

THE MAX MEDICAL JOURNAL

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25
YEARS OF
SERVICE AND
EXCELLENCE

ORIGINAL ARTICLES

REVIEW ARTICLES

PATH-BREAKING CASES

THE IMAGES

STUDENTS' CORNER

FROM PARALYSIS TO PRIDE:

Managing Spinal Injury in a Young Artist with Down Syndrome



In November 2024, a young girl with Down Syndrome, also an artist with remarkable talent, was involved in an accident that resulted in a traumatic C1–C2 dislocation. The injury left her paralysed and severely impacted her quality of life. Due to the severity and complexity of the injury, her condition was critical.

Her journey towards recovery was made possible through the integrated efforts of the multidisciplinary team at Max Super Speciality Hospital, Saket, comprising neurosurgeons, neuro-anaesthesiologists, critical care nurses, and physiotherapists. The team undertook a complex surgical intervention, followed by an intensive rehabilitation programme aimed at restoring neurological function and promoting independent mobility. Despite the initial paralysis, the patient made steady progress under close medical and rehabilitative supervision.

Just two months after the surgery, she returned to the hospital, walking independently, to present the team with one of her paintings—a deeply moving gesture that reflected both her spirit and the impact of collaborative care.

The treatment not only helped her recover physically but also enabled her to return to her art. Six months later, her passion and focus to her art were recognised when she was honoured by the President of India for her artistic accomplishments. Her journey stands as a powerful testament to what personalised, patient-centred, multidisciplinary care can achieve.

This case exemplifies not only the complexities of managing spinal injuries in patients with special needs but also the transformative potential of integrated care and early intervention.

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Message from the Chairman & Managing Director



Dear Friends,

I am delighted to present the 6th edition of *The Max Medical Journal*—our prestigious publication, set up with the collaboration of our dedicated doctors and researchers.

This year, as we mark 25 years of Max Healthcare, it is only fitting that we reflect on this milestone through a lens most foundational to our journey: the pursuit of clinical excellence, academic inquiry, and the advancement of medical science.

Over the past two and a half decades, we have evolved from a modest healthcare venture into India's most trusted healthcare organisation. Today, we are recognised not only for our scale but for our enduring leadership in clinical outcomes, research, digital innovation, and patient-centric

medical practices. This milestone reaffirms our core commitment — to our patients, our people, our planet, and above all, to our purpose — To Serve. To Excel.

With a network of 22 world-class facilities and over 5,100 beds, Max Healthcare has had the privilege of treating patients from over 560 cities in India and 182 countries worldwide—each placing their trust in our blend of clinical excellence and compassionate care. In FY25 alone, over 3.46 lakh patients received free treatment—demonstrating our unwavering belief in equitable access to quality care.

At the centre of this achievement are our people. Our team of more than 35,000 dedicated professionals—including over 5,000 doctors and 12,500 nurses and paramedics—represent a formidable reservoir of medical talent, united by a culture rooted in empathy and backed by world-class infrastructure. With 4 JCI-accredited, 3 AACI accredited and 18 NABH-accredited hospitals, our expanding global reach is further supported by 15 international patient assistance centres.

Max Healthcare's true distinction lies not merely in the number of patients served, but in the way we extend care—anchored in compassion, integrity, and clinical precision. This philosophy, embodied by our clinicians and academics, has defined our journey for the past 25 years and will continue to guide us in the future.

I take immense pride in this edition of The Max Medical Journal, a publication that reflects our unwavering commitment to clinical excellence, research, and the open sharing of knowledge. The journal was born from the belief that medical knowledge should be a universal right, not a privilege. By offering this platform freely to professionals, researchers, and students worldwide, we reaffirm our dedication to academic inclusivity and the global advancement of clinical expertise.

Our academic ecosystem today is a powerful expression of this vision. We are currently driving over 645 research projects and clinical trials, and have contributed more than 2,550 peer-reviewed publications to global medical literature. Over 1,20,000 students have engaged with our learning platforms, which offer a curriculum spanning 250+

courses delivered by a distinguished faculty of approximately 1,500 experts.

As we commemorate 25 years of transformative healthcare, let us celebrate the ideas that will shape the next 25. *The Max Medical Journal* is not just a publication, it is a promise! A promise to democratize medical knowledge, to foster inquiry, and to continually expand the boundaries of possibility in medicine.

With warm regards,

Abhay Soi

Chairman and Managing Director

The Inheritance of Loss



“If the pigeon closes his eyes and pretends that the cat cannot see him, he ends up in the cat’s belly pretty soon. So is the case with hereditary cancers. Genetic screening as a follow up of appropriate counselling makes sense.”

This is the story of one of the most beautiful women in the world. She underwent a ‘prophylactic’ bilateral mastectomy in 2013 after she discovered that she had the breast cancer gene 1 (BRCA1) mutation, which put her at a very high risk of breast and ovarian cancer. Of course, there was breast reconstruction involved. In 2015, she went under the scalpel a second time for a salpingo-oophorectomy, to reduce her chances of ovarian cancer. Her public disclosure led to heightened awareness, genetic testing and more acceptance of these risk-reducing prophylactic surgeries. Today, we call it ‘The Angelina Jolie Effect’. It must have been a very brave and difficult decision, considering Jolie’s mother had died of ovarian cancer at the age of 56.

About 12% of women will develop breast cancer in their lifetime, but the odds become 60% if you inherit the BRCA1 or breast cancer gene 2 (BRCA2) mutation. If two close relatives have had breast or ovarian cancer, the probability skyrockets. Men with these mutations also have increased chances of developing carcinoma of the breast. Since Angelina, Sharon Osbourne and Christina Applegate consented to these surgeries, the celebrity fan-following has seen prophylactic mastectomy

rates doubling. Cancer susceptibility genes such as BRCA1, BRCA2, tumour protein p53 (TP53) or phosphatase and tensin homolog (PTEN) are being tested routinely. The bilateral mastectomy reduces the risk of breast cancer by at least 90%-95%, but cannot be 100% effective, as some amount of breast tissue will be left behind despite surgery.

The more important questions are the awareness and the willingness to undergo genetic testing, the pre-test and post-test probability of getting a positive result, the impact of a positive test report on the psyche of a relatively healthy individual, and how proactive an individual’s attitude and approach might be.

Under the Human Genome Project, it took 13 years for scientists to decipher the 3 billion base pairs of human deoxyribonucleic acid (DNA). From mere conjecture about the genetic basis of various diseases, we suddenly found ourselves thrown into an ocean of medical genomics. What we inherit from our parents is not just limited to our height and eye colour, but a whole lot more. Whether we like it or not, the medical world is now being driven by only two revolutions — artificial intelligence (AI) and

genetics. Genetics has become the keyword for how we approach a disease. It is not restricted to the realm of oncology. We talk of genetic predisposition for practically every disease, from Alzheimer's to cardiomyopathy, congenital hearing loss to polycystic kidney disease. It is ironical that most patients with diabetes will not even talk about their lifestyle but put the entire blame on their parents for inheriting bad genes.

Coming back to the subject at hand, most cancers are not hereditary. They are a complex interplay of ageing, environment and lifestyle including smoking. In fact, only 5%-10% are hereditary cancers, but these strike at a younger age. Yet, there are multiple hereditary cancer syndromes, including hereditary breast and ovarian cancer syndrome (HBOC), Lynch syndrome associated with endometrial, colon and ovarian cancers or familial adenomatous polyposis (FAP) linked to colon cancer, or the Li-Fraumeni syndrome associated with breast cancer, sarcomas, leukaemias and childhood cancers. Von Hippel-Lindau disease increases the risk of eye, renal and adrenal tumours. An understanding of cancer biology and molecular fingerprinting has changed our entire approach to the treatment of cancers. Clustered regularly interspaced short palindromic repeats (CRISPR) is a technology that is a game-changer and allows us to selectively modify the DNA of living organisms.

It is our duty to ask the relevant family history from our patients, screen them and refer them to the experts for genetic counselling and testing. One pathogenic gene variant, like BRCA1 or BRCA2, increases the risk of multiple cancers, including

breast, ovaries, fallopian tubes, prostate and pancreas. Similarly, the adenomatous polyposis coli (APC) gene associated with FAP is linked to colon, rectal, small intestine, stomach, pancreas, thyroid, brain and liver cancers. Genetic testing cannot be offered to the entire population. At the same time, counselling and a plan of action are important. Put yourself in the patient's shoes. In fact, he is not even a patient yet, but just a common man on the street at a higher risk of cancer. He is not even sure if he will not be killed by a hit-and-run before he gets any life-threatening disease. How do you convince him to get genetic testing done? Would you and I want to undergo genetic testing for cancer? If yes, would it make sense to just increase screening and surveillance, or be radical enough to get multiple prophylactic surgeries done? If the pigeon closes his eyes and pretends that the cat cannot see him, he ends up in the cat's belly pretty soon. So, screening after appropriate counselling makes sense.

It's a game of chess, and it is up to an individual as to how aggressive or passive an approach he adopts. The King has to survive at all costs. His predecessors may have been bad, but it's not always about inheritance. Whether he wins or loses depends on how he plays the game. The aim is to provide a genetically informed, personalised approach to win the fight against cancer.

Dr. Monica Mahajan

Editor-in-chief,
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Orchestrating Urgency: Leadership in Emergency Protocols Through Administrative-Clinical Synergy – **Ashwini Jogade Pandhare**

Enhancing Patient Care Through a Quality Improvement Project: A Before-and-After Study of Nurse Training on Effective Fluid Balance Monitoring and Charting

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Abstract:

Fluid balance (FB) charting is a common practice in wards across all levels of care — primary, secondary, and tertiary. These charts enable treating physicians to accurately assess the patient's volume status and to prescribe drug therapies for those suffering from cardiovascular, renal, hepatic, and surgical conditions. However, in practice, glaring lapses in FB documentation frequently occur. Nursing staff and caregivers often provide estimates of fluid inputs and outputs that are recorded inconsistently, resulting in inadequate clinical assessment. This project aimed to enhance the quality of FB chart documentation by nursing staff through a comprehensive approach to FB monitoring with a reduction in error rates and enhanced efficiency, thereby favourably impacting patient outcomes and minimising transfers from the ward to the intensive care unit (ICU). A pre-intervention audit was conducted over 15 consecutive days on 246 patients' FB charts. This was followed by a quality improvement intervention, involving nursing education, and a post-intervention audit in a 38-bed multi-speciality ward to analyse the impact on the accuracy and completeness of the input/output charts. In conclusion, this quality improvement project demonstrated that a targeted, robust nursing education programme, along with the introduction of a redesigned colour-coded FB chart can significantly improve the accuracy and completeness of FB documentation, potentially enhancing patient care and reducing the length of hospitalisation.

Key words: Fluid Balance, Fluid Balance Chart (Input/Output Charting), Nursing Training Initiative, Quality Improvement Project.

Introduction

While the nursing staff diligently care for patients, several recurring issues have emerged as areas of concern. These include incomplete recording of the fluid balance (FB) chart due to insufficient manpower and a lack of understanding of its importance. The inspiration for this study came from observed lapses in patient care noted by the authors during their routine ward rounds, which were attributable to poor FB documentation and perceived to be preventable. A literature review reveals several quality improvement projects in this domain that have shown improvement in their primary objectives, particularly an

article in 2023 by Barretto, Cayla Marie *et al.*,¹ which echoes the objectives of the present study.

Study Design

A before-and-after study design was chosen for this quality improvement initiative (QII).

Pre-intervention audit: In June 2024, a detailed audit was conducted on the prevalent nursing documentation practices in a 38-bed multi-speciality ward (medical and surgical) on the 2nd floor of Max Smart Super Speciality Hospital, specifically

related to FB charting. (see Appendix-1- existing FB chart). A set of eight variables was assessed on the FB chart of the study day, on a sample size of 246 patient records (both manual and digital records), spanning 15 consecutive days, from 4 pm to 5 pm each day. The variables assessed were as follows:

- Accuracy of documenting patient demographic details on the FB chart
- Mathematical error in the calculation of input/output/both
- Fictitious entries on the chart at variance with the clinical progress notes
- Significant gap(s) in the documentation of input/output
- Compliance with measurement and documentation of the daily weight in the FB chart
- Compliance with documentation of intravenous (IV) infusions/IV bolus fluids in the FB chart
- Compliance with documentation of fluid losses other than urine (e.g., ultrafiltration with dialysis, nasogastric aspirate, vomiting, stool losses, and others)
- Compliance with documentation related to the previous day's cumulative balance on the FB chart

QII: From July to August 2024, five nursing education classroom sessions were conducted, emphasising the importance of FB in managing various disease states. The importance of accurate documentation related to the eight variables listed above was also highlighted. Through an interactive PowerPoint presentation, we introduced a newly designed, colour-coded FB chart (Appendix-2).

Post-intervention audit (August-September 2024): This was conducted on a fresh batch of 246 patient records with the same

Statistical analysis:

Pre-intervention data

Variables							
Was the patient catheterised?	Yes	5	35	-9.76%	-15.02% to -4.49%	0.0005	Highly significant
	No	11	195				
Patient demographic details accurately filled	Yes	192	24	0.81%	-4.82% to 6.45%	0.8877	Not significant
	No	26	4				
Mathematical error in calculation of input/output/both	Yes	5	56	-17.48%	-23.7% to -11.23%	< 0.0001	Highly significant
	No	13	172				
Fictitious chart entries	Yes	16	73	-23.98%	-30.78% to -17.18%	< 0.0001	
	No	14	143				
Significant gaps in documentation	Yes	51	138	-48.78%	-56.65% to -40.91%	< 0.0001	
	No	18	39				
Daily weights measured and documented	Yes	0	0	2.85%	0.77% to 4.92%	0.0156	Significant
	No	7	239				
Intravenous infusions/ intravenous boluses documentation	Yes	108	22	28.86%	21.12% to 36.61%	< 0.0001	Highly significant
	No	93	23				
Fluid losses other than urine documented	Yes	86	8	53.66%	46.66% to 60.66%	< 0.0001	
	No	140	12				
Previous day's cumulative balance entered	Yes	178	24	7.32%	0.91% to 13.72%	0.0356	Significant
	No	42	2				
Unmeasurable losses (diaper wets, patient' bias) measured or not?	Yes	0	1	-0.41%	-1.20% to 0.39%	0.999	Not significant
	No	0	245				

Table 1: Efficacy of nursing education and training using McNemar's test.

set of eight variables, five days after the completion of the QII. This phase also spanned 15 consecutive days between 4 pm and 5 pm in the same 38-bed multi-speciality ward.

Initial sample size: The total number of FB charts reviewed pre- and post-intervention was 570.

Inclusion and exclusion criteria: The inclusion criteria for the study was that the duration of admission in the hospital or duration of stay in the designated study ward to be greater than 24 hours. The exclusion criteria was that the duration of admission to the hospital or duration of stay in the designated study ward to be less than 24 hours.

Final sample size: n=246 (pre-intervention); n=246 (post-intervention).

Study objective: The primary objective of this study was to improve the quality of FB chart documentation by nursing staff through a comprehensive approach to monitoring, with reduced error rates and enhanced efficiency, thereby favourably impacting patient outcomes and minimising transfers from the ward to the ICU.

Data handling: Google Forms were utilised for data collection before and after the intervention. Subsequently, data on each of the eight variables from 246 pre-intervention records and 246 post-intervention records were collated using Microsoft Excel. The data was recorded in a Yes/No format for each variable. McNemar's test was applied to determine the significance of the QII.

Results

Each measure was subjected to McNemar's test to determine the intervention's significance concerning each variable (as shown in Table 1). The McNemar test is beneficial when binary data are generated in pairs and a change in behaviour or practice needs to be determined.

Patient demographic details accurately filled

The test statistics, $z = -0.878$ and $p = 0.8877$ were not significant, implying that nursing education and training yielded a mere 0.81% increase in the completion of demographic information, suggesting that the nursing staff has already been performing well in this documentation domain.

Mathematical error in calculation of input/output/both

This was highly significant ($p < 0.0001$). The QII significantly reduced mathematical errors in input/output, calculations, with a reduction of 17.48% in the intervention phase.

Fictitious chart entries

This was also highly significant ($p < 0.0001$). The intervention reduced false data entry by 23.98%.

Significant gaps in documentation

Highly significant ($p < 0.0001$). This huge negative deviation of -48.78% implies that the QII significantly closed documentation gaps in the FB chart, improving the continuity and completeness of the recorded information.

Daily weights measured and recorded

Significant ($p = 0.0156$). A 2.85% in post-intervention weight recording was achieved following the intervention.

Intravenous infusions/intra-venous boluses documentation

Highly significant ($p < 0.0001$). Compliance in documenting of this parameter increased by 28.86%.

Fluid losses other than urine documented

Highly significant ($p < 0.0001$). Here was a 53.66% improvement in recording all types of fluid losses — crucial for accurate FB charting.

Previous day's cumulative balance entered

Significant ($p = 0.0356$). Implying a 7.32% improvement in this aspect of nursing documentation performance following the intervention.

Subset of patients with an indwelling urinary catheter

This subset was analysed separately during the audit. In the pre-intervention phase, 40 out of 246 samples had a catheter, compared to 16 out of 246 in the post-intervention phase. Given the ease of monitoring such patients, this subset was expected to demonstrate the most accurate output recording. In the pre-intervention audit, an abysmal 19% of the patients with a Foley catheter ($n=40$) had timely FB entries. This figure improved to 66.7% in the post-intervention audit ($n=16$). The reduced number of catheterised patients in the second phase was attributed to the high prevalence of thrombocytopenic dengue cases during the autumn season in New Delhi.

Discussion

The root causes of inaccuracies in FB documentation in nursing care are multifactorial.¹⁻¹¹ These include insufficient and inconsistent training in FB charting, inadequate awareness of the importance of accurate monitoring, and poor communication between medical personnel and caregivers, resulting in uninformative FB charts. The lack of a standardised process flow to capture the input and output data, delays in documentation due to hectic nursing shifts, and unclear FB chart format all contribute to fictitious entries and significant gaps in documentation. Deficiency or malfunctioning of monitoring devices such as IV infusion pumps and confusion related to manual charts viz-a-viz electronic medical record charts further adds to unsatisfactory documentation. There is too much process — more about the system than about the patients. Additionally, there is a significantly high nursing turnover in most tertiary hospitals with inadequate induction of the incoming staff. Poorly designed FB charts (small font size, poorly spaced rows and columns with inadequate demarcation, unclear sub-headers) contribute to nurses' apathy concerning proper documentation. These issues were considered when formatting a new colour-coded chart, with each row or column coded in different coloured shades to highlight the importance of each column. The rows were split according to the nursing shift duties, ensuring the assigned nurse would be solely responsible for documentation and providing an efficient handover to subsequent staff. The chart aimed to facilitate early detection of critical outcomes such as oliguria, high nasogastric aspirate volumes, fluid overload, high drain outputs, and diarrhoeal losses. These improvements could lead to enhanced patient outcomes, fewer incidences of nosocomial acute kidney injury (AKI) and acute pulmonary oedema leading to fewer ICU transfers. A further barrier identified was a lack of encouragement from senior nursing staff, which can demotivate front-line nurses.

This QII was implemented in a 38-bed multi-speciality ward and focused on improving the accuracy of FB monitoring through nursing education and redesigned documentation tools. The findings from this study align with existing literature, which emphasises the importance of accurate FB monitoring in improving patient outcomes, particularly in managing cardiovascular, renal, and hepatic conditions.^{1,2}

Key Findings

The pre-intervention audit revealed several areas of concern, including significant gaps in documentation, mathematical errors in input/output calculations, and fictitious entries in FB charts. These issues are consistent with findings from other studies that have identified similar challenges in FB documentation.^{3,4} Post-intervention, there was a marked improvement in the accuracy of documentation, particularly in output charting in catheterised patients (71%), IV infusion recording (28.86%), and documentation of fluid losses other than urine (53.66%). Reducing mathematical errors (17.48%) and fictitious entries (23.98%) was particularly noteworthy, as these are critical to ensuring accurate FB management.

The intervention also significantly improved documentation of daily weights (2.85%) and the carry-over of the previous day's

cumulative balance (7.32%), both of which are essential for analysing a patient's volume status. These findings are supported by prior research highlighting the importance of continuous and accurate tracking of FB in preventing complications such as AKI and pulmonary oedema.^{5,6}

Strengths of the Study

A key strength lies in the study's practical approach to addressing a common yet critical issue in patient care. By focusing on nursing education and redesigning the FB chart, our intervention was feasible and scalable. A before-and-after study design clearly compared pre- and post-intervention outcomes, providing robust evidence of the intervention's effectiveness. Furthermore, the involvement of nursing staff in the design and implementation of our QII ensured that the solutions were tailored to the ward's specific needs and challenges.

Another strength is the comprehensive nature of the audit, which covered multiple aspects of FB documentation, including demographic details, mathematical accuracy, and the documentation of various fluid losses. This holistic approach allowed for a thorough assessment of the intervention's impact on different aspects of patient care.

Limitations

Despite the positive outcomes, several limitations should be acknowledged. First, the study was conducted in a single ward within a single hospital, which may limit the generalisability of the findings. While the results are promising, further research is needed to determine whether similar interventions would be effective in other settings, such as smaller hospitals with different staffing levels.

Second, the study relied on self-reported data from nursing staff, which may be subject to bias. Although the audit was conducted rigorously, there is always a possibility of some inaccuracies or omissions in documentation. Moreover, the short duration of the post-intervention audit (15 days) may not fully reflect the long-term sustainability of the improvements. At a personal level, we observed that post-completion of the study, the accuracy of nursing documentation declined after a month, suggesting that ongoing training and reinforcement may be necessary to maintain the gains achieved.

Finally, while the intervention significantly improved documentation, it did not address all areas of concern. For example, the documentation of unquantifiable losses (e.g., diaper wets) remained unchanged, indicating that further refinements to the charting process may be needed, especially in patients who require diapers. This is consistent with findings from other studies, which have highlighted the challenges of documenting subjective or unmeasurable data.^{8,9}

Implications for Practice

The findings from this study have several important implications for clinical practice. First, they underscore the importance of ongoing nursing education and training in improving the quality of patient care. The significant improvements observed in this study suggest that even relatively simple interventions, such as targeted training sessions and the introduction of more user-friendly documentation tools, can substantially impact patient outcomes.

Secondly, the study highlights the need for standardised protocols and tools for FB monitoring. The success of the colour-coded FB chart demonstrates the value of a clear and intuitive framework for documentation. This finding is consistent with previous research, emphasising the importance of standardised processes in reducing errors and improving the accuracy of FB monitoring.^{8,9}

Finally, the study suggests regular audits and feedback loops are essential for maintaining documentation quality over time. The decline in documentation accuracy observed by the authors during their ward rounds one month after the intervention, highlights the need for ongoing monitoring and reinforcement of best practices. This is particularly important in high-pressure environments, where staff may be more prone to errors due to workload and time constraints.

Disclaimer: This project did not require ethical approval. However, it was approved by the Audit & Administration department, the Nursing department, and the Medical Superintendent of Max Smart Super Specialty Hospital, Saket, New Delhi.

Conclusion

This QII demonstrated that a targeted, robust nursing education program and the introduction of a redesigned colour-coded FB chart can significantly improve the accuracy and completeness of FB documentation by nurses. While the study had some limitations, the findings provide valuable insights into the factors contributing to effective FB monitoring and the potential for simple, scalable interventions to enhance patient care and reduce the length of hospitalisation and cost of care.

Praveen Arumugam, Bijjam Venkata Vijay Kumar Reddy, Medam Ashok Kumar Reddy, Kshitij Makarand Gokhale, Alka Bhasin. Enhancing Patient Care Through a Quality Improvement Project: A Before-and-After Study of Nurse Training on Effective Fluid Balance Monitoring and Charting. MMJ. 2025, June. Vol 2 (2).

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Appendix-1: Existing fluid balance chart



AFFIX PATIENT LABEL

INTAKE OUTPUT SHEET

Date: Previous Day's Intake: Output: Balance: Stool Passed: Y/N

Time	INTAKE								OUTPUT								
	Oral	RT	IV Fluids		Medications			Hourly Total	Grand Total	Urine	RTASP/Vomiting	Drain I	Drain II	Drain III	Stool	Hourly Total Output	Grand Total Output
			I	II	I	II	III										
6 AM																	
7 AM																	
8 AM																	
9 AM																	
10 AM																	
11 AM																	
12 PM																	
1 PM																	
2 PM																	
3 PM																	
4 PM																	
5 PM																	
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7 PM																	
8 PM																	
9 PM																	
10 PM																	
11 PM																	
12 AM																	
1 AM																	
2 AM																	
3 AM																	
4 AM																	
5 AM																	

MSSSH/Intake-Output Chart/Ver 1.2/July 2021

Appendix-2: Newly developed colour-coded fluid balance chart

FLUID BALANCE CHART-Sep-2024											all values in "ml"	
Patient Label							Date:					
							Yesterday's Input/Output					
							Today's Weight					

INPUT							OUTPUT					
	Oral	IV bolus	IV infusion	RT-feed / TPN	BT	Hourly total	Urine output	Vomit Loose stools	Drain		UF with Dialysis	Irrigation I/O
									I	II		
08:00												
09:00												
10:00												
11:00												
12:00												
13:00												
14:00												
Total-												
15:00												
16:00												
17:00												
18:00												
19:00												
20:00												
Total-												
Total Input Over 12hours-							Total Output over 12 hours-					
21:00												
22:00												
23:00												
24:00												
00:00												
01:00												
02:00												
03:00												
04:00												
05:00												
06:00												
07:00												
Total-												
Total Input Over 12hours-							Total Output over 12 hours-					

Grand Total Input	
Grand Total Output	
[+ / -] Balance	

Pictures taken during the “Quality Improvement Intervention” training session



Analysis of the Transepicondylar Angle in the Indian Population: A Single-Centre Study Using CUVIS Robot and Computed Tomography Scan Data

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Abstract:

The transepicondylar angle (TEA) serves as a crucial reference for determining femoral component rotation in total knee replacement (TKR). This study aims to determine the average TEA and its variation in the Indian population, using data collected from a single centre via the CUVIS robot and preoperative computed tomography (CT) scans. A total of 200 cases were analysed. The mean TEA was found to be $1.83^\circ (\pm 1.13^\circ)$, ranging from 0.00° to 5.80° . Compared to the posterior condylar angle (PCA) in the Indian population (mean PCA $\sim 4.67^\circ$), this study suggests significant anatomical differences requiring ethnicity-specific considerations in TKR.

Key words: Transepicondylar Angle, CUVIS Robot, Orthopaedic Robotics, TEA Measurement.

Introduction

Total knee replacement (TKR) is one of the most common orthopaedic procedures performed worldwide. The success of TKR largely depends on precise implant positioning, particularly the rotational alignment of the femoral component.¹ In this context, the transepicondylar axis (TEA) — the line connecting the medial and lateral epicondyles of the femur — serves as a critical reference. Proper alignment along this axis ensures balanced flexion gaps and optimal patellofemoral tracking, which are vital for long-term joint stability and function.²

In most surgical protocols, the posterior condylar axis (PCA) and TEA are used interchangeably or in combination to determine femoral rotation.³ However, studies suggest considerable variability between these axes depending on individual anatomy and ethnicity. The angle between TEA and PCA, referred to as the posterior condylar angle (PCA) value, plays an essential role in identifying rotational mismatches that could lead to complications such as pain, stiffness, patellar maltracking, or even early prosthetic failure.⁴

Previous anatomical studies in Western populations have reported the average PCA value (i.e., TEA-PCA difference) to range from 3.5° to 5° .⁵ For instance, Dennis *et al.* (2001)⁶ and

Whiteside *et al.* (2003)⁷ emphasised the importance of using TEA over PCA for consistent alignment in femoral component positioning due to its reproducibility. However, Asian and Indian populations, owing to genetic and functional anatomical differences such as habitual squatting and cross-legged sitting, exhibit different morphometric characteristics. Indian studies have reported lower PCA values ($\sim 4.67^\circ$), suggesting a more externally rotated distal femur compared to Western populations.⁸

Such ethnic differences are often overlooked in the design of TKR instrumentation and surgical planning, which predominantly rely on datasets derived from Caucasian morphologies. A few magnetic resonance imaging (MRI)-based morphometric studies in India (Gupta *et al.*, 2015¹) have indicated the necessity of ethnicity-specific implant design and preoperative planning using CT or MRI data to account for these variations. Furthermore, the introduction of robotic-assisted systems (like CUVIS, MAKO, and ROSA) has enhanced the ability to accurately measure such parameters, thereby personalising TKR planning.⁵

This study contributes to the growing body of evidence advocating for population-specific references in TKR. It leverages CT-based data and robotic precision to analyse TEA in the Indian population — data which may be pivotal in optimising rotational alignment, minimising intraoperative guesswork, and improving long-term clinical outcomes.

Methods

This retrospective study analysed 200 patients who underwent preoperative CT scans as part of robotic TKR planning at a single centre. The TEA was measured using the CUVIS robotic

system, ensuring accurate and consistent angle measurements. Data were categorised and analysed for statistical variation. Statistical analysis included mean, standard deviation, range, and interquartile range (IQR). The distribution and variation of TEA values were illustrated using data visualisation tools such as histograms and box plots, presented in Figure 1 and Figure 2, respectively.

Results

- **Mean TEA:** $1.83^\circ (\pm 1.13^\circ)$
- **Range:** 0.00° to 5.80°
- **25th percentile:** 0.90°
- **Median:** 1.80°
- **75th percentile:** 2.60°
- **No significant correlation** was observed between TEA and patient age

Discussion

The TEA observed in the Indian population was significantly lower than the PCA ($\sim 4.67^\circ$), consistent with previous findings that suggest that Indian knees may require different rotational alignment approaches compared to Western populations.

The implications for TKR include:

1. **Potential malalignment risks** if using Western-derived femoral component guides.
2. **Ethnicity-based surgical modifications** to prevent excessive internal rotation.
3. **Importance of preoperative CT-based planning** to customise alignment for Indian knees.

Rotational malalignment of the femoral component can lead to complications such as patellar maltracking, joint instability, increased polyethylene wear, and reduced implant lifespan. Literature indicates that even small deviations from optimal femoral rotation (3° to 5°) can alter joint kinematics and increase complication rates.

The use of robotic-assisted surgery offers precision and individualised patient care. Robotic systems such as CUVIS not only improve the accuracy of TEA measurement but also facilitate intraoperative modifications tailored to patient-specific anatomy. This is particularly beneficial for populations with known anatomical variability.

From a broader perspective, this study highlights the need for more inclusive implant designs and emphasises the clinical importance of customising surgical approaches based on ethnic differences. Future directions should focus on integrating these findings into surgical training, national guidelines, and implant manufacturing processes.

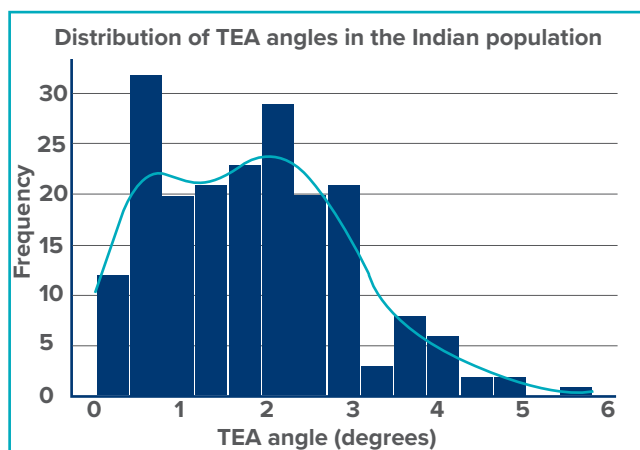


Figure 1: Histogram showing the distribution of transepicondylar angle (TEA) values in the Indian population.

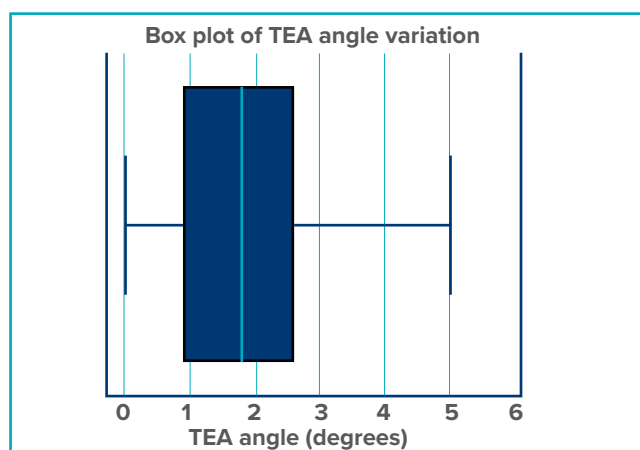


Figure 2: Box plot representing the variation in transepicondylar angle (TEA) values across the sample of 200 patients.

Conclusion

This study establishes the TEA values for the Indian population and underscores the need to consider anatomical variations in TKR planning. Future studies should incorporate multicentre data to further validate these findings. The use of robotic-assisted measurements (CUVIS) and CT-based evaluations ensures precise data collection, which may guide improved implant alignment strategies.

Lakshay Goel, Simon Thomas, Divesh Gulati, Devan P Nambiar. Analysis of the Transepicondylar Angle in the Indian Population: A Single-Centre Study Using CUVIS Robot and Computed Tomography Scan Data.

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Vestigial to Wonders: Appendicular Interposition in Complex Ureteric Strictures

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Abstract:

The case report aims to explore the role of the appendix as an interposition graft or flap for the reconstruction of right-sided ureteric strictures. We present two cases in which the appendix was utilised — one as a flap and the other as a complete interposition graft. The appendiceal onlay flap was applied using robotic surgery, while the interposition graft was placed via a laparoscopic approach. Both procedures resulted in good long-term surgical outcomes. The appendix, although a vestigial organ, can play a remarkable role in ureteric reconstruction in clinically complex cases.

Key words: Appendix, Flap, Ureteric Stricture, Interposition.

Introduction

Stricture of the ureters may develop after endourological treatments such as retrograde intrarenal surgery (RIRS) or various gynaecological or surgical procedures. For long pelvic strictures, the Boari flap or psoas-hitch operation is performed. However, long strictures of the proximal ureter are a real challenge to reconstruct. In these cases, it is possible to perform an intestinal ureteroplasty, or the Yang–Monti principle can be applied. Nonetheless, surgical and metabolic complications are observed after intestinal plastic surgery. Over the past decade, onlay ureteroplasty using grafts from the buccal mucosa has been actively introduced.¹ We have previously published a series of 12 patients who underwent buccal mucosal graft ureteroplasty by robotic and laparoscopic approaches.¹ In rare cases, in the presence of a long and wide appendix, it can be used to replace a long stricture of the ureter. The appendix can be used both as an interposition graft or as an onlay flap.

Case Reports

We recently performed two such interesting cases in which the appendix was used in different ways to reconstruct ureteric strictures. We used the appendix as a total interposition in the first case via laparoscopy, and as an appendiceal flap in the second case via a robotic approach.

Case 1

A 35-year-old male with history of failed right laparoscopic pyeloplasty at a different hospital presented to us with a percutaneous nephrostomy (PCN) tube *in situ*. His right ureter

was completely obstructed, and he was on PCN for the last three months. He was planned for right retrograde pyelography with possible ureteric reconstruction.

Laparoscopic ports were placed, and ureteric dissection was performed. There was a 6 cm stricture in the upper ureter starting from the pelviureteric junction. His appendix was quite healthy and long, so we transposed the appendix as a substitute for the lost ureteric segment. The appendix was detached from the caecum, but its blood supply was kept intact (Figure 1A). The appendix was anastomosed to both the ureteric ends with the help of 4-0 Vicryl sutures over a double J (DJ) stent. The stent was removed after 6 weeks, and the patient maintained a patent ureteric lumen. His PCN was removed ten days after surgery.



Figure 1A: Final picture after the appendix is anastomosed with the ureter as a tubular graft.

Case 2

A 47-year-old female presented with a history of open abdominal hysterectomy and left salpingo-oophorectomy for endometriosis, performed two years ago. She developed a right endometriotic cyst which engulfed the right ureter, forming a stricture and obstruction of the right kidney. A computed tomography (CT) scan revealed right hydronephrosis with partial lower ureteric stricture of 6 cm in length. Right retrograde pyelography (RGP) confirmed a 5 cm partial ureteric stricture on the lower ureter. A DJ stent was placed on the right side, and robotic ports were inserted. Intraoperatively, the right ovarian endometriotic cyst was found to be densely adherent to the ureter. Careful dissection was carried out and right oophorectomy was performed. The right ureteric stricture segment was opened along its axis. Her appendix was opened longitudinally and converted into a vascularised pedicle. An appendiceal onlay flap was applied over the ureteric segment with a DJ stent in situ. The patient recovered well, and the stent was removed after 6 weeks (Figure 1B).



Figure 1B: Representation of an appendiceal onlay flap on the right ureter.

These two cases were pilot cases in which the appendix was used as a substitute, either as a tubular graft or an onlay flap. The appendix, although a vestigial organ, can be remarkably effective in ureteric reconstruction in complex cases.

Both cases resulted in good long-term surgical outcomes. At a follow-up of 24 to 30 months, neither patient showed any evidence of obstruction in the reconstructed ureter.

Discussion

Ureteral replacement is an important procedure for managing complex ureteral strictures in the field of ureteral reconstruction. Currently, autologous tissues can be used to repair ureteral

strictures, including the intestines (ileum and colon), oral mucosa (lingual and buccal mucosa), and the appendix. Melnikoff first attempted to use the appendix to replace the ureter in 1912.² For long proximal and middle ureteral strictures, the treatment options include downward nephropexy, renal autotransplantation, nephrectomy, and ureteral substitution. These interventions are rarely required for complex ureteral strictures and should be used only when the previously discussed repairs are not possible or are contraindicated.³ The alternative tissues that can be used for ureter reconstruction include the ileum, buccal or lingual mucosa grafts and the appendix.⁴

The concept of onlay grafts, initially developed for the management of urethral stricture disease, was first applied to ureteral reconstruction in 2009. Reggio *et al.* described laparoscopic appendiceal onlay flap ureteroplasty, which was successful with 8 months of follow-up.⁵ Yarlagadda *et al.* were the first to perform robotic-assisted laparoscopic appendiceal interposition for a 5 cm obliterative right ureteral stricture, and achieved a successful outcome.⁶ An appendiceal onlay flap is mainly suitable for the repair of right proximal and middle ureter strictures. Appendix interposition for left or right ureteral reconstruction in paediatric renal transplantation patients has been reported in several studies.^{7,8} The appendix interposition technique may be a viable solution for managing ureteral stricture in selected cases. However, fistula formation and anastomosis stenosis are the common complications that have been reported.⁹

The onlay graft concept was first used to treat urethral stricture disease in 1996.¹⁰ Appendiceal onlay ureteroplasty provides a solution for urologists to repair complex ureteral strictures. For 2-6 cm ureteral stenoses that are not suitable for direct anastomosis, especially in the proximal and middle ureters, an appendiceal onlay can be used as an alternative to an ileal ureter. To date, no cases of left ureteral stenosis repair using the appendiceal onlay have been reported, and this procedure warrants further exploration.

Robotic assistance offers several advantages such as a magnified view, three-dimensional (3D) visualisation, and better articulation, facilitating delicate suturing. Our study was limited by a small sample size and short follow-up period. We plan to continue monitoring these patients closely in subsequent follow-ups and collect longer-term recovery data. Simultaneously, additional cases will be accumulated. We aim to summarise our comprehensive experience with robot-assisted laparoscopic and ureteral posterior wall reconstruction techniques in the future.

Conclusion

Appendiceal flap or interposition graft is a useful option for managing long-segment (3-6 cm) proximal and middle ureteral strictures on the right side. The outcomes at 24-months follow-up are satisfactory. A robotic or laparoscopic approach helps in achieving effective results of minimally invasive surgery.

Suresh Chandra Sahay, Pawan Kesarwani, Abhijeet Jha, Shashwat Singh, Shubhankar Powar. Vestigial to Wonders: Appendicular Interposition in Complex Ureteric Strictures. MMJ. 2025, June. Vol 2 (2).

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Leadership Styles in Hospital Administration and Their Impact on Organisational Performance: A Literature Review

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Abstract:

In healthcare administration, leadership is essential because it affects personnel morale, organisational performance, and care quality. This study of the literature examines the many leadership philosophies that are common in hospital environments and how they affect organisational outcomes. Based on regional and international research, the review emphasises the effects of transformational, transactional, servant, and autocratic leadership styles on performance metrics like financial management, innovation, staff happiness, and the quality of patient care. According to the review's findings, high organisational performance in hospitals is most favourably correlated with transformational and servant leadership.

Key words: Hospital Administration, Leadership Styles, Organisational Performance, Transformational Leadership, Healthcare Management.

Introduction

In hospital management, strong leadership is essential to ensure the efficient, moral, and patient-centred delivery of healthcare services.¹ Today's hospitals must contend with several issues, such as growing patient volumes, staff shortages, regulatory requirements, and the complexity of healthcare technology. In this situation, hospital organisations' ability to function effectively under these challenges is significantly influenced by their leadership style.² Patient outcomes, staff morale, and the long-term viability of a business are all impacted by a leader's capacity to engage his or her team, foster trust, communicate effectively, and adjust strategically.³

In the healthcare industry, leadership is about impact and teamwork, not just power. Team dynamics, clinical practice adoption, and motivation and retention of healthcare professionals are all impacted by leadership styles in hospital settings.⁴ To improve healthcare systems, the World Health Organisation (WHO) and other international health organisations have highlighted leadership development as a top goal. For health managers, politicians, and practitioners alike, it is crucial to comprehend which leadership philosophies yield the best outcomes.⁵

In the literature on healthcare, several leadership ideas are prevalent. Often praised for its inspiring and visionary traits, transformational leadership fosters innovation and ongoing learning among employees. Research has indicated a positive correlation between this style and improved patient safety, lower burnout, increased organisational agility, and staff satisfaction.^{6,7} On the other hand, transactional leadership has been linked to increased efficiency but decreased engagement and innovation, as it emphasises job completion through reward-based incentives and set policies.⁸

Servant leadership is another increasingly popular structure that emphasises employee empowerment, trust-building, and prioritising team members' welfare. Despite being more prevalent in community or non-profit settings historically, servant leadership has drawn interest in hospital administration due to its association with enhanced team cohesion, ethical climate, and communication.⁹ On the other hand, authoritarian leadership, which is typified by tight control and centralised decision-making, can occasionally be effective in emergencies, but frequently lowers morale and inhibits innovative problem-solving.¹⁰

These leadership philosophies are not exclusive, and depending on the situation, actual hospital administrators may display characteristics from several philosophies. However, existing research indicates that certain approaches are better suited to encourage innovation, employee retention, and high-quality care.¹¹ The importance of emotionally aware and adaptable leadership in handling the complexity of contemporary hospitals is becoming increasingly apparent. To give readers a comprehensive understanding of how various leadership philosophies affect organisational performance in hospital settings, this review synthesises the body of available empirical and theoretical material. The evaluation provides insights that help guide hospital administration training, policy, and strategic planning by identifying effective leadership approaches.¹²

Aim and Objectives

Aim: To review existing literature on leadership styles in hospital administration and their impact on organisational performance.

Objectives:

1. To identify and describe common leadership styles employed in hospital settings.
2. To evaluate the impact of each leadership style on organisational performance indicators.
3. To highlight the most effective leadership approaches based on empirical evidence.

Methodology

A narrative literature review methodology was adopted. Articles published between 2010 and 2024 were sourced from databases including PubMed, Scopus, Web of Science, and Google Scholar. Keywords used for the search included "leadership styles," "hospital administration," "organisational performance," and "healthcare leadership."

Inclusion criteria:

- Peer-reviewed journal articles
- English language
- Studies focused on hospital or healthcare settings

Exclusion criteria:

- Non-peer-reviewed articles
- Editorials or opinion pieces without empirical data

A total of 45 articles were selected based on relevance and quality of evidence. The data was synthesised thematically, and key findings were summarised in tables and figures.

Results

The review identified four predominant leadership styles in hospital administration: transformational, transactional, servant, and autocratic. Their effects on various performance metrics are summarised below (Table 1).

Leadership Style	Key Features	Positive Outcomes	Negative Outcomes
Transformational	Visionary, inspiring, innovative	High staff morale, better patient care	Requires emotional intelligence
Transactional	Reward/punishment-based	Efficiency, clarity in roles	Risk of employee disengagement
Servant	Focus on team needs and development	Increased trust, job satisfaction	May be time-consuming
Autocratic	Centralised decision-making	Quick decisions in crises	Poor team morale, low innovation

Table 1: Summary of leadership styles and organisational outcomes.

Leadership Styles in Hospital Administration



Figure 1: Impact of leadership styles on hospital performance indicators.

The analysis found that hospital administration frequently employs four main leadership concepts — transformational, transactional, servant, and autocratic (Figure 1). Each of these philosophies has a unique effect on healthcare outcomes and organisational performance.

Across several performance metrics, transformational leadership was found to be the most advantageous. This type of leader is distinguished by an inspiring and imaginative attitude, which frequently stimulates creativity and cultivates a sense of unity among employees. According to several studies, transformational leaders greatly increased healthcare systems' capacity for adaptation, patient satisfaction, and workforce engagement. Its efficacy, however, often depends on the leader's interpersonal skills and emotional intelligence.

Increased trust, employee loyalty, and a positive work environment have all been linked to servant leadership, which emphasises attending to employees' needs and fostering their professional development. Although it could take more time and work to implement effectively in busy hospital environments, this approach promotes teamwork and long-term staff development.

Structured incentive and accountability systems underpin transactional leadership, which fosters role clarity and operational effectiveness. It is effective in maintaining order

and following protocol. However, it often lacks the adaptability and creativity required in fast-paced healthcare settings, and if applied too strictly or excessively, it may lower motivation. Centralised decision-making, which is a hallmark of autocratic leadership, has proven useful in emergency or time-sensitive scenarios where prompt, decisive action is crucial. Despite this, it is often associated with low employee morale, a lack of innovation, and a greater incidence of turnover, making it less suitable for collaborative healthcare settings.

Conclusion

In hospital administration, leadership is more than just a managerial role; it is a strategic tool that affects every facet of organisational performance, from financial results to patient care. Transformational, transactional, servant, and autocratic are the four main leadership philosophies that have been studied in this literature review, along with how they affect important performance metrics in hospital environments.

When it comes to encouraging innovation, patient safety, and employee satisfaction, transformational leadership has continuously been the most successful of these. Its emphasis on motivation, personalised support, and a shared vision aligns well with the intricate, multidisciplinary nature of medical settings. Servant leadership also holds great promise, especially in developing moral corporate cultures and boosting employee confidence. By empowering and engaging frontline staff, these approaches promote sustainable improvements in patient care and healthcare delivery.

However, transactional leadership may not adequately inspire healthcare teams or promote long-term development, even though it is advantageous in preserving operational structure and accountability. Autocratic leadership is generally linked to lower morale and reduced flexibility, even if it may be appropriate in some high-pressure situations or emergencies.

The main conclusion drawn from the literature is that healthcare leadership must be adaptable, emotionally intelligent, and responsive to context. Hospital executives are best positioned to attain high organisational performance if they can combine elements of servant and transformational leadership, while also utilising transactional tools when necessary. Hospital systems should place a high priority on communication, strategic thinking, emotional intelligence, and ethical decision-making in their leadership development programmes.

Future research should also examine hybrid leadership models and assess how organisational, demographic, and cultural factors affect the effectiveness of leaders. Leaders in the ever-changing healthcare industry must be mentors, innovators, and advocates for both employees and patients in addition to being administrators.

In summary, implementing and developing effective leadership styles in hospital administration is not only advantageous but also necessary for providing high-quality healthcare in a way that is efficient, equitable, and sustainable.

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A Correlation Study to Determine the Prevalence of Depression and Connected Risk Factors Among Patients with Chronic Obstructive Pulmonary Diseases

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Abstract:

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition that often presents with comorbid mental health disorders, particularly depression, which significantly influences patients' quality of life and disease outcomes. This study aimed to determine the prevalence of depression in COPD patients and identify the associated risk factors while also evaluating their health-related quality of life (HRQoL). A cross-sectional observational study was conducted at Max Healthcare's pulmonology outpatient department (OPD). 124 patients aged over 35 years with confirmed COPD and no recent hospitalisations were enrolled. Data were collected using the patient health questionnaire-9 (PHQ-9) to assess depression and the short form-36 (SF-36) questionnaire to evaluate HRQoL. Descriptive statistics, logistic regression, and Tukey's honest significant difference (HSD) tests were applied to identify significant associations. Depression was prevalent among COPD patients, with significant associations found between higher disability grades and global initiative for chronic obstructive lung disease (GOLD) stages with increased PHQ-9 scores ($p = 0.003$ and $p < 0.001$, respectively). Similarly, lower SF-36 scores were significantly correlated with more advanced disease severity ($p < 0.001$). No statistically significant differences in depression or HRQoL were observed based on gender, age, occupation, education, diet, smoking, or alcohol consumption. Depression is a significant comorbidity in COPD, particularly in patients with severe disease and higher disability grades. Timely psychological assessment and integrated care approaches are essential to improve patient outcomes.

Key words: COPD, Depression, PHQ-9, SF-36, Quality of Life, Risk Factors.

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic, progressive, and largely preventable lung condition marked by persistent respiratory symptoms and airflow limitation caused by airway and/or alveolar abnormalities. It is primarily due to significant exposure to noxious particles or gases, most commonly tobacco smoke. Globally, COPD poses a major public health challenge and is currently the third leading cause of death, accounting for approximately 3.23 million deaths in 2019 alone.¹

Although dyspnoea, persistent coughing, and sputum production are the hallmarks of COPD, its effects go well beyond the lungs. A variety of comorbid illnesses are exacerbated by the disease's systemic character, with psychological disorders — especially anxiety and depression being among the most common.^{2,3} Reduced physical capacity, social isolation, anxiety of dyspnoea, and recurrent exacerbations are some of the factors that contribute to the multifactorial depression associated with COPD.⁴ In addition to lowering patients' health-related quality of life (HRQoL),

it also makes it harder for patients to follow their treatment plans, which increases the likelihood of hospital stays and raises healthcare expenses.^{5,6}

Depression among individuals with COPD frequently remains underdiagnosed and inadequately treated, despite its common occurrence. While medical professionals may ignore psychological symptoms in favour of treating respiratory conditions, many people mistakenly ascribe mood swings to physical sickness or ageing.⁷ Additionally, there are gaps in the delivery of care, since conventional COPD management guidelines frequently lack strong foundations for routine mental health screening.⁸

There appears to be a reciprocal association between depression and COPD. While untreated depression can hinder self-care, reduce medication adherence, and hasten physical deterioration, worsening respiratory function and exacerbations can cause or exacerbate depressive symptoms.^{9,10} Anxiety and depression frequently combine, with anxiety exacerbating dyspnoea and causing avoidance of activities, which reinforces physical deconditioning.¹¹

Studies have shown that depressive symptoms occur in 10%–60% of COPD patients, depending on the disease stage and methodology.¹² Additionally, irrespective of lung function, depression is a significant predictor of death.¹³ Reduced health-related quality of life (HRQoL), elevated symptom burden, and compromised social functioning are all closely linked to these psychiatric comorbidities.¹⁴

There is growing agreement that managing COPD requires a multidisciplinary approach that considers both the psychological and physical aspects of the illness. Interventions that have demonstrated encouraging effects in improving outcomes include cognitive behavioural therapy, pulmonary rehabilitation, and pharmaceutical treatment for depression.¹⁵

Designing comprehensive care models that promote better quality of life and long-term disease control requires an understanding of the prevalence, severity, and correlates of depression in patients with COPD.

Aim and Objectives

Primary objective: To determine the prevalence of depressive symptoms among COPD patients.

Secondary objectives:

1. To assess the severity of depression in COPD patients.
2. To identify demographic, clinical, and lifestyle risk factors associated with depression.

3. To evaluate HRQoL using the short form-36 (SF-36) questionnaire.

Methodology

This cross-sectional observational study was conducted at the pulmonology outpatient department (OPD) of Max Healthcare. Patients over 35 years of age with a confirmed diagnosis of COPD were enrolled after providing informed consent. Participants with recent hospitalisations or known psychiatric illnesses were excluded to minimise confounding factors.

Depression was assessed using the patient health questionnaire-9 (PHQ-9), while HRQoL was measured using the SF-36 questionnaire. Additional demographic and clinical data, such as age, sex, body mass index (BMI), dietary habits, smoking and alcohol history, and disability grades, were recorded. Statistical analysis was performed using the statistical package for the social sciences (SPSS) version 25.0. Descriptive statistics, Pearson's correlation, logistic regression, and Tukey's honest significant difference (HSD) tests were used. A $p < 0.05$ was considered statistically significant.

Results

Gender, age, education, occupation, diet, smoking, and alcohol use were among the demographic and lifestyle factors that did not significantly differ in depression (PHQ-9) or quality of life (SF-36) scores, according to the risk factor analysis ($p > 0.05$) (Table 1). This implies that socio-behavioural factors do not significantly affect depression symptoms and decreased health-related quality of life in individuals with COPD. Figure 1 illustrates the gender distribution among participants, showing a near-equal representation of male and female patients, further supporting the lack of significant association between gender and psychological outcomes. Similarly, Figure 2 depicts the age distribution, which demonstrates that depressive symptoms and quality of life scores were not markedly different across age groups. Regardless of their history or lifestyle choices, these findings underscore the necessity of frequent psychological assessment and comprehensive management strategies for all patients with COPD.

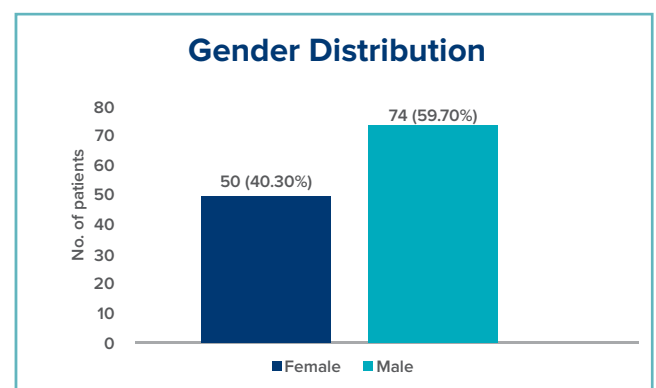


Figure 1: Gender-wise distribution.

Variable	Category	Frequency (n)	Percentage (%)	p-value (PHQ-9)	p-value (SF-36)
Gender	Male	74	59.7	0.947	0.154
	Female	50	40.3		
Age Group	35–44	21	16.9	0.617	0.132
	45–54	33	26.6		
	55–64	26	21.0		
	65–74	25	20.2		
Diet	Vegetarian	33	26.6	0.172	0.801
	Non-Vegetarian	59	47.6		
	Eggetarian	32	25.8		
Smoking history	Yes	64	51.6	0.999	0.399
	No	60	48.4		
Alcohol use	Yes	55	44.4	0.175	0.410
	No	69	55.6		

Table 1: Demographics and baseline characteristics.

Abbreviations : SF-36: Short form-36; PHQ-9: Patient health questionnaire-9.

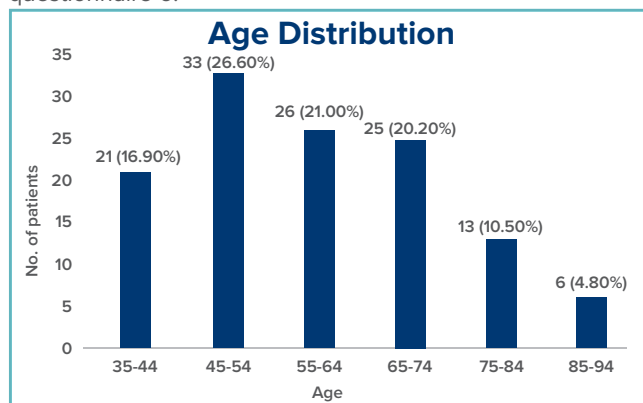


Figure 2: Age group distribution.

Significant associations were observed between disability grades and both depression (PHQ-9) and quality of life (SF-36) scores:

- Grade 5 disability was significantly associated with higher PHQ-9 scores ($p = 0.013$) and lower SF-36 scores ($p = 0.003$) (Table 2) and (Figure 3).
- GOLD stage 4 showed a significantly higher depression score ($p < 0.001$) and lower HRQoL score ($p < 0.001$) compared to GOLD stage 1 (Table 3) and (Figure 4).

Assessing Disability in COPD	Total	Percentage	p-value (PHQ-9)	p-value (SF-36)
Grade 1	15	12.1	0.003	0.002
Grade 2	30	24.2		
Grade 3	30	24.2		
Grade 4	34	27.4		
Grade 5	15	12.1		

Table 2: Correlation between disability grade and PHQ-9 scores.

Abbreviations : SF-36: Short form-36; PHQ-9: Patient health questionnaire-9.

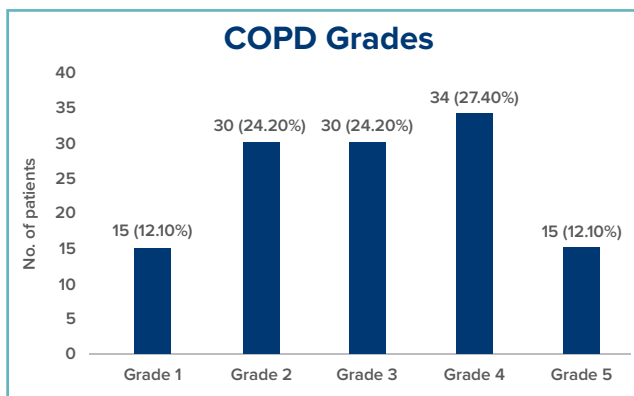


Figure 3: Disability grades in chronic obstructive pulmonary disease (COPD).

GOLD Criteria	Total	Percentage	p-value	p-value (SF-36)
GOLD 1 (Mild COPD)	28	22.6	0.001	<0.001
GOLD 2 (Moderate COPD)	40	32.3		
GOLD 3 (Severe COPD)	30	24.2		
GOLD 4 (Very severe COPD)	26	21.0		

Table 3: Global initiative for chronic obstructive lung disease (GOLD) criteria.

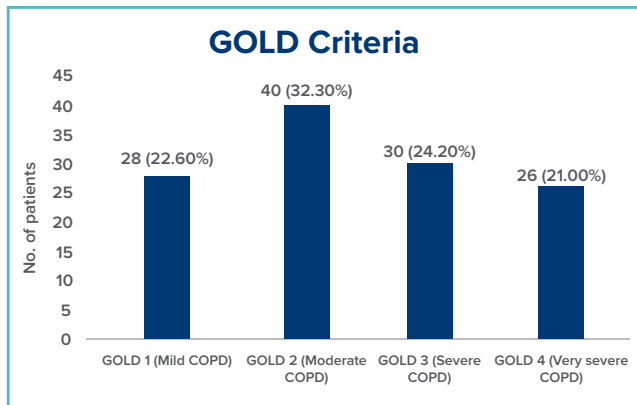


Figure 4: Global initiative for chronic obstructive lung disease (GOLD) criteria and mean patient health questionnaire-9 (PHQ-9) scores criteria.

A statistically significant inverse association between the severity of depression and health-related quality of life in patients with COPD was found by the correlation analysis using Pearson's coefficient, which showed a substantial negative correlation between PHQ-9 and SF-36 scores ($r = -0.807$, $p < 0.001$). This indicates that the overall quality of life significantly decreased as depression symptoms rose. The correlation's strength emphasises the significant psychological toll that people with COPD endure and reaffirms how closely mental and physical health are related. These results highlight how crucial it is to detect and treat depression early to potentially enhance the patients' mental health and general quality of life.

Discussion

The present study provides compelling evidence of the substantial burden of depression among patients with COPD, a finding that aligns with existing literature. The observed prevalence of depression in our cohort underscores the psychological vulnerability of COPD patients, likely attributable to the chronic nature of the disease, persistent dyspnoea, activity limitation, and social isolation. These factors synergistically diminish patients' quality of life (QoL), further highlighting the bidirectional relationship between COPD and mental health deterioration.

This is consistent with previous research indicating that lower socioeconomic status and unhealthy lifestyle practices exacerbate both physical and psychological morbidity in COPD populations.^{1,2} Furthermore, the inverse relationship between physical activity and depression severity observed in our study echoes findings from Dogra *et al.*, who emphasised the role of sedentary behaviour in deteriorating mental health among individuals with obstructive lung disease.³

Importantly, our findings also demonstrate a clear link between depression and lower scores on the SF-36, indicating impaired HRQoL. Mental health conditions such as depression can negatively influence COPD self-management, treatment adherence, and engagement in pulmonary rehabilitation, thereby continuing a cycle of poor health outcomes.⁴ This insight is crucial for clinicians and health policymakers, as it emphasises the need for integrated care models that incorporate routine mental health screening and multidisciplinary interventions for COPD patients.

Although pulmonary rehabilitation has been shown to enhance QoL and reduce depressive symptoms in COPD patients,⁵ its utilisation remains limited due to accessibility issues and a lack of awareness. Addressing these gaps through targeted public health strategies and patient education may lead to significant improvements in both psychological well-being and functional status.

Conclusion

This study emphasises the substantial prevalence of depression in individuals with COPD, especially in those with more severe GOLD stages and higher disability grades. The results show a strong relationship between poor respiratory function and a rise in depression symptoms, supporting the idea that patients' physical and mental health significantly deteriorate as the severity of COPD increases.

It is interesting to note that the study found no statistically significant correlations between depression and lifestyle or demographic factors, including age, gender, occupation, food, smoking, or alcohol use. This implies that rather than socio-behavioural factors, depression in COPD may be more closely related to the physiological course of the illness. These results highlight how crucial it is to regularly incorporate psychological screening, especially with validated instruments like the PHQ-9, into the clinical evaluation of patients with COPD, irrespective of their behavioural history or background.

Additionally, patients with higher degrees of depression may experience significantly worse HRQoL, as seen by the substantial inverse association between PHQ-9 and SF-36 scores. This emphasises the two-fold burden that people with COPD bear and necessitates a thorough, multidisciplinary management strategy that considers their psychosocial and pulmonary demands. To improve long-term results, early psychological interventions, counselling, and access to mental health services may be essential.

Patients with COPD are very likely to experience depression, particularly if their illness is more advanced and they have more physical limitations. According to the study, depression is more strongly correlated with the severity of the illness than with lifestyle or demographic characteristics. The necessity of routine mental health screening and integrated care that addresses the psychological and physical elements of COPD is further highlighted by a strong negative correlation between depression and quality of life (QoL).

Limitations and Future Scope of the Study

There are various limitations to this study that need to be considered. Determining whether depression causes or contributes to developing COPD is challenging due to the cross-sectional design, which limits causal inferences. Because it was only done at one tertiary care facility, the results might not apply to larger or more varied populations. While the smaller sample size is adequate for preliminary analysis, it may not possess sufficient power to detect variations among smaller subgroups, such as age or occupation. A larger sample size would enhance the robustness of the analysis and improve the ability to identify

these differences. Patients with the greatest psychological burden might have been disregarded since those who had just been admitted to the hospital were not included. Self-reported instruments such as the SF-36 and PHQ-9 add subjectivity and possible reporting bias as well.

To better examine the temporal link between depression and the advancement of COPD, future research should use longitudinal methods. Generalisability would be enhanced by expanding to multicentre studies in a range of socioeconomic

and geographic contexts. Biological pathways may become clearer with the use of clinical indicators like oxygen saturation and C-reactive protein (CRP). It is necessary to conduct intervention-based studies to evaluate the effectiveness of pharmacological and psychological interventions in this population. Additionally, incorporating telemedicine and mobile health (mHealth) tools could improve mental health screening and assistance in the treatment of COPD, particularly in settings with low resources or distant locations.

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Orchestrating Urgency: Leadership in Emergency Protocols Through Administrative-Clinical Synergy

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Abstract:

Healthcare excellence is no longer the result of clinical brilliance alone — it now demands agile administration, system-driven processes, and seamless coordination between clinical and non-clinical domains. At Nanavati Max Super Speciality Hospital, this transformation is evident in the implementation of time-sensitive emergency protocols — Code White for stroke, Code Green for cardiac emergencies, and the emerging Code Orange for surgical crisis. These protocols represent a new era of administrative leadership and teamwork, where hospital administrators serve as real-time enablers of clinical outcomes. This article outlines how integrated teamwork, strategic foresight, and responsive governance contribute to improved patient outcomes and client satisfaction.

Key words: Emergency Protocols, Code White / Code Green / Code Orange, Healthcare Leadership, Patient-Centric Care.

Introduction

The evolving landscape of tertiary care demands that healthcare administrators go beyond operational oversight to take on dynamic leadership roles. From aligning interdepartmental workflows to driving emergency response mechanisms, administrators today are not just facilitators — they are core enablers of clinical excellence.¹

At Nanavati Max Super Speciality Hospital, a 350-bed tertiary care institution in Mumbai, the administration has consistently demonstrated its commitment to patient-centric care and process improvement. Through a series of collaborative emergency response systems: Code White, Code Green and Code Orange — the hospital has institutionalised a culture of clinical-administrative synergy that saves lives, ensures efficiency, and strengthens patient safety.^{2,3}

Code White: Rapid Stroke Response – A Model of Collaborative Leadership

A three-year longitudinal internal study assessed the impact of sensitisation, training, and multidisciplinary coordination in delivering treatment for stroke patients within the “golden hour”.^{2,4,5}

Activation of Code White involved synchronised efforts from:

- Neurology teams
- Accident & emergency (A&E) department
- Magnetic resonance imaging (MRI)/Computed tomography (CT) suite
- Critical care unit (CCU)
- Pharmacy/Catheterisation laboratory (Cath lab)/Administrative departments

The administrator's role in this initiative was pivotal — overseeing the expedited clearance for MRI, coordinating intensive care unit (ICU) bed management, aligning pharmacy and finance functions, and serving as the link between clinical urgency and systemic readiness. An assembly-line approach was used to move patients efficiently through triage, diagnostics, and intervention.²

Outcomes:

- Enhanced stroke outcomes (Figure 1)
- Minimised treatment delays.
- Reduced average length of stay (ALOS)
- Embedded a culture of team-based rapid response
- Strengthened community connect

Code Green: Saving Time, Saving Myocardium

The Code Green protocol for acute cardiac emergencies such as ST-elevation myocardial infarction (STEMI) embodies cross-functional responsiveness.⁶

Administrative interventions included:

- Rapid coordination between Emergency, Cath lab, and Cardiology departments
- Use of fast-tracked elevators and bypass corridors

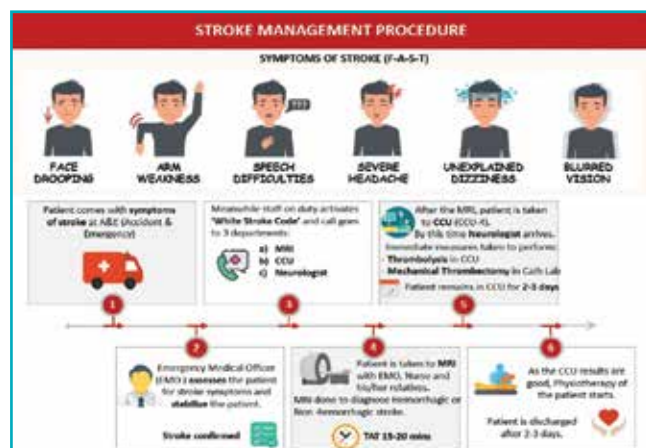


Figure 1: Stroke management procedure.

- Real-time coordination with patient relatives and financial clearances
- Ensuring Cath lab readiness with materials, manpower, and documentation

Administrators were hands-on — often physically present — to troubleshoot real-time issues. The hospital achieved electrocardiogram (ECG)-to-balloon times under 60 minutes. It is pertinent to note that as an institution, we set this stringent turnaround time (TAT) after discussions with our consultants, though international guidelines recommend a door-to-balloon TAT of 90 minutes.⁶

Outcomes:

- Improved TAT for primary angioplasty in myocardial infarction (PAMI)
- Improved cardiac intervention success rates
- Reinforced the symbiotic culture

Code Orange: Surgical Emergency Activation — The Next Frontier

Currently under implementation, Code Orange is Nanavati Max Super Speciality Hospital's emergency response protocol for life-saving surgical crisis, including ruptured

ectopic pregnancies, perforated peritonitis, major trauma, gastrointestinal obstructions.⁷

This ingenious concept was introduced following a multidisciplinary symposium and literature review.⁷⁻⁹

Administrative focus areas included:

- Immediate mobilisation of surgical, anaesthetist, critical care, and related teams
 - Ensuring availability of operation room (OR), sterilised instruments, blood products, pharmacy, and consumables
 - Fast-tracking investigations — laboratory, radiology
 - Parallel management of patient-family communications and consent documentation
 - Streamlined patient transfers without corridor bottlenecks
- The pilot rollout has already demonstrated significant reductions in decision-to-incision time.

Leadership by Coordination: The Administrator's Role Redefined

Methodology:

1. Patient identification in A&E

- **Initial triage:** Upon arrival, the A&E team quickly assesses and identifies patients with stroke, STEMI, or surgical emergencies through a robust triage system
- **Rapid diagnosis:** Involves preliminary clinical evaluation, point-of-care diagnostics, and imaging to confirm the critical condition (e.g., MRI scan for stroke or ECG for STEMI)

2. Code activation

- **Code system initiation:** Once identified, the respective code (Code Green for STEMI, Code White for stroke, or Code Orange for surgical emergencies) is activated
- **Alert system:** Automatically notifies a pre-defined group of 40 key personnel, including:
 - **Clinicians:** Emergency physicians, neurologists, cardiologists, surgeons, and related teams
 - **Nurses:** For immediate patient care and preparation for procedures
 - **Radiology team:** For immediate imaging (e.g., CT/MRI for stroke, chest X-ray for surgical emergencies)
 - **Laboratory and blood bank:** Prompt investigations and arrangement of blood
 - **Pharmacy:** To ensure the readiness of medications
 - **Technicians:** For operating ECG machines, ventilators, etc.
 - **Security:** To facilitate smooth patient transport and area access
 - **Administrative staff:** For documentation, patient registration, and movement facilitation

3. Coordination and readiness

- **Immediate activation:** The team is already prepared and on standby to ensure rapid readiness
- **Preparation for movement:** While the patient is stabilised in A&E, necessary equipment and staff in related departments (e.g., Cath lab, Stroke unit, Surgical theatre) are prepared in advance⁹

4. Patient transfer

- **Swift patient movement:** Patients are transferred promptly from A&E to the ICU, Cath lab, Stroke unit, or OR
- **Escorted transport:** Security and nursing staff ensure safe and swift movement through the hospital, avoiding delays in corridors

5. Emergency measures and immediate care

- **Continuous monitoring:** Upon arrival in the respective department, emergency measures are immediately initiated:
 - **For stroke:** Administration of thrombolytics (if within the time window), setting up for potential thrombectomy
 - **For STEMI:** Preparation for percutaneous coronary intervention (PCI)
 - **For surgical emergencies:** Stabilisation, anaesthesia, and immediate surgical intervention

6. Multi-disciplinary involvement and communication

- **Centralised communication:** Throughout the process, a central communication hub ensures updates are shared between all involved teams, ensuring a collaborative response
- **Documentation:** Administrative staff ensures that patient documentation, consent forms, and any required statutory documents are processed simultaneously

7. Post-procedure coordination

- Follow-up care and transitions (e.g., ICU for post-surgical recovery, stroke rehabilitation) are arranged
- Regular monitoring and protocols for potential complications are in place

This comprehensive methodology ensures timely, efficient, and collaborative emergency care, ultimately improving patient outcomes.

Toward a Collaborative Healthcare Culture

Nanavati Max Super Speciality Hospital's clinical-administrative model promotes integrated leadership rather than parallel operations.^{3,8,9}

The message is clear: Administrative leadership is now transformational, ensuring better patient care, faster responses, and higher client satisfaction.

Conclusion

Code White, Code Green, and Code Orange are not just emergency protocols — they are case studies in agile leadership, strategic planning, and collaborative healthcare delivery. Nanavati Max Super Speciality Hospital demonstrates that administrative foresight, when aligned with clinical expertise, creates healthcare models that are both patient-centred and outcome-driven. By institutionalising these protocols, the institution is saving lives and creating a new healthcare leadership blueprint.

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Leadless Cardiac Pacing: A Narrative Review

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Abstract:

Pacemakers were developed with the aim of enhancing quality of life and diminishing morbidity and mortality in patients with bradycardia (reduced heart rate). An ageing population, accompanied by increasing life expectancy, has led to a steady increase in the demand for pacemaker implantation. The disadvantages of the transvenous pacemaker system have driven the evolution of leadless pacemakers (LPMs). Since their inception, LPMs have undergone improvements in design and technology, leading to their present-day performance. In this review, we provide a comprehensive review of the evolution of LPMs, the clinical usefulness of the current generation of pacemakers, and future trends in technology.

Key words: Leadless Pacemakers, Leadless, Pacemakers, Single Chamber, Dual Chamber.

Introduction

Pacemakers were developed with the aim of enhancing quality of life and diminishing morbidity and mortality in patients with bradyarrhythmias.¹ As a result of an ageing population and increasing life expectancy, the rates of pacemaker implantation have increased steadily. Transvenous pacing systems are life-saving and improve patient quality of life through the treatment of symptomatic bradycardias. Nevertheless, they come with the potential for procedure and device-related complications such as infections, lead displacement, and fractures.² The advent of leadless pacemakers (LPMs) has revolutionised this field, offering a promising alternative that mitigates many of these issues. LPMs are about ten times smaller than traditional pacemakers and do not require leads. These pacemakers utilise a percutaneous catheter-based approach to introduce the self-contained device into the right ventricle. In this review, we present the contemporary experience and future technologies in leadless pacing opportunity in the clinical practice.

Early Developments of Leadless Pacemakers

LPMs were initially conceptualised in the 1970s and successfully implanted in dogs using a mercury battery-powered capsule. With advancements in miniaturisation, nanotechnology, battery technology, communication capability, and catheter-based delivery systems, LPMs became a reality. The first commercial LPM was approved and implanted in a patient in 2012.³ It eliminated the need

for leads and a subcutaneous pocket, significantly reducing the risk of infections and other complications. The leadless permanent pacemaker (LPPM) system was developed to bypass these areas of vulnerability. LPPM constitutes an excellent alternative to the epicardial approach in patients with specific comorbidities, such as limited upper venous access, recurrent or bilateral permanent pacemaker (PPM) infection, and kidney failure with limited venous access.⁴

Benefits of LPMs

LPMs offer several advantages over traditional pacemakers:^{5,6}

- **Reduced risk of complications:** By eliminating leads and the need for a subcutaneous pocket, LPMs significantly reduce the risk of infections, lead dislodgement, and fractures.
- **Minimally invasive procedure:** The implantation procedure is less invasive, involving a catheter-based approach that shortens recovery time and hospital stay.
- **Cosmetic benefits:** Without a visible chest incision or pacemaker pocket, there are no scars on the chest or arm movement restrictions, offering patients better cosmetic outcomes.
- **Long-lasting:** Newly available pacemakers last almost twice as long as traditional transvenous pacemakers.

- **Unrestricted magnetic resonance imaging (MRI) access:** MRI scans can be safely performed on patients with LPMs.
- **Upgradability to dual-chamber:** Recently available pacemakers can be upgraded to dual-chamber function based on clinical needs.
- **Chronic retrievability:** These devices can be retrieved and replaced, ensuring patients receive the most up-to-date technology and optimal pacing therapy over their lifetime, making them suitable even for younger patients.

Since 2012, three different LPMs have been introduced:

1. Nanostim LPM (St. Jude Medical/Abbott, Chicago, IL, USA)
2. Micra™ transcatheter pacing system (Medtronic, Minneapolis, MN, USA) (Figures 1-3)
3. AVEIR™ LPM (Abbott) (Figure 4)

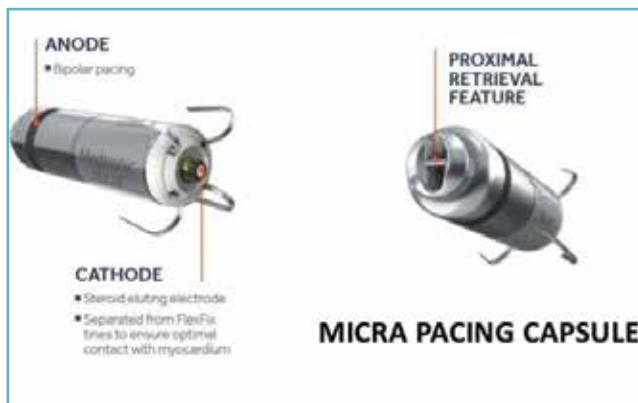


Figure 1: Micra pacemaker.

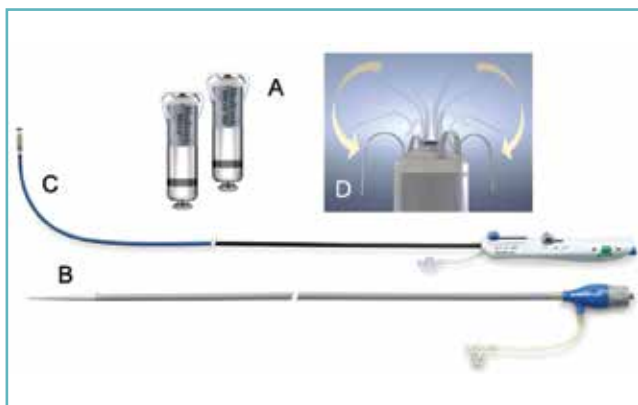


Figure 2: Micra pacemaker and delivery system.

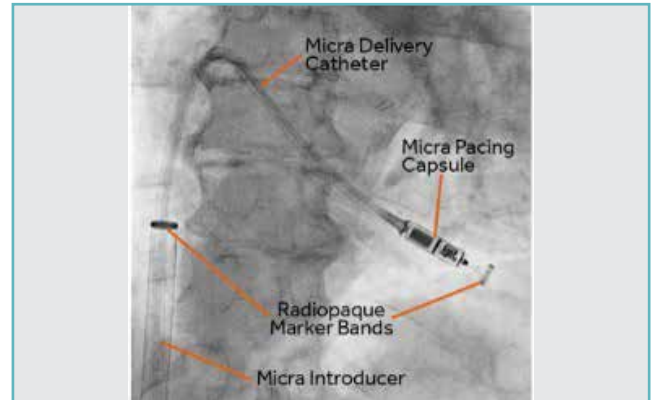


Figure 3: Micra pacemaker delivery: The procedure is guided by fluoroscopy (an X-ray imaging technique). If the position is suboptimal, both leadless pacemakers are repositionable and retrievable in the short-term using a specific catheter.



Figure 4: Final deployment of AVEIR leadless pacemaker.

The first LPMs were indicated only for a selective group of patients requiring ventricular pacing in VVI(R) mode. Subsequent generations aimed to widen their applicability, such as the Micra AV for atrioventricular (AV) synchronous ventricular pacing, and more recently, the first dual-chamber LPM (AVEIR DR), offering all pacing modes including AAI(R), VVI(R), and DDD(R) (Figure 5).

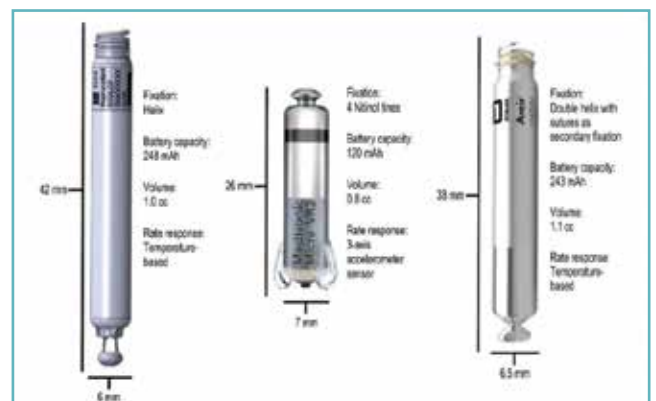


Figure 5: Comparison of the size and volume of the different leadless pacemakers. The Nanostim leadless pacemaker, the Micra leadless pacemaker, and the AVEIR leadless pacemaker with device characteristics.⁶

LPMs: The Past

The first LPM was the Nanostim (St. Jude/Abbott), which was implanted 1,423 times globally between 2012 and 2017.⁷ It was a single-chamber LPM, able to pace and sense in the ventricle and deliver rate response (VVI[R] mode). Although studies reported a high success rate, serious concerns arose over early battery depletion in 7 of the 1423 implanted devices (0.5%) within 29-37 months post-implantation, leading to its withdrawal and cancellations of future implantations.⁸

LPMs: The Current Status

The first Micra VR LPM was implanted in 2013. Since then, more than 200,000 devices have been implanted. Compared to Nanostim, the Micra is shorter (25.9 vs. 42 mm), and occupies < 2% of the right ventricular (RV) volume. Published studies have shown excellent implantation success and stable electrical parameters with Micra LPM.^{9,13}

LPMs: The Future

Although current LPM use is mostly confined to single-chamber right ventricular pacing, most pacemaker patients require dual-chamber pacing.¹⁰ Significant advancements in LPM technology have been observed in recent years. A notable development is the Micra AV, a second-generation device offering AV synchrony via a new pacing algorithm that relies on sensing mechanical atrial contraction. This feature allows the pacemaker to coordinate the timing between the atria and ventricles, providing a more natural heart rhythm for patients with AV block. It suits patients with AV block and intact sinus node function but may be less effective in older adults with frequent sinus node dysfunction.

The development of true dual chamber LPMs (Figure 6) represents a breakthrough. In this approach, two miniaturised pacemakers are implanted, one in the atrium and one in the ventricle, that communicate wirelessly to ensure optimal heart function. This innovation expands the use of LPMs to a broader patient population, including those who require pacing in both heart chambers.



Figure 6: Dual chamber pacing.⁶

The AVEIR VR (ventricular rate-responsive) and AVEIR AR (atrial rate-responsive) represent further advancements in LPM technology. These are designed for long-term retrieval and extended battery life, making them suitable for even younger populations. It has mapping capabilities prior to fixation, which aid in optimal device placement and reduces the need for repositioning. The AVEIR AR is part of a dual-chamber system that allows for atrial and ventricular pacing, providing comprehensive cardiac rhythm management.

Dual Chamber Leadless Pacing

The AVEIR DR dual-chamber LPM by Abbott represents a significant advancement in leadless pacing technology. It consists of two devices implanted percutaneously, one in the right atrium and one in the right ventricle. In the AVEIR DR i2i (implant-to-implant) study, the procedural success rate was 98.3%.¹¹ This system allows for synchronised dual-chamber pacing using proprietary i2i™ communication technology, which transmits high-frequency electrical impulses to relay messages between co-implanted leadless pacemakers via the naturally conductive characteristics of the blood. This ensures continuous AV synchrony, which is crucial for patients with conditions like sick sinus syndrome or AV block. These co-implanted LPMs are fully capable of pacing, just like the traditional dual chamber pacemakers. The system is upgradeable, supporting tailored therapy as patient needs evolve.

Leadless Conduction System Pacing (CSP)

CSP is an evolving technique in which a traditional pacemaker wire is implanted deep into the interventricular septum (wall separating the left and right chambers of the heart). This approach activates the left bundle branch (LBB) area enabling physiological pacing which mimics the heart's natural electrical current. As a result, this pacing approach offers more physiological pacing than standard options. The future of LPMs includes the development of leadless CSP systems. Abbott's investigational AVEIR CSP is designed to deliver pacing to the LBB area, a key part of the heart's electrical conduction system. This approach aims to mimic the heart's natural beat more closely, offering a new treatment option for patients with slow or irregular heart rhythms.

Remote monitoring and programming capabilities are also under investigation, as is the integration of LPMs with other traditional cardiac implantable electronic devices (CIEDS) for dual functioning.

The evolution of LPMs represents a significant leap forward in cardiac care. The seamless integration of CSP procedures with leadless pacemaker technology has the potential to deliver unique benefits over traditional pacemakers. With continuous advancements in technology and research, these devices are set to become even more effective and accessible, offering hope to millions of patients worldwide. As we look to the future, the potential for LPMs to transform the landscape of cardiac pacing is immense.

LPMs and the Subcutaneous Implantable Cardioverter-Defibrillator (S-ICD)

The S-ICD is an established alternative to the transvenous ICD.¹² However, S-ICDs lack pacing for bradycardia or anti-tachycardia pacing (ATP). For such patients, requiring both defibrillation and pacing, co-implantation with an LPM offers an extravascular solution. Case reports show that currently

available LPMs can be co-implanted with S-ICDs to provide anti-bradycardia pacing. However, potential issues include double counting (leading to inappropriate shocks) and under-sensing of ventricular arrhythmias due to pacing artefacts. Also, no ATP can be provided. A coordinated system with wireless communication between S-ICD and LPM may overcome these potential problems.

Conclusion

Over the past decade, LPM therapy has matured from an experimental to an established treatment option. A substantial body of observational evidence suggests that single-chamber VVI(R) LPMs are associated with fewer infections and complications, compared to transvenous pacemakers, particularly over the long term. While acute perforations may be more frequent and severe, they are often mitigated by operator training and experience. The introduction of leadless VDD(R), and more recently DDD(R) pacing has expanded the indications for LPM therapy to considerably more patients. With promising early data on LBB-area LPM implantation, the future for LPM therapy looks very promising. These advances offer a pathbreaking opportunity to reshape the landscape of cardiac pacing.

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New Therapeutic Vistas in Carpal Tunnel Syndrome Management

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Abstract:

Carpal tunnel syndrome (CTS) represents the most common entrapment neuropathy, affecting approximately 8% of the adult population worldwide. This review examines the pathophysiological mechanisms of CTS and provides a critical evaluation of contemporary interventional approaches that bridge the gap between conservative treatment and surgical management. Particular emphasis is placed on emerging techniques such as ultrasound-guided hydrodissection (HD), prolotherapy, platelet-rich plasma, and hyaluronic acid injections. A systematic analysis of randomised controlled trials and meta-analyses was conducted to evaluate the efficacy, safety, and long-term outcomes of these interventions. The evidence suggests that ultrasound-guided techniques offer significant advantages over blind injections, with dextrose prolotherapy and platelet-rich plasma demonstrating promising results for long-term symptom management. This review provides clinicians with evidence-based recommendations for the appropriate selection of interventional techniques based on disease severity and patient-specific factors, potentially reducing the need for surgical intervention in selected patients.

Key words: Carpal Tunnel Syndrome (CTS), Neuropathy, Emerging Interventional Approaches.

Introduction

Carpal tunnel syndrome (CTS) represents the most prevalent entrapment neuropathy, affecting approximately 8% of the adult population.¹ Characterised by compression of the median nerve as it traverses the carpal tunnel, CTS presents with a classic constellation of symptoms including paraesthesia, numbness, and pain in the median nerve distribution, often accompanied by diminished grip strength and fine motor dexterity.^{2,3} The condition significantly impacts the quality of life and work productivity, with economic implications extending beyond direct healthcare costs to include lost workdays and decreased occupational performance.⁴

The management landscape for CTS has traditionally been dichotomised between conservative approaches and surgical intervention. Conservative management typically includes splinting, activity modification, oral anti-inflammatory

medications, and local corticosteroid injections.⁵ While these approaches may provide temporary relief, their long-term efficacy remains limited, particularly in moderate to severe cases.⁶ Conversely, surgical decompression, while generally effective, carries inherent risks including scar formation, pillar pain, and prolonged recovery periods.⁷

The gap between these conventional treatment paradigms has spurred interest in minimally invasive interventional techniques that may provide more durable relief than conservative management while avoiding the morbidity associated with surgery. These intermediate interventions, including ultrasound-guided hydrodissection (HD), prolotherapy, platelet-rich plasma (PRP) injections, and hyaluronic acid applications, represent an evolving frontier in CTS management.^{8,9}

This review aims to critically examine the pathophysiological mechanisms underlying CTS and provide a comprehensive analysis of contemporary interventional approaches based on current evidence from randomised controlled trials and meta-analyses. By synthesising this information, we seek to establish evidence-based recommendations for the appropriate selection and implementation of these techniques in clinical practice.

Pathophysiology of CTS

Anatomical considerations

The carpal tunnel is a fibro-osseous canal bounded dorsally by the carpal bones and ventrally by the transverse carpal ligament (TCL). This confined space houses the median nerve and nine flexor tendons – the flexor pollicis longus and eight flexor digitorum superficialis and profundus tendons.¹⁰ The median nerve, positioned superficially beneath the TCL, is particularly vulnerable to compressive forces within this restrictive environment (Figure 1).

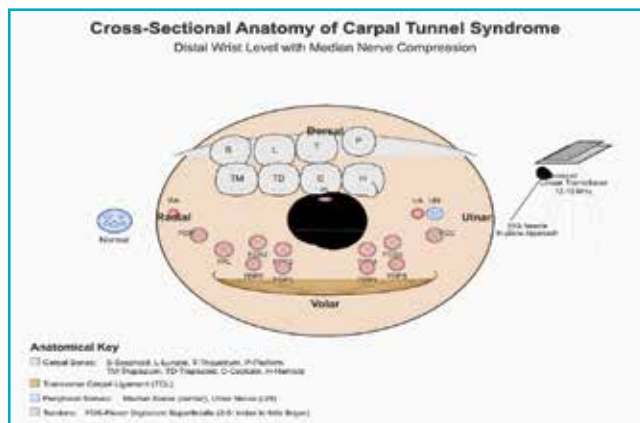


Figure 1: Anatomical site of carpal tunnel with compression of median nerve (Drawn by Dr. Abhishek Dixit using Python Software).

Compression mechanisms

The pathophysiology of CTS involves a cascade of events initiated by increased pressure within the carpal tunnel. Normal pressure ranges from 2-10 mmHg, but can exceed 30 mmHg in CTS patients, particularly during wrist flexion or extension.¹¹ This elevated pressure leads to several pathophysiological changes:

- Vascular compromise:** Initial compression affects venous outflow from the epineurial veins of the median nerve, leading to venous stasis, oedema, and subsequent ischaemia. The compression of the vasa nervorum results in the accumulation of metabolic toxins in the affected segment.¹²
- Lymphatic obstruction:** Prolonged compression impairs lymphatic drainage, which normally occurs through vessels located outside the epineurium, further exacerbating local oedema and intraneural pressure.¹³
- Demyelination and axonal injury:** Persistent ischaemia leads to focal demyelination, particularly affecting large, myelinated fibres, resulting in slowed nerve conduction. If compression continues, axonal degeneration may occur, leading to permanent neurological deficits.¹⁴
- Mechanical disruption:** Beyond vascular effects, direct mechanical forces impair axonal transport and disrupt the nerve's gliding mechanisms. The median nerve normally exhibits longitudinal excursion during wrist and finger movements. Reduced nerve mobility due to fibrosis and adhesions represents a critical factor in symptom development and persistence.¹⁵
- Neurogenic inflammation:** Compression triggers the release of inflammatory mediators including substance P, calcitonin gene-related peptide, and pro-inflammatory cytokines, perpetuating a cycle of inflammation, oedema, and increased pressure.¹⁶

Role of nervi nervorum

An important pathophysiological consideration is the impact on nervi nervorum, the free nerve endings supplying the connective tissue sheaths of the main nerve. These structures mediate nociception from the nerve itself and play a critical role in neurogenic inflammation. Compression of nervi nervorum contributes significantly to pain symptomatology in CTS, even before notable conduction abnormalities in the main trunk.¹⁷

This understanding provides a mechanistic rationale for HD techniques that aim to separate the nerve from surrounding structures, potentially relieving pressure on these pain-mediating nerve fibres.

Progression and Severity Classification

CTS typically progresses through three stages: (1) intermittent symptoms with reversible conduction changes, (2) persistent symptoms with demonstrable sensory and motor deficits, and (3) severe, constant symptoms with muscle atrophy and significant electrophysiological abnormalities.¹⁸ This progression correlates with pathophysiological changes from transient ischaemia to demyelination and ultimately axonal loss. Severity classification guides treatment approaches, with early intervention potentially preventing progression to irreversible neural damage. Electrodiagnostic findings typically correlate with severity:

- Mild:** Prolonged sensory latencies with normal motor studies
- Moderate:** Abnormal sensory and motor latencies
- Severe:** Absence of sensory responses and prolonged motor latencies with reduced amplitude¹⁹

The cross-sectional area (CSA) of the median nerve on ultrasound represents another important parameter for severity assessment and treatment monitoring, with values greater than 12 mm² considered abnormal.²⁰

Emerging Interventional Approaches

Ultrasound-guided HD

HD represents a novel technique involving the injection of fluid to separate the nerve from surrounding structures, thereby potentially addressing both mechanical compression and vascular compromise.²¹

Mechanisms of action

HD operates through several proposed mechanisms:

- 1. Mechanical separation:** Creating a fluid plane between the median nerve and adjacent structures, reducing direct compression²²
- 2. Improvement in nerve gliding:** Decreasing the gliding resistance of the median nerve, which is considered a principal patho-mechanical factor in CTS²²
- 3. Relief of nervi nervorum compression:** Releasing pressure on the pain-mediating nerve fibres supplying the main nerve²³
- 4. Restoration of vascular flow:** Improving microcirculation by separating the nerve from compressive structures and reducing venous congestion²³
- 5. Disruption of adhesions:** Breaking fibrous connections that restrict nerve movement²³

Technical approaches

Two primary approaches have been described for ultrasound-guided HD:

- 1. In-plane approach:** The needle is positioned in-plane with the ultrasound transducer, perpendicular to the long axis of the nerve. The tissues above and below the nerve are hydrodissected sequentially. This can be performed from either the ulnar or radial side, with some evidence suggesting the radial approach may offer more prolonged pain relief.²⁴

- 2. Out-of-plane approach:** The needle is advanced parallel to the long axis of the nerve, with the probe initially perpendicular and then parallel to the nerve. This facilitates HD of longer nerve segments but may be technically more challenging.²⁵

Comparative studies suggest the in-plane ulnar approach may be more effective than out-of-plane or blind injections in terms of symptom improvement and electrophysiological outcomes.²⁶

Efficacy and safety

Multiple randomised controlled trials have demonstrated the efficacy of ultrasound-guided HD. Wang *et al.* conducted a study with 64 patients randomised to HD or control groups, finding improvements in both functional and electrophysiological parameters in the HD group.²⁷ Similarly, Wu *et al.* demonstrated that HD with 5 mL normal saline was superior to subcutaneous injection above the carpal tunnel, supporting the mechanical separation hypothesis.²⁸

A systematic review by Yang *et al.* concluded that ultrasound-guided injections yielded favourable results for symptom severity and functional status compared to conventional approaches.²⁹ The safety profile appears excellent, with nerve damage being exceptionally rare due to the polyfascicular architecture of peripheral nerves and real-time visualisation provided by ultrasound guidance.³⁰

Long-term outcomes are encouraging, with a retrospective study by Li *et al.* reporting effective outcomes in 88.6% of patients after a mean follow-up of 1-3 years. Notably, the number of injections required correlated with initial severity, with mild, moderate, and severe grades requiring an average of 1.7, 2.4, and 2.6 injections, respectively.³¹

Injectate Options for Interventional Approaches

The evolution of interventional management has seen experimentation with various injectates, each with unique properties and proposed mechanisms of action (Table 1).

Injectate	Mechanism of Action	Key Evidence	Advantages	Limitations
Normal saline	• Mechanical separation of nerve from surrounding tissues • Promotion of blood flow • Reduction of nerve compression	Wu <i>et al.</i> 2019 ²⁸	• Cost-effective • Minimal side effects • Safe for repeat injections	• Limited durability • Primarily mechanical effect • Less effective than bioactive injectates
Corticosteroids	• Anti-inflammatory effect • Reduction of local oedema • Inhibition of fibroblast activity and collagen formation	Babaei-Ghazani <i>et al.</i> 2018 ³³	• Rapid onset of action • Strong evidence base • Effective for acute symptoms	• Limited long-term efficacy • Potential for tissue atrophy with repeated use • Risk of tendon weakening • Particulate steroids pose risk of neural damage
Dextrose 5% (D5W)	• Inhibition of TRPV1 receptors • Reduction of neurogenic inflammation • Correction of perineural glycopenia • Modulation of nerve hyperexcitability	Wu <i>et al.</i> 2017 ³⁹ Wu <i>et al.</i> 2018 ⁴⁰	• Superior long-term outcomes • Non-toxic to neural tissue • Safe for repeat injections • May promote tissue healing	• Slower onset of action • May require multiple treatments • Mechanism not fully elucidated
Platelet-rich plasma (PRP)	• Delivery of growth factors (TGF-β, PDGF, VEGF) • Promotion of tissue repair and regeneration • Modulation of inflammatory response	Wu <i>et al.</i> 2017 ⁴³ Raeissadat <i>et al.</i> 2018 ⁴⁴	• Long-lasting effects • Potential regenerative properties • Autologous nature reduces reaction risk • May reduce need for surgery	• Preparation complexity • Higher cost • Standardisation challenges • Requires special equipment
Hyaluronic acid	• Anti-adhesion properties • Anti-inflammatory effect • Promotion of nerve regeneration • Enhancement of nerve gliding	Su <i>et al.</i> 2021 ⁴⁶ Elawamy <i>et al.</i> 2020 ⁴⁷	• Rapid onset of action • Natural component of human tissues • Improves tissue hydration and gliding • Favourable safety profile	• Higher cost • Variable molecular weights available • Less durable than PRP or D5W
Ozone (O₂-O₃)	• Improved tissue oxygenation • Enhancement of cellular metabolism • Anti-inflammatory properties • Reduction of oxidative stress	Bahrami <i>et al.</i> 2019 ⁵⁰	• Potent anti-inflammatory effect • Antimicrobial properties • Improvement in tissue oxygenation	• Limited standardisation • Specialised equipment required • Variable concentration protocols • Less robust evidence base

Table 1: Comparison of different injectates for carpal tunnel syndrome.

Abbreviations: TRPV1: Transient Receptor Potential Vanilloid 1; TGF- β : Transforming Growth Factor Beta; PDGF: Platelet-derived Growth Factor; VEGF: Vascular Endothelial Growth Factor.

Corticosteroids

Corticosteroid injections remain the most widely studied intervention for CTS. Their anti-inflammatory properties reduce swelling within the carpal tunnel, potentially alleviating pressure on the median nerve.³² While traditionally administered using anatomical landmarks, ultrasound-guided corticosteroid injections have demonstrated superior efficacy.

A meta-analysis by Babaei-Ghazani *et al.* examining 10 randomised controlled trials (n=633) found ultrasound-guided corticosteroid injections provided significantly greater improvement in symptom severity compared to landmark-guided injections (standardised mean difference [SMD]=-0.82; 95% CI, -1.14 to -0.50; $p < 0.001$).³³ However, the duration of benefit appears limited, with effects typically waning after 3-6 months.³⁴

The choice of corticosteroid may influence outcomes and safety profiles. Triamcinolone acetonide, a commonly used particulate steroid, carries a risk of permanent nerve injury if accidentally injected intraneurally. Conversely, dexamethasone sodium phosphate, a non-particulate steroid, may offer a more favourable safety profile while maintaining efficacy.³⁵

Dextrose prolotherapy (5% dextrose in water, D5W)

Dextrose prolotherapy has emerged as a promising approach for CTS, particularly for its potential neuromodulatory and regenerative properties. D5W is iso-osmolar, minimising irritation to neural structures while potentially offering therapeutic benefits.³⁶

The mechanism of action remains incompletely understood but may involve inhibition of transient receptor potential vanilloid receptor-1 (TRPV1), blocking the release of substance P and calcitonin gene-related peptide, key mediators in neurogenic inflammation.³⁷ Additionally, chronic neuropathic pain may reflect relative glycopenia around affected nerves, with dextrose potentially correcting this metabolic imbalance.³⁸ Wu *et al.* conducted a pivotal randomised controlled trial comparing 5 mL of D5W against placebo in 54 patients with mild-to-moderate CTS. At 6-month follow-up, the dextrose group demonstrated significantly greater improvements in the Boston Carpal Tunnel Syndrome Questionnaire symptom severity score (-0.8 ± 0.5 vs -0.2 ± 0.4 ; $p < .001$) and functional status score (-0.7 ± 0.6 vs -0.1 ± 0.3 ; $p < .001$).³⁹

In a subsequent study comparing D5W to triamcinolone injection, Wu *et al.* found superior long-term outcomes with dextrose. While both treatments showed initial efficacy, the dextrose group-maintained improvements at 4-6 months, whereas the steroid group demonstrated regression toward baseline.⁴⁰

Dosage considerations may be relevant, with Lin *et al.* demonstrating that 4 mL of D5W provided better efficacy than 1 mL or 2 mL volumes based on symptom relief and functional improvement at 1-, 4-, and 12-weeks post-injection.⁴¹

Platelet-rich plasma (PRP)

PRP represents an autologous concentration of platelets containing numerous growth factors, including transforming

growth factor- β , platelet-derived growth factor, and vascular endothelial growth factor. These bioactive components potentially promote tissue repair and nerve regeneration.⁴²

Wu *et al.* conducted a randomised controlled trial comparing single ultrasound-guided PRP injections against night splinting in 60 patients with mild-to-moderate CTS. At 6-month follow-up, the PRP group demonstrated significantly greater improvements in pain, symptom severity, functional status, and CSA of the median nerve.⁴³

Similarly, Raeissadat *et al.* compared PRP to corticosteroid injections in 41 patients, finding comparable short-term outcomes but superior long-term efficacy with PRP at 10-week follow-up.⁴⁴

Hyaluronic acid (HA)

HA has gained attention for its potential anti-adhesion, anti-inflammatory, and nerve regeneration properties. As a glycosaminoglycan naturally present in human tissues, HA may improve nerve gliding mechanics while modulating inflammatory responses.⁴⁵

Su *et al.* conducted a randomised trial comparing HA to normal saline in CTS patients, demonstrating superior outcomes in the HA group regarding symptom severity, functional status, and electrophysiological parameters.⁴⁶ Similarly, Elawamy *et al.* found that HD with HA offered more rapid onset of pain relief and better median nerve conduction compared to HD with normal saline alone over a 6-month follow-up period.⁴⁷

When compared directly to corticosteroids, a study by Alsaied demonstrated that HA significantly outperformed dexamethasone in terms of Boston Carpal Tunnel Questionnaire scores, electrophysiological studies, and sonographic parameters at 1 week, 1 month, 3 months, and 6 months post-intervention.⁴⁸

Ozone therapy

Ozone therapy represents an emerging approach for various musculoskeletal disorders, including CTS. The proposed mechanisms include improved tissue oxygenation, enhanced cellular metabolism, anti-inflammatory effects, and reduction of oxidative stress.⁴⁹

Bahrami *et al.* conducted a randomised controlled trial of 40 patients with mild or moderate CTS, comparing ozone injection to corticosteroid. At 10-week follow-up, the ozone group demonstrated superior improvements in functional scales and visual analog scale scores.⁵⁰

However, when compared directly to corticosteroid injection in another study, both treatments showed improvement in symptom severity and pain at 6 and 12 weeks, but electrophysiological parameters improved significantly only in the corticosteroid group.⁵¹

Comparative Efficacy of Different Injectates

Wu *et al.* conducted a comparative study of commonly used injectates in patients with severe CTS (CSA > 15 mm²).

Intervention	Symptom Improvement	Functional Improvement	Electrophysiological Improvement	Sonographic Improvement	Onset of Action	Duration of Effect	Recommended for
Conservative Management							
Splinting	+	+	+/-	-	Slow (weeks)	Temporary	Mild CTS, initial management
Oral NSAIDs	+	+/-	-	-	Moderate (days)	Short-term	Acute symptoms, mild CTS
Intermediate Interventions							
US-guided corticosteroid injection	+++	++	++	+	Rapid (days)	3-6 months	Moderate CTS, acute symptoms
US-guided D5W HD	++	+++	++	++	Moderate (1-2 weeks)	6+ months	Mild to moderate CTS, patients seeking durability
US-guided PRP injection	++	+++	++	+++	Moderate (1-2 weeks)	6+ months	Moderate to severe CTS, failed conservative treatment
US-guided HA injection	+++	++	++	++	Rapid (days)	3-6 months	Moderate CTS, patients needing rapid relief
US-guided ozone therapy	++	++	+	+	Moderate (1-2 weeks)	3-4 months	Alternative for patients with contraindications to other treatments
Surgical Approaches							
Endoscopic release	++++	++++	+++	+++	Delayed (weeks)	Long-term/permanent	Severe CTS, failed conservative/interventional approaches
Open release	++++	++++	+++	+++	Delayed (weeks)	Long-term/permanent	Severe CTS, recurrent CTS, complicated cases

Table 2: Comparative efficacy of interventional approaches for carpal tunnel syndrome.

Rating scale: - = no effect; + = minimal effect; ++ = moderate effect; +++ = significant effect; ++++ = maximum effect

Abbreviations: US: Ultrasound; D5W: 5% Dextrose in Water; PRP: Platelet-Rich Plasma; HA: Hyaluronic Acid; CTS: Carpal Tunnel Syndrome; NSAIDs: Non-steroidal Anti-inflammatory Drugs.

Comparing normal saline, D5W, PRP, and HA, they found that single doses of PRP, D5W, and HA were significantly more effective than normal saline regarding symptomatic improvement, functional outcomes, and reduction in median nerve cross-sectional area.⁵²

For long-term efficacy, PRP and D5W demonstrated greater durability than HA at 6-month follow-up, although PRP showed slightly superior results. For early response, HA demonstrated the most rapid effect at 1-month post-intervention.⁵³

This differential temporal response pattern may guide clinical decision-making, with HA potentially preferred for rapid symptom relief, while PRP or D5W may be superior choices for sustained long-term outcomes (Table 2).

Volume Considerations in HD

The optimal volume for HD remains an area of active investigation. Traditional approaches typically utilise larger volumes (5-10 mL) to achieve mechanical separation of the nerve from surrounding structures.⁵⁴ However, the minimum required volume for therapeutic effect remains undefined.

Wang *et al.* conducted a randomised trial comparing ultrasound-guided HD with 10 mL of solution (1 mL triamcinolone, 1 mL lidocaine, 8 mL saline) versus 2 mL (1 mL triamcinolone, 1 mL lidocaine). Both groups demonstrated comparable functional and electrophysiological improvements, suggesting volume may not be the primary determinant of efficacy.²⁷

Conversely, Lin *et al.* found that ultrasound-guided injection of 4 mL of D5W provided superior efficacy compared to 1 mL or 2 mL volumes based on symptom relief and functional improvement at 1-, 4-, and 12-weeks post-injection.⁴¹ In a subsequent analysis, they demonstrated that higher volumes (4 mL) yielded better nerve mobility and more significant reductions in median nerve cross-sectional area compared to smaller volumes.⁵⁵

This discrepancy may reflect differences in the primary mechanism of action between various injectates. Corticosteroids may exert their effect predominantly through anti-inflammatory properties, with volume playing a lesser role. In contrast, D5W may require sufficient volume to achieve

both mechanical separation and adequate distribution of the dextrose solution to modulate neurogenic inflammation and local metabolism.

Ultrasound-Guided Versus Blind Injections

The role of ultrasound guidance in CTS interventions has been extensively studied, with compelling evidence supporting its superiority over traditional landmark-guided approaches. Chen *et al.* conducted a double-blind randomised controlled trial comparing ultrasound-guided versus direct approach corticosteroid injections in CTS patients. The ultrasound-guided group demonstrated earlier and more profound symptom relief, greater improvements in sensory testing, and superior gains in sensory nerve conduction velocity.⁵⁶

A comprehensive meta-analysis by Babaei-Ghazani *et al.* synthesising data from 10 randomised controlled trials (n=633) found ultrasound-guided injections significantly outperformed landmark-guided approaches in symptom severity improvement (SMD=-0.82; 95% CI, -1.14 to -0.50; $p < 0.001$). While functional status showed a trend favouring ultrasound guidance, this did not reach statistical significance.³³

The advantages of ultrasound guidance include:

- 1. Precise medication delivery:** Ensuring the injectate reaches the intended target³⁰
- 2. Avoidance of iatrogenic injury:** Minimising risk to neurovascular structures³⁰
- 3. Confirmation of spread patterns:** Visualising the distribution of injectate around the nerve³⁰
- 4. Potential diagnostic information:** Providing real-time assessment of neural morphology and surrounding structures³⁰
- 5. Improved patient satisfaction:** Potentially reducing procedural anxiety and discomfort³⁰

The safety profile of ultrasound-guided procedures appears excellent, with nerve injury exceptionally rare due to the polyfascicular architecture of peripheral nerves and real-time visualisation.³⁰

HD Versus Surgical Management

For patients with refractory symptoms or severe CTS, surgical decompression has traditionally been considered the gold standard. However, emerging evidence suggests HD techniques may offer a viable alternative in selected cases. Zeng *et al.* directly compared ultrasound-guided HD versus surgery in CTS patients. While both approaches demonstrated efficacy, HD offered several advantages including smaller incision, lower cost, shorter procedural time, and faster recovery.⁵⁸

The decision between interventional approaches and surgery should consider several factors:

- 1. Disease severity:** Severe CTS with significant axonal loss and muscle atrophy may necessitate surgical intervention
- 2. Failed conservative management:** Patients who have not responded to initial conservative measures
- 3. Patient preferences:** Consideration of recovery time, procedural invasiveness, and risk tolerance
- 4. Comorbidities:** Medical conditions that may increase surgical risk.
- 5. Occupational demands:** Requirements for rapid return to function versus long-term outcome optimisation⁵⁹

For mild to moderate CTS, or in patients with contraindications to surgery, HD with appropriate injectates may offer a reasonable alternative with potentially equivalent long-term outcomes in selected cases.

Clinical Recommendations

Based on the current evidence, several practical recommendations emerge for the interventional management of CTS:

- Ultrasound guidance is preferred over blind or landmark-guided injections for all interventional procedures, offering superior precision, safety, and potentially improved outcomes.
- The in-plane ulnar approach generally provides optimal results for HD, although the radial approach may offer longer pain relief in some cases.
- Injectate selection should be tailored to patient-specific factors:
 - For rapid symptomatic relief: Corticosteroids or hyaluronic acid
 - For durable long-term results: D5W or PRP
 - For patients with contraindications to other injectates: Normal saline
- Volume considerations suggest 4-5 mL may represent an optimal balance for HD, particularly when using D5W, though this may vary based on injectate type.
- Disease severity influences treatment selection:
 - Mild CTS: Conservative management initially; if unsuccessful, consider D5W or HA HD
 - Moderate CTS: Consider ultrasound-guided interventions as first-line therapy; PRP or D5W may offer optimal long-term results
 - Severe CTS: Surgical intervention is typically preferred; in patients declining surgery or with contraindications, multiple sessions of HD (particularly with PRP) may provide benefit
- Combination approaches may offer synergistic benefits, such as initial corticosteroid injection for rapid relief followed by D5W or PRP for long-term management,

though evidence for such sequential therapy remains limited.

7. Safety considerations favour non-particulate steroids (dexamethasone) over particulate options (triamcinolone) when corticosteroids are selected, due to reduced risk of intraneural injection complications.
8. Monitoring response should include patient-reported outcomes (Boston Carpal Tunnel Questionnaire), objective measures (grip strength, sensory testing), and where available, serial ultrasound assessment of median nerve CSA and mobility.
2. Identification of predictive factors for response to specific interventions, potentially including ultrasound parameters, electrodiagnostic findings, or symptom characteristics
3. Exploration of combination therapies utilising sequential or simultaneous application of different injectates or techniques
4. Standardisation of techniques including optimal needle approach, volume, concentration, and post-procedural recommendations
5. Investigation of regenerative approaches beyond PRP, potentially including stem cell therapies or nerve growth factors
6. Development of novel injectates specifically designed to address the pathophysiological mechanisms of CTS
7. Cost-effectiveness analyses comparing interventional approaches to conventional management strategies

Future Directions

Several areas warrant further investigation to refine our understanding and optimisation of interventional approaches for CTS:

1. Comparative effectiveness research directly contrasting various injectates in large, well-designed randomised controlled trials with extended follow-up periods

Conclusion

The management of CTS continues to evolve, with ultrasound-guided interventional techniques offering a promising middle ground between traditional conservative measures and surgical decompression. Current evidence supports the efficacy and safety of HD techniques utilising various injectates, each with unique properties and potential advantages.

Ultrasound guidance significantly enhances precision and outcomes compared to landmark-guided approaches. Among available injectates, dextrose prolotherapy and PRP demonstrate particular promise for durable long-term outcomes, while hyaluronic acid may offer more rapid symptomatic relief.

Patient selection remains crucial, with disease severity, prior treatment response, comorbidities, and patient preferences informing the appropriate intervention strategy. For mild to moderate CTS, ultrasound-guided HD may provide a viable alternative to surgery in many cases, potentially reducing healthcare costs and recovery time while maintaining comparable outcomes.

As our understanding of CTS pathophysiology continues to deepen, and interventional techniques are further refined, the management paradigm will likely continue shifting toward minimally invasive, targeted approaches that address the underlying mechanisms of neural compression and dysfunction.

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Re-emerging Zoonotic Diseases in India: Insights and Evolving Challenges

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Abstract:

The majority of humans interact with animals in some form, creating opportunities for disease transmission. A zoonotic disease is a disease or infection that can be transmitted naturally from vertebrate animals to humans or from humans to vertebrate animals. Common examples include bacterial infections such as salmonellosis, brucellosis, plague, and leptospirosis; fungal diseases like cryptococcosis and histoplasmosis; parasitic infections such as leishmaniasis, hydatid disease, schistosomiasis, and toxoplasmosis; and viral illnesses including rabies, influenza, and yellow fever.

Throughout history, zoonotic pathogens have been responsible for major pandemics, such as the Black Death, the Plague of Justinian, and the 1918 Spanish flu. More recently, the Nipah virus, causing severe encephalitis, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for the coronavirus disease 2019 (COVID-19) pandemic, are believed to have zoonotic origins. India, with its predominantly agriculture-based economy and high dependence on animal husbandry, faces heightened vulnerability to zoonotic diseases. Other contributing factors, including population growth, urbanisation, deforestation, and inadequate public health infrastructure, all of which pose serious threats. This review aims to examine the landscape of emerging zoonotic diseases in India and underscore the urgent need for integrated One Health approaches in policy and practice.

Key words: Zoonotic Diseases, Climate Change, Antimicrobial Resistance.

Emergence of Zoonotic Disease

According to the World Health Organization (WHO), zoonotic diseases are infections transmitted from animals to humans and can be caused by bacteria, viruses, fungi, or parasites (Table 1).¹ Emerging zoonotic diseases are newly identified infections transmitted from animals to humans that are increasing in

incidence or geographic spread, while re-emerging zoonotic diseases are previously known animal-to-human infections that had declined but are now resurging in incidence or distribution.

Bacterial Pathogens - Hosts	Viral Pathogens - Hosts	Fungal Pathogens - Hosts	Parasitic pathogens
Brucella - Raccoon, hare	Rabies - Dogs, bats	Cryptococcus and histoplasmosis - Bats	Leishmaniasis - Sandfly
Leptospira - Rats, cattle, buffalo	Influenza- Bats, camel		Hydatid disease - Dogs
Salmonella - Poultry and eggs	Dengue and chikungunya - Aedes Mosquito		Schistosoma - Snails
Bubonic plague - Rats	Japanese encephalitis virus - Pond herons, cattle egrets		Toxoplasma - Cats
	Hanta virus - Bandicots, rats, shrews		
	CrimeanCongo haemorrhagic virus - Shrews, bats		
	Kyasanur forest disease virus - Sick/dying monkeys, birds, ticks		

Table 1: Classification of zoonotic diseases based on the type of pathogen.²

A reservoir host is the one that serves as a source of infection and potential reinfection to animals/humans by harbouring a pathogen, without itself suffering from significant illness. While, an amplifier host is the one in which the pathogen multiplies to high levels, providing an important source of infection for target

host and vectors. Transmission of pathogen from reservoir or amplifier hosts to humans can occur through various routes such as direct contact, ingestion of contaminated food or water, or via vector organisms (Figure 1).

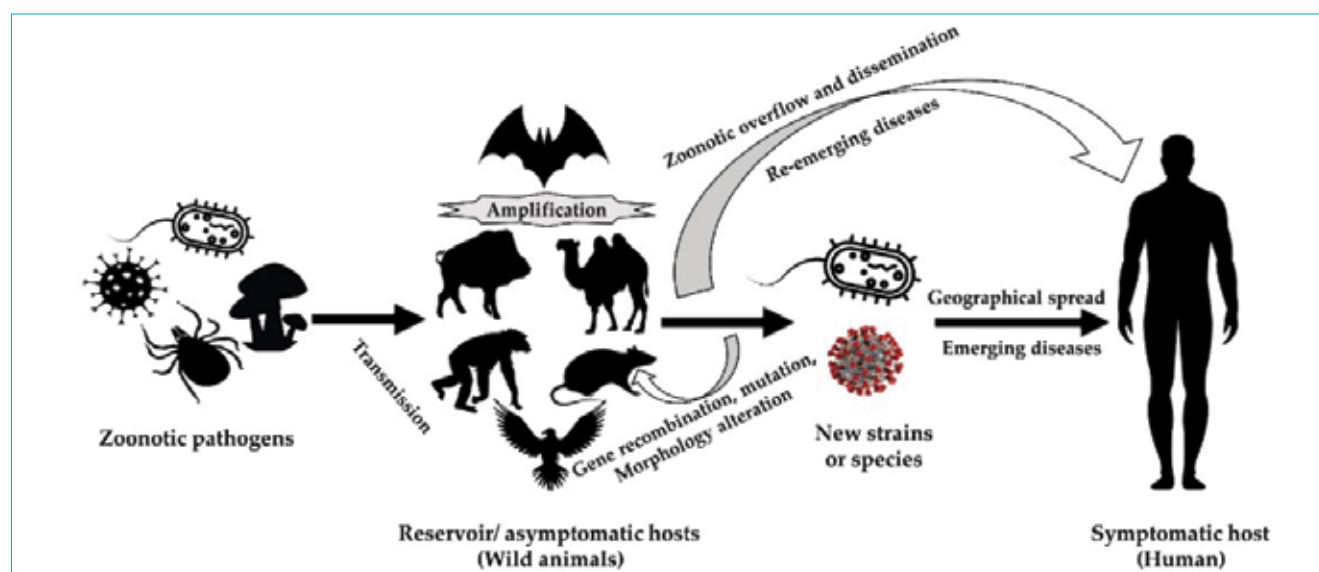


Figure 1: The involvement of the wild animals in the transmission and amplification of aetiological agents of emerging and re-emerging zoonoses.³

The unpredictable emergence of zoonotic diseases poses significant challenges for pandemic forecasting. To address this, the Daszak model was proposed⁴ which conceptualises zoonotic spillover in three progressive stages (Figure 2).

1. Stage 1 represents the pre-emergence phase, during which microbes circulate within their natural animal reservoirs without infecting humans. ecological disruptions — such as land-use changes — can alter host and microbial dynamics, potentially increasing the risk of spillover to other non-human species, including wildlife and livestock, although not yet to humans.
2. Stage 2 marks localised emergence, characterised by limited spillover events. These may be small and self-limiting (depicted by green peaks and troughs, reflecting fluctuating case numbers over time) or more extensive spillovers (red peaks), leading to short chains of human-to-human transmission.
3. In stage 3, certain spillover events result in sustained human transmission, which can escalate to widespread outbreaks, cross-border dissemination, and ultimately, the development of a true pandemic.

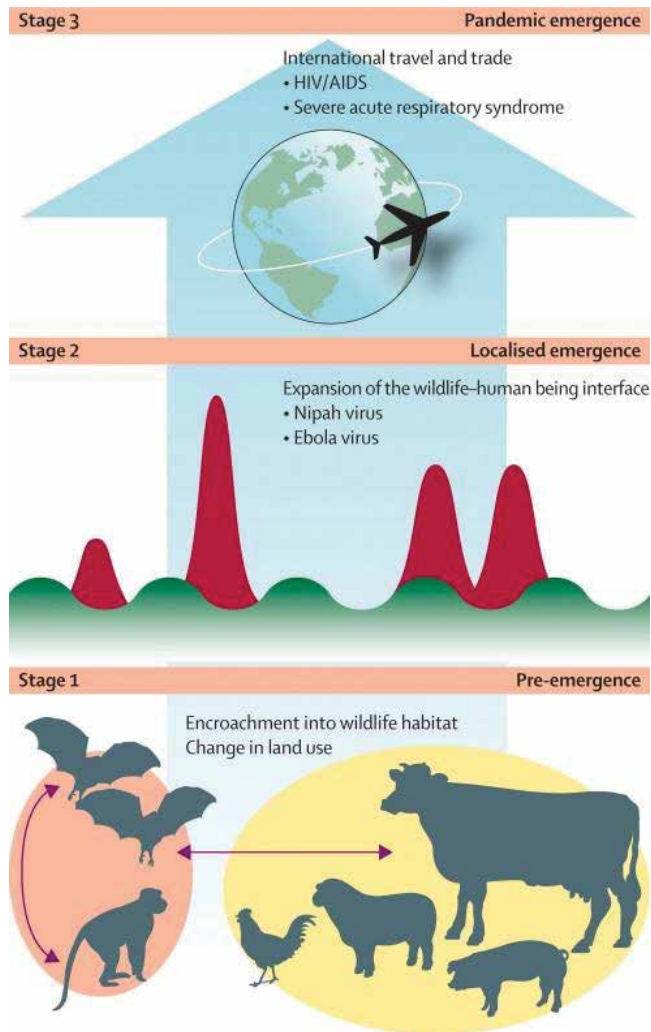


Figure 2: Stages of zoonotic spillover.⁵

While the potential impact and geographic reach of each stage increase from stages 1 through 3, the frequency of such events declines, with stage 3 pandemics being relatively rare. For healthcare professionals, it is imperative to understand the factors contributing to the resurgence of zoonotic diseases and to be prepared for the challenges they present.

A detailed understanding of this progression, along with its ecological and epidemiological drivers, can inform more targeted strategies for pandemic prevention. Ideally, effective control measures should aim to intervene at stage 1, preventing pathogens from ever reaching the human population.

1. Factors driving the Re-emergence of Zoonoses in India

1.1. Urbanisation and population growth

India's rapid urbanisation, combined with a burgeoning population, has resulted in increased human-wildlife interactions. This disrupts forest ecosystems and allows previously hidden forest pathogens to enter newly formed human settlements. Examples include diseases like Nipah virus (NiV) and Kyasanur forest disease.⁶ Urbanisation, closely linked to population growth, leads to accumulation of waste and poor sanitation. This creates ideal conditions for rodents and stray

animals to thrive and for stagnant water to accumulate — providing breeding grounds for mosquitoes. These factors contribute to the emergence and re-emergence of zoonotic diseases of rodent and arthropod origin, (Figure 3) such as Japanese encephalitis, dengue, and leptospirosis.

1.2. Climate change and environmental disruption

Climate change has profound effects on zoonotic disease dynamics. Warmer temperatures, altered

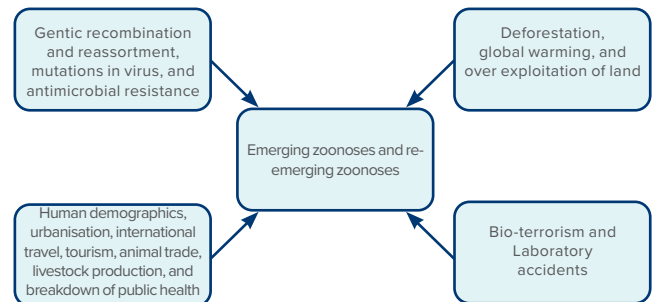


Figure 3: Major factors responsible for emerging and re-emerging zoonoses.³

precipitation patterns, and changing ecosystems influence the distribution and behaviour of vector species, such as mosquitoes, ticks, and rodents. Diseases like dengue, malaria, and chikungunya, which are transmitted by vectors, are becoming more widespread in India due to shifting climate conditions.⁷

1.3. Agricultural practices and livestock management

India's agricultural sector is a key driver of zoonotic disease emergence. The close proximity of humans, livestock, and wildlife increases the chances of disease transmission. Practices such as the intensive farming of poultry, dairy, and other livestock can facilitate the spread of diseases like avian influenza, brucellosis, and tuberculosis. Additionally, the lack of proper veterinary surveillance systems further exacerbates the problem.⁸

1.4. Globalisation and movement of people and goods

India's interconnectedness with the global community also poses a significant risk in terms of zoonotic disease spread. The movement of people, animals, and goods across borders facilitates the rapid spread of infectious diseases. The recent outbreaks of coronavirus disease 2019 (COVID-19), originating from animal-human interactions, have demonstrated the vulnerability of human populations to emerging zoonotic threats in a globalised world.⁹

1.5. Antimicrobial resistance

Biological factors like mutations in genome of virus, are also a significant factor. Drug-resistant pathogen strains can emerge as a consequence of chemical and antimicrobial agent exposure, making disease management and therapeutic interventions more challenging.¹⁰ The overuse of antibiotics and antivirals in both human and veterinary medicine contributes

to the development of resistant strains of pathogens, complicating therapeutic efforts. Illustrative examples are shown in Table 2.

Disease	Contributing Factor
Middle East respiratory syndrome	Wildlife, travel
Highly Pathogenic Avian Influenza (HPAI) viruses	Animal-animal influenza virus gene reassortment; emergence of H5N1 avian influenza, extensive chicken farming
Ebola virus	Technology and industry developments (healthcare)
Leptospirosis	Developments (Health care)
Severe acute respiratory syndrome	Ecosystem change
Crimean-Congo Haemorrhagic fever	Ecological changes favouring increased human exposure to ticks of sheep and small wild animals
Lassa Fever	Hospital exposure to index case – rodent exposure
Cryptosporidiosis	Inadequate control of water supply, international travel, increased use of child-care facilities
Rabies	Breakdown in public health measures, change in land use, travel, bites from rabid dogs
Rift valley fever	Climate change
Tuberculosis	Drug resistance; Breakdown in public health or control measures

Table 2: Some examples of emerging and re-emerging infections and their root cause.¹⁰

2. Key Re-emerging Zoonoses in India

2.1. Rabies

Rabies, a viral zoonosis primarily transmitted through the bite of an infected animal, remains a major public health issue in India. Despite advances in vaccination and post-exposure prophylaxis (PEP), India continues to bear a significant rabies burden, accounting for approximately 36% of global rabies deaths, with an estimated 18,000 - 20,000 fatalities annually.¹¹ Stray dogs, which are abundant in urban and rural areas, are the primary source of rabies transmission. Rabies has a high case fatality rate, and the lack of consistent vaccination campaigns in both dogs and humans contributes to the persistence of the disease.

2.2. Nipah virus

NiV, a deadly zoonotic virus from the *Paramyxoviridae* family, is transmitted by Pteropus fruit bats and has caused high-mortality outbreaks in South Asia, including Malaysia, Singapore, Bangladesh, and India. India has seen outbreaks in West Bengal (2001, 2007) and Kerala (2018, 2021), with high fatality rates.³ First identified in 1998 in Malaysia, NiV spreads to humans via intermediary hosts like pigs or directly through bat-contaminated sources such as date palm sap. NiV infection can cause encephalitis and respiratory distress, with a high mortality rate.¹² Human encroachment into wildlife habitats, intensive farming, and genetic factors contribute to NiV's emergence.

Classified as a potential bioterrorism agent (Centers for Disease Control and Prevention [CDC] category C), NiV prevention requires surveillance, safe pig-rearing, protecting food sources from bats, and limiting habitat disruption.

2.3. Scrub typhus

Scrub typhus is a vector-borne zoonotic disease caused by the bacterium *Orientia tsutsugamushi* and is a significant contributor to rickettsial infections worldwide. Each year, nearly one million cases are reported globally, with a notable mortality rate. In 2023, multiple outbreaks were reported across the country, resulting in several fatalities, with Himachal Pradesh and Odisha among the hardest-hit states.¹³ The disease typically presents with symptoms such as fever, cough, nausea, headache, breathlessness, and, in some cases, altered sensorium. Around one-third of affected individuals may develop severe multiorgan dysfunction involving the heart, kidneys, lungs, and liver. Its characteristic sign includes an eschar at the site of bite of the vector. Treatment includes twice-daily dose of 100 mg of doxycycline and other supportive therapy.

2.4. Leptospirosis

Leptospirosis, a bacterial infection caused by the *Leptospira* species, is another re-emerging zoonosis in India. This disease is transmitted through contact with water or soil contaminated by the urine of infected animals, particularly rodents. Leptospirosis is often associated with flooding, as seen during the monsoon season in states like Kerala, Maharashtra, and Tamil Nadu.¹⁴ The disease presents with flu-like symptoms but can progress to severe liver and kidney damage, haemorrhagic fever, or meningitis in some cases.

2.5. Avian influenza (bird flu)

Avian influenza, caused by the H5N1 virus, is another zoonotic threat that has periodically emerged in India. In March 2025, a two-year-old girl in Andhra Pradesh succumbed to H5N1 infection, marking the country's first human fatality from avian influenza in the last four years. The transmission of this virus from poultry to humans, although rare, poses significant public health risks. The outbreaks of avian influenza in poultry farms have caused alarm, particularly with the potential for genetic mutations that might make the virus more transmissible between humans. Efforts to control the spread of bird flu include mass culling of infected poultry and surveillance of migratory birds.

2.6. Plague

While the plague is no longer a major threat in many parts of the world, India has experienced several outbreaks in the past, particularly in rural areas. The disease is primarily transmitted through flea bites from infected rodents, and although it has been largely controlled through antibiotics, occasional cases continue to emerge, particularly in states like

Rajasthan.¹⁵ Surveillance and vector control measures remain critical in preventing further outbreaks.

2.7 Other zoonotic diseases

Zoonotic diseases, a constant threat to the world, are still underrated in many aspects. COVID-19 emerged as a hazard, leaving a bruise on the planet and an example to humankind about the potential threat zoonotic diseases could cause. Anthrax, brucellosis, bovine tuberculosis, cysticercosis, Japanese encephalitis, echinococcosis, toxoplasmosis, and nontyphoidal salmonellosis are the most significant neglected zoonotic diseases, particularly in India.¹⁶

Similarly, Zika virus, another zoonotic disease, is due to a virus transmitted by *Aedes aegypti* mosquitoes, which bite during the daytime. This virus was primarily detected in monkeys in the Zika forest in Uganda and gradually appeared in humans with time. Symptoms of this virus include headache, malaise, muscle, and joint pain, fever, rash, and conjunctivitis. Other complications are caused during pregnancy. Infants born with congenital Zika syndrome have microcephaly and other congenital abnormalities. The Zika virus may cause a pregnant woman to be prone to preterm birth and miscarriage. Guillain–Barre syndrome, neuropathy, and myelitis are a few of the neurological symptoms most commonly seen with the Zika virus.

Dengue, the most prevalent arboviral illness in humans, transmitted by female *Aedes* mosquito, is frequently reported in India, especially from July to November. The upsurge of dengue fever is a potential threat to society, and timely treatment is vital to prevent mortality.

The febrile illness known as Kyasanur forest disease is accompanied by haemorrhages. It is brought on by a flavivirus spread through a tick bite. Patients experience symptoms ranging from fever and headaches to myalgia, haemorrhages, and neurological symptoms.

3. Diagnostic approaches

The diagnosis of zoonotic diseases requires a combination of clinical suspicion, epidemiological understanding, and laboratory investigations. Therefore, a thorough clinical history, especially regarding animal exposure, is essential for guiding diagnosis.¹⁷

3.1. Diagnostic challenges

The diagnostic challenge lies in differentiating zoonotic diseases from other endemic conditions, particularly in a country like India where multiple infectious diseases circulate simultaneously.

Zoonoses often present with nonspecific symptoms, such as fever, headache, fatigue, and muscle pain, which overlap with many other infectious diseases. For example, leptospirosis and dengue fever both present with acute febrile illness and may show overlapping clinical features like headache, muscle pain, and fatigue.

Similarly, malaria and typhoid fever are common in endemic areas and can mimic symptoms of zoonotic diseases like brucellosis or rickettsial infections.

The key to distinguishing between zoonotic infections and other differential diagnoses lies in:

1. **Clinical clues:** It is crucial to inquire about recent travel to areas with known outbreaks, exposure to animals (including domestic pets, livestock, and wildlife), consumption of undercooked meat, or exposure to vectors like mosquitoes or ticks. The patient's occupation — whether they are involved in farming, veterinary work, or wildlife conservation — also provides important clues. Knowing if the patient has been exposed to water sources potentially contaminated by animal urine or faeces can also guide diagnosis, especially for leptospirosis.¹⁸
2. **Laboratory testing:** Rapid antigen tests, polymerase chain reaction (PCR), and serological assays are essential tools for confirming zoonotic diseases. For instance:
 - o PCR-based assays can detect specific pathogen DNA or RNA, which is useful for diagnosing viral diseases like NiV, Hantavirus, and avian influenza.
 - o Serological tests to detect antibodies (IgM or IgG) against pathogens like *Brucella*, *Leptospira*, or *Rickettsia* help confirm infection.
 - o Blood cultures in cases of leptospirosis or rickettsial infections and urinary antigen tests for *Leptospira* are particularly important.

3.2. Syndrome-based approach to diagnosis

A physician should consider zoonotic diseases in the differential diagnosis while evaluating a patient. For instance:

- **Fever of unknown origin (FUO):** In a country like India, where diseases such as tuberculosis, malaria, and typhoid are endemic, FUO is a common presentation. However, if a patient has a history of animal exposure, zoonotic infections like brucellosis, leptospirosis, dengue, or rickettsial diseases should be high on the differential.¹⁸
- **Acute encephalitis:** In a patient presenting with acute encephalitis, particularly with a history of exposure to bats or other animals, must be considered. Patients with Nipah can present with rapidly progressing encephalitis, requiring immediate isolation and management.
- **Acute respiratory distress:** In patients presenting with severe respiratory distress and a history of rodent exposure, Hantavirus pulmonary syndrome should be considered. Similarly, avian influenza should be considered in patients with a history of close contact with infected poultry.

- **Muscle pain and hepatic involvement:** In patients presenting with muscle pain and evidence of hepatic involvement (elevated liver enzymes, jaundice), leptospirosis should be considered, especially if there's a history of exposure to contaminated water during flooding or water sports.

4. Treatment approaches in Zoonotic Diseases

The treatment plan will depend on the type of pathogen, its severity, and the patient's overall condition. Some zoonotic diseases are treatable with antibiotics, antivirals, or supportive care, while others may require more intensive interventions.

4.1. Antibiotic therapy for bacterial zoonoses

- **Brucellosis:** This is a major zoonotic bacterial infection, especially in India, where patients may present with fever, arthralgia, and splenomegaly. A combination of doxycycline (100 mg twice daily) and rifampin (10 mg/kg/day) for at least 6 weeks is recommended, with possible extension depending on the severity and complications such as osteoarticular or genitourinary involvement.¹⁹
- **Leptospirosis:** This often presents with a mild or moderate febrile illness but can progress to severe disease with liver failure, kidney damage, or haemorrhagic manifestations. For mild cases, oral doxycycline (100 mg twice daily for 5–7 days) may be sufficient. However, for severe cases, intravenous penicillin G (24 million units/day) or ceftriaxone is indicated.¹⁷
- **Rickettsial infections (e.g., scrub typhus, Rocky Mountain spotted fever):** The treatment of choice is doxycycline (100 mg twice daily for 7-10 days). Early antibiotic therapy is essential to prevent complications like organ failure or death.¹⁸
- **Tularemia and plague:** Though these diseases are relatively rare in India, both can be life-threatening and require aggressive antibiotic treatment. Streptomycin or gentamicin are used for tularemia, and streptomycin or doxycycline for plague.¹⁹

4.2. Antiviral therapy for viral zoonoses

- **NiV:** For Nipah virus, there is no specific antiviral treatment, but supportive care is crucial. Intensive care management, including mechanical ventilation, is often required for patients with respiratory failure or encephalitis.

- **Avian Influenza (H5N1):** Early antiviral treatment with oseltamivir (75 mg twice daily for 5 days) can help reduce mortality and morbidity. However, the emergence of antiviral-resistant strains remains a significant challenge.¹⁷

4.3. Symptomatic and supportive care

Many zoonotic diseases require extensive supportive care, especially those with multisystem involvement. This includes managing electrolyte imbalances, hydration, and organ support (especially renal and hepatic support). For diseases like leptospirosis, scrub typhus, and malaria, early supportive care can reduce complications and improve outcomes.

- **Hydration and electrolyte management:** In patients with leptospirosis or scrub typhus, especially those with renal or hepatic dysfunction, careful fluid management is essential to prevent acute kidney injury (AKI) or hepatic failure.
- **Ventilatory support:** For patients with severe respiratory involvement due to Hantavirus pulmonary syndrome, NiV, or avian influenza, timely initiation of mechanical ventilation and oxygen therapy can be life-saving.
- **Post-exposure prophylaxis (PEP):** There is role of PEP in some zoonotic diseases. For example, rabies requires immediate administration of the rabies vaccine and immunoglobulin (RIG) following exposure to a potentially rabid animal.

5. Prevention and Control Strategies

The control of emerging zoonotic diseases is often hindered by a limited understanding of how these diseases are transmitted. Additionally, there are significant gaps in knowledge about the role animals play in the emergence of such diseases, as efforts typically focus on treating human cases rather than addressing the animal reservoirs. Effective prevention and control strategies must target the weakest links in the transmission chain — this includes managing animal reservoirs, interrupting transmission pathways, and immunising vulnerable human populations. (Figure 4).

Although most emerging diseases originate from animals, research in human and animal health is often carried out separately. To effectively predict, prevent, and manage emerging zoonotic diseases, there is a need for a unified, multidisciplinary approach. The 'One Health' strategy, which brings together experts in human, animal, and environmental health, offers a comprehensive solution to address these complex and interconnected public health threats.

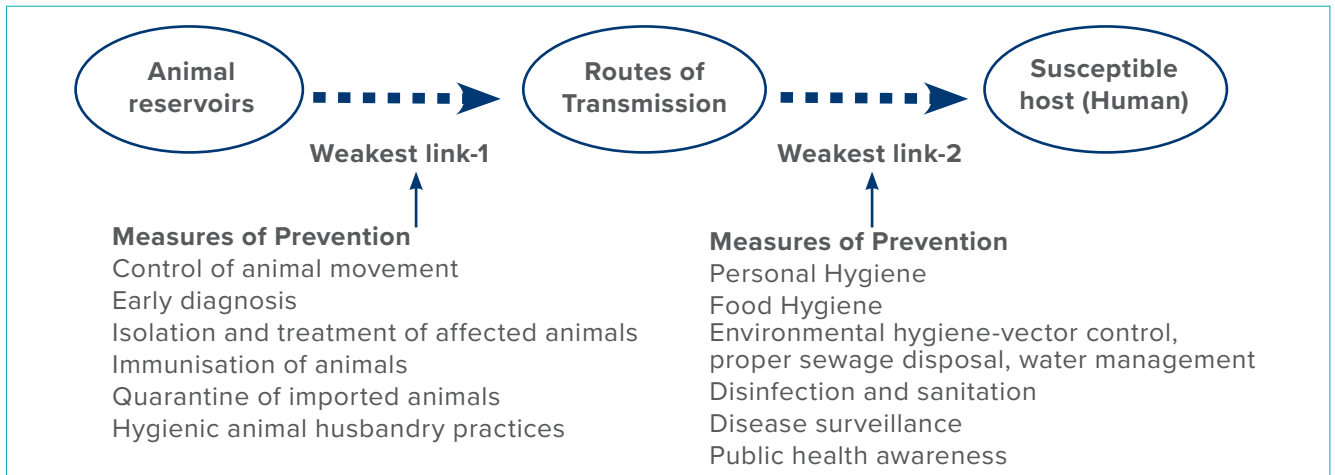


Figure 4: Measures for prevention at the weakest link for blockage of the Transmission.³

5.1. Implementing the One Health approach

One Health framework recognises the interconnectedness of human, animal, and environmental health, emphasising the need for collaboration between healthcare professionals, veterinarians, environmental scientists, and policymakers. For clinicians, this holistic approach involves understanding the role of animal reservoirs, vector species, and environmental factors in the transmission of zoonotic pathogens.²⁰

In India, a concerted effort to adopt One Health strategies is still in embryonic stages.¹⁶ The government initiated the National One Health Mission with the assistance of the Ministries of Health, Agriculture, and Environment. This mission aims to enhance disease surveillance, promote intersectoral cooperation, and strengthen response systems.

Initiatives such as the Integrated Disease Surveillance Programme (IDSP) and the National Animal Disease Reporting System (NADRS) are also enhancing early warning systems. Research institutions such as the Indian Council of Medical Research (ICMR) and the Indian Council of Agricultural Research (ICAR) are working to research on zoonotic diseases.

But One Health must do more. Wildlife health needs to be incorporated into surveillance, and environmental monitoring needs to improve. Health workers and veterinarians must be trained to identify early symptoms of zoonotic diseases. Livestock vaccination programs and rural hygiene practices have to be enhanced. Public awareness campaigns in high-risk regions can prevent outbreaks from spreading. (Figure 5).



Figure 5: Schematic representation of One Health approach.²¹

5.2. Enhanced diagnostic capacities

One of the biggest challenges is the lack of reliable and rapid diagnostic tools for zoonotic diseases. Clinicians in India, particularly in rural or under-resourced areas, often struggle to identify zoonotic infections accurately and promptly due to limited diagnostic capabilities. The reliance on clinical signs alone can lead to misdiagnosis, which is particularly concerning for diseases with overlapping symptoms, such as leptospirosis, malaria, and dengue fever.

The implementation of improved diagnostic tools, such as PCR-based assays and rapid antigen tests, is crucial to ensure quick and accurate diagnosis. Furthermore, making these diagnostic tools more accessible to healthcare providers in both public and private settings, especially in rural areas, would drastically improve the outcome for patients.

Conclusion

The re-emergence of zoonotic diseases in India presents a complex challenge that requires a multifaceted approach, one that involves healthcare professionals, veterinarians, environmental scientists, and policymakers working in unison. From a clinician's perspective, there is a need for heightened awareness, improved surveillance, better diagnostic tools, and public education. With India's rich biodiversity and increasing urbanisation, the risks of zoonotic disease outbreaks are significant. However, with strong interdisciplinary collaboration and a commitment to implementing One Health principles, we can mitigate these risks and safeguard public health for future generations.

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Neuromyelitis Optica (NMO) and Myelin Oligodendrocyte Glycoprotein (MOG)-Associated Autoimmune Neurological Disorders and Recent Management

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Abstract:

Neuromyelitis optica (NMO) is a devastating demyelinating syndrome characterised by optic neuritis (ON) and myelitis, occurring either simultaneously or in sequential relapses. Classical symptoms of NMO include ON, myelitis or area postrema syndrome. The key diagnostic test is the NMO antibody (anti aquaporin-4 antibody [AQP4]) with a sensitivity of 70%-80% and specificity close to 100%. There may be overlap syndromes with Sjögren's syndrome, systemic lupus erythematosus (SLE), and positive vasculitis antibodies. Cerebrospinal fluid (CSF) analysis shows oligoclonal bands in only 10% of patients, with a mild elevation in white blood cell (WBC) count and protein being commonly observed. There is no cure for NMO, but it is treatable. Some patients recover, but many are left with impaired vision and limb function, which can be severe in some cases. A high dose of intravenous (IV) methylprednisolone pulse is given for 5 days, followed by a prednisolone taper. Depending on treatment response, plasmapheresis or IV immunoglobulin (IVIG) may be used for relapses with incomplete recovery after steroids. Azathioprine, mycophenolate mofetil, rituximab, cyclophosphamide, and mitoxantrone have all been used as preventive treatments. Some improvement may be seen within a few weeks, but disability may persist. Unlike multiple sclerosis (MS), NMO rarely progresses to a secondary progressive phase. Approximately 20% of patients with monophasic NMO experience permanent visual loss, and 30% develop permanent paralysis in one or both legs.

Key words: Neuromyelitis Optica (NMO), Demyelinating Syndrome, Autoimmune Disorders.

Introduction

Neuromyelitis optica (NMO) is a devastating demyelinating syndrome characterised by optic neuritis (ON) and myelitis, occurring either simultaneously or in sequential relapses. It was coined by Eugène Devic in the late 1800s. In 2004, NMO was considered a severe variant of multiple sclerosis (MS). However, in 2004, the anti-aquaporin-4 (AQP4) antibody was identified in most patients with the clinical syndrome of NMO with high specificity.¹ Thus, it was reclassified as a distinct entity from MS.¹

Pathophysiology

NMO antibody (AQP4)

AQP4 is a transmembrane protein that facilitates water transport in the central nervous system (CNS). It is expressed at the astrocytic foot processes at the blood-brain-barrier (BBB). There is complement activation, leading to a "rim and rosette" pattern of immune complexes in NMO lesions, causing astrocyte death and tissue necrosis in both grey and white matter. There is accumulation of T cells, B cells, and macrophages, similar to MS, but with additional infiltration by neutrophils and eosinophils, which also contribute to tissue damage.^{2,3}

Epidemiology

NMO is a rare condition, with a prevalence of 2-4/100,000 in most populations. The female: male ratio is 9:1. The age of onset is older, with a median age of 40 years. It is more common in non-Caucasian populations, especially those of Hispanic and African descent. The course of NMO is more devastating, with greater disability accumulated through relapses, including total blindness and paralysis, which are uncommon in MS. The majority of NMO patients have no affected relatives, and it is regarded as a non-familial condition.⁴

Clinical features

Classical symptoms of NMO are ON, myelitis or area postrema syndrome.⁵

Optic neuritis

ON is typically, severe and more often bilateral; recovery may be incomplete, and total blindness can also occur.

Longitudinally extensive transverse myelitis (LETM)

Spinal cord relapses are a hallmark of NMO. LETM is defined as a spinal cord lesion that is contiguous and spans more than 3 vertebral segments. It often extends from the cervicomedullary junction to the cervical and thoracic spinal cord, with motor, sensory, and/or bladder and bowel function involvement.

Area postrema syndrome

Although NMO typically spares the brain, involvement is seen in 10% of patients. Brainstem symptoms include intractable nausea, vomiting, hiccups (area postrema syndrome), double vision, dysphagia and respiratory compromise. Cerebral symptoms include motor or sensory deficits and encephalopathy.

Diagnosis

The key diagnostic test is the NMO antibody (AQP4) with a sensitivity 70%-80% and specificity close to 100%. There may be overlap syndromes with Sjögren's syndrome and systemic lupus erythematosus (SLE), with vasculitis antibodies being positive. Cerebrospinal fluid (CSF) analysis shows oligoclonal bands in only 10% patients, with a mild elevation in white blood cell (WBC) count and protein commonly observed.

Wingerchuk diagnostic criteria (2015)

A diagnosis of NMO can be made in a patient who is AQP4-IgG positive and has a history of one or more core clinical syndromes (ON, myelitis, area postrema syndrome, brainstem syndrome, narcolepsy, acute diencephalic syndrome, or symptomatic cerebral syndrome), with exclusion of alternative diagnoses (Table 1).

Diagnostic criteria for NMOSD with AQP4 IgG⁵

- At least one core clinical characteristic
- Positive AQP4 IgG test
- Exclusion of other alternative diagnosis

Diagnostic criteria for NMO without AQP4 IgG or NMOSD with unknown AQP4 IgG status

- At least two core clinical characteristics occurring because of one or more clinical attacks and meets all requirements:
 - o At least one core clinical characteristic; acute LETM or area postrema syndrome.
 - o Dissemination in space (2 or more different clinical characteristics)
 - o Fulfilment of additional MRI requirements
- Negative test for AQP4 IgG or unavailable
- Exclusion of alternate diagnosis

Core clinical characteristics

- Optic neuritis (ON)
- Acute myelitis (LETM)
- Acute postrema syndrome: episodes of unexplained hiccups or nausea and vomiting
- Acute brainstem syndrome
- Symptomatic narcolepsy or acute diencephalic syndrome with NMOSD typical diencephalic MRI lesions.
- Symptomatic cerebral syndrome with NMOSD typical brain lesions³⁹

Additional MRI requirements for NMOSD without AQP4 IgG and NMOSD with unknown AQP4-IgG status

- **Acute ON:** Brain MRI showing: a) normal findings or only non-specific white matter lesions or b) optic nerve MRI with T2 hyperintense lesions or T1-weighted gadolinium-enhancing lesions extending over more than half the length of the optic nerve, or involving the optic chiasma.
- **Acute myelitis:** associated intramedullary MRI lesions over >3 contiguous segments of focal spinal cord atrophy in patients with history of acute myelitis
- **Acute postrema syndrome:** Associated lesions in the dorsal medulla/area postrema
- **Acute brainstem syndrome:** Associated periependymal brainstem lesions



Table 1: Diagnostic criteria for NMO spectrum disorder (NMOSD) with AQP4 IgG.⁵

Abbreviations: AQP4 IgG: Aquaporin-4 Immunoglobulin G; LETM: Longitudinally Extensive Transverse Myelitis; MRI: Magnetic Resonance Imaging; NMOSD: Neuromyelitis Optica Spectrum Disorder; ON: Optic Neuritis.

Myelin oligodendrocyte glycoprotein (MOG)-associated autoimmune disorders vs NMOSD (Table 2)⁶⁻⁹

- MOG antibody is seen in a subset of AQP4-seronegative NMOSD patients^{6,7}
- Transient seropositivity of MOG antibody is associated with a monophasic disease course
- Persistently high titres are associated with a higher risk for relapsing disease
- MOG-associated disorders also include ON, myelitis, and brain stem syndrome, with subtle differences compared to NMO disorders^{8,9}
- More common in males
- Acute disseminated encephalomyelitis (ADEM) is a common presenting feature
- ON: presents with disc oedema; involves a long section of the optic nerve and is often bilateral
- Myelitis: Typically affects the lower spinal cord (can be LETM or involve only a short segment).
- Area postrema syndrome: Less common
- Prognosis: Better than AQP4-IgG-associated disorders.
- Relapses: Less likely to result in severe neurological deficits. Most patients retain motor function, though bladder, bowel, or erectile dysfunction may be permanent^{6,9}

Feature	NMOSD	MOG disease
Mean age at onset	40-46 years	27-37 years
Female to male ratio	7.2:1-10:1	1:1.6-1.3:1
Median EDSS at last follow up	4.0-5.8	0-1.5
Coexisting autoimmune disease	16%-45%	6%-11%
Localisation of optic nerve lesions	Orbital, chiasma	Orbital, canalicular, intracranial
Features of optic neuritis	OCT: prominent RNFL thinning	Severe optic nerve swelling at onset; frequently simultaneous or rapidly sequential optic neuritis and LETM

Localisation of spinal cord lesions	Cervical, thoracic	Thoracic, lumbar, conus
MRI brain lesions	Frequently lesions in medulla oblongata, area postrema (Figure 1)	ADEM-like brain lesions; deep grey matter lesions; lesions in pons, thalamus.

Table 2: Differences between NMOSD and MOG disease.

Abbreviations: ADEM: Acute Disseminated Encephalomyelitis; EDSS: Expanded Disability Status Scale; LETM: Longitudinally Extensive Transverse Myelitis; MOG: Myelin Oligodendrocyte Glycoprotein; MRI: Magnetic Resonance Imaging; NMOSD: Neuromyelitis Optica Spectrum Disorder; OCT: Optical Coherence Tomography; RNFL: Retinal Nerve Fibre Layer.

Management

The approach to treatment in both disorders is identical and consists of three parts:

- Treatment of relapse
- Prevention of relapse
- Treatment of chronic symptoms

Treatment of relapse¹⁰

- Treatment should be prompt and aggressive.
- There is no cure for NMO, but it is treatable. Some patients recover, but many are left with impaired vision and limb function, which can be severe in some cases.
- High-dose IV methylprednisolone pulse therapy is given for 5 days, followed by a prednisolone taper.
- Depending on the treatment response; plasmapheresis or IVIG may be used for relapses with incomplete recovery after steroids.
- Early plasmapheresis is encouraged for patients with serious deficits or those who do not respond to steroids. Treatment of subsequent attacks with plasmapheresis has shown better outcomes. This treatment involves the patient's own blood being pumped out, blood cells being removed from the plasma and mixed with a solution, and then the new blood mixture being pumped back in.

Prevention of relapse^{10,11}

Low dose prednisolone or prednisone

- Low-dose oral corticosteroids are used in many neurological diseases. Tapering doses of oral steroids are given for a few months.
- Data on long-term use of steroids are limited. A few studies show a decrease in annual relapse rate by low-dose steroid therapy.

- It is known from treatment with azathioprine that additional oral prednisone is effective to reduce disease activity during the first 3-6 months until azathioprine reaches full efficacy.
- In MOG disease, low treatment failure rates were achieved with oral prednisone. There can be occurrence of relapses post tapering and stopping of IV methylprednisolone. But a long-term therapy should be carefully used in view of known side effects.⁹
 - Azathioprine mycophenolate mofetil, rituximab, cyclophosphamide, and mitoxantrone all have been used for preventive treatments (Table 3).
 - Eculizumab, a complement inhibitor is now the United States Food and Drug Administration (US FDA)-approved for the treatment of NMOSD. It showed a 94% risk reduction for new relapses when added on to patients who were on placebo and continued their previous disease-modifying treatment (DMT).¹¹
 - Satralizumab and inebilizumab both showed marked reduction in new NMOSD relapses versus the comparison group.¹²
- Multiple DMTs used in MS, like interferons and natalizumab can worsen the disease course of NMO. Therefore, early and accurate diagnosis is critical in the management of NMO.

Abbreviations: DNA: Deoxyribonucleic acid; NMO: Neuromyelitis Optica; NMOSD: Neuromyelitis Optica Spectrum Disorder.

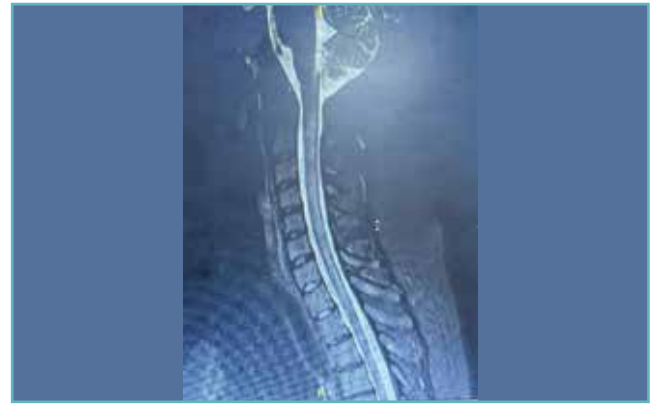


Figure 1: Longitudinally extensive cervical and dorsal spine lesions. Spared brain parenchyma.

It is important to note that interferon beta, fingolimod, natalizumab and alemtuzumab worsen NMO disease progression and should not be used to treat NMO.¹²

Prognosis

Some improvement typically occurs in a few weeks, but disability may persist. Although it has a monophasic phase, approximately 85% have a relapsing course with repeated episodes of transverse myelitis and/or optic neuritis. In the monophasic form, transverse myelitis and optic neuritis occur simultaneously, but in the relapsing form, there are typically weeks or months between initial attacks, and patients have better motor recovery after the initial transverse myelitis event. Around 55% have a relapse in the first year and 90% in the first five years. Unlike MS, NMO rarely enters a secondary progressive phase. Approximately 20% with monophasic NMO have permanent visual loss, and 30% experience permanent paralysis in one or both legs.⁵

Drug	Mechanism of Action	Note
Azathioprine	Inhibits purine metabolism	Reported effective in 1998; a mainstay of treatment combined with steroids due to delayed onset of action (takes months)
Mycophenolate mofetil	Inhibits purine metabolism	Better efficacy and tolerability. Combined with steroids due to delayed onset of action
Methotrexate	Inhibits folate metabolism	-
Cyclophosphamide	DNA cross-linker	
Rituximab	Anti-CD20 antibody; depletes B cells	Most commonly used treatment for NMOSD
Intravenous immunoglobulins	-	-
Mitoxantrone	Inhibits DNA synthesis/repair	-
Haematopoietic stem cell transplantation	-	Used in severe case of NMO. Provides short term benefit by inflammation reduction. But most patients relapse within 5 years

Table 3: Preventive treatment for NMOSD.

Conclusion

It is very important to diagnose NMO and MOG-associated disorders as early as possible to ensure proper management and avoid complications and poor long-term prognosis. IVIG, plasma exchange and IV rituximab have revolutionised the management and early recovery of most cases, resulting in reduced disability and an intermediate prognosis. MOG disorders carry a more favourable prognosis compared to NMO, with better recovery with supportive care. IVIG and plasma exchange, when administered in good neurology intensive care units, worldwide, are associated with low mortality.

Manoj Khanal. Neuromyelitis Optica (NMO) and Myelin Oligodendrocyte Glycoprotein (MOG)-Associated Autoimmune Neurological Disorders and Recent Management. MMJ. 2025, June. Vol 2 (2).

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Robotic-Assisted Adrenalectomy: A Novel Approach to Manage Conn's Adenoma

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Abstract:

Primary hyperaldosteronism (PHA), also known as Conn's syndrome, accounts for 5%-10% of hypertensive cases. It is a condition caused by an adrenal tumour that produces excess aldosterone. This hormonal excess leads to high blood pressure and is referred to as Conn's syndrome, named after the doctor who first described it. Although, symptoms may be mild, prolonged exposure to high aldosterone levels is very toxic, and can cause stroke and heart attacks. This report presents a patient who came with paralytic symptoms due to severe hypokalaemia. On investigation, he was diagnosed with a Conn's adenoma, which was subsequently treated by adrenalectomy. This is a rare presentation of Conn's adenoma and was managed in a timely manner through a multidisciplinary approach. Robotic-assisted surgery benefited the patient by enabling a rapid recovery with minimal blood loss. The patient's blood pressure normalised following the adrenalectomy.

Key words: Primary Hyperaldosteronism, Conn's Syndrome, Conn's Adenoma, Hypokalaemic Paralysis, Robot-Assisted Laparoscopic Adrenalectomy.

Introduction

Primary hyperaldosteronism (PHA) is a condition caused by an adrenal tumour that produces excess amounts of the hormone aldosterone. PHA, also known as Conn's syndrome, accounts for 5%-10% of hypertensive cases.¹ While the majority of hypertensive patients with PHA are normokalaemic, around half of those with aldosterone-producing adrenal adenomas are hypokalaemic.²

This report presents a case of hypokalaemic paralysis as the presenting symptom in a patient with an aldosterone-producing adrenal adenoma. The initial symptoms were suggestive of a neurological event leading to paralysis, but subsequent investigations revealed hypokalaemia induced by hyperaldosteronism. This paper highlights this rare presentation of hypokalaemic paralysis due to Conn's adenoma and the advantages of robotic-assisted surgery in the management of such tumours.

Case Report

A 30-year-old gentleman presented with left lower limb weakness and stiffness lasting 24 hours. He experienced difficulty in weight bearing and walking and reported muscle

cramps in both lower limbs over the preceding two days. He was hypertensive (blood pressure: 180/100 mmHg) and was taking telmisartan 40 mg, ramipril 2.5 mg, and hydrochlorothiazide 12.5 mg once daily.

He was conscious and oriented, and on clinical examination found to have left lower limb weakness. On biochemical evaluation, his sodium was 144 mEq/L and serum potassium was 1.55 mEq/L. His creatine phosphokinase (CPK) was elevated at 5909 U/L, and urine spot potassium was 7.88 mmol/L. Urine pH was alkaline, and arterial blood gas analysis showed alkalosis. Ultrasound (USG) of the whole abdomen revealed a 3-4 cm mass in the left adrenal gland. His serum aldosterone level was elevated at 26 ng/dL and direct renin concentration was 0.5 ng/dL, giving an aldosterone-renin ratio of 503. Co-secretion of cortisol and dehydroepiandrosterone sulphate (DHEAS) was ruled out by doing overnight dexamethasone suppression tests and DHEAS levels.

He was diagnosed as a case of PHA. A 5-fluorodeoxyglucose positron emission tomography-computed tomography (5-FDG PET-CT) scan revealed a 3-4 cm well defined, minimally

peripherally enhancing FDG-avid mass in the left adrenal region, suggestive of a functional adrenal adenoma (Figure 1a and b). The endocrinologist team managed him with intravenous (IV) potassium and spironolactone. His limb weakness recovered on the same day, and he was planned for a left robotic-assisted adrenalectomy. The Da Vinci Xi robotic system (Intuitive Surgical, USA) was used. The adrenalectomy was performed without any challenges, as the plane around the adrenal was well preserved (Figure 1c and d). He recovered well, with stable serum potassium levels and blood pressure postoperatively.

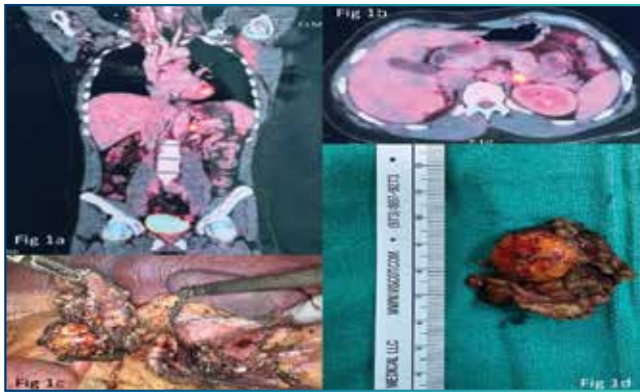


Figure 1: (a) sagittal section, (b) transverse section of 5-fluorodeoxyglucose positron emission tomography-computed tomography (5-FDG PET-CT) scan showing FDG-avid lesion in left adrenal gland, (c) intraoperative image, (d) image of the excised tumour.

Anti-hypertensive medications were discontinued on the post-operative day two, and the patient was discharged the same day. Histopathology was consistent with the diagnosis of an adrenal adenoma. His blood pressure gradually normalised, and his antihypertensive medications were discontinued.

Discussion

This case highlights an unusual presentation of Conn's adenoma or PHA with severe hypokalaemia manifesting as acute lower limb weakness. Excess aldosterone can lead to hypokalaemic rhabdomyolysis, and metabolic alkalosis.¹ A suppressed renin level and elevated aldosterone-to-renin ratio confirmed the diagnosis of PHA,² while USG and CT scan detected a functional adrenal adenoma.³ The patient was stabilised preoperatively with IV potassium and spironolactone.⁴ Robotic-assisted adrenalectomy, using the Da Vinci Xi system, enabled precise dissection and successful removal of the functional adrenal adenoma, with minimal blood loss and rapid recovery.^{5,6} Postoperatively, the patient experienced resolution of hypokalaemia, limb weakness, and hypertension, enabling discontinuation of antihypertensive medications.

Hypokalaemic periodic paralysis is a rare disorder with an estimated prevalence of 1 in 100,000. It is characterised by transient attacks of flaccid paralysis of varying intensity and duration, which, if not recognised in time, has the potential to be life-threatening.⁷ In this case, the patient presented with sudden-onset flaccid quadriparesis. On clinical examination, his blood pressure was 180/100 mmHg, and laboratory tests revealed hypokalaemia and metabolic alkalosis. He was initially managed with potassium supplementation and antihypertensives. His weakness completely improved within 12 hrs. Based on the clinical triad of hypertension, hypokalaemia, and metabolic alkalosis, a presumptive diagnosis of PHA was made. Screening with plasma aldosterone and plasma renin activity confirmed a high aldosterone-to-renin ratio.

PHA or Conn's syndrome is characterised by suppressed plasma renin activity, elevated and non-suppressible plasma aldosterone and hypokalaemia.⁸ Its presentation is highly variable and typically occurs in patients who are in the third to sixth decade of life. Hypertension is often the sole presenting feature and may be refractory to treatment. Interestingly, hypokalaemia is less common in PHA than previously thought. Kuo *et al.*⁹ found that plasma potassium levels were < 3.3 mEq/L in only 18% of confirmed PHA cases.

While hypokalaemic periodic paralysis may result from thyrotoxicosis and Conn's syndrome, it is rarely reported as a presenting manifestation of Conn's syndrome and is rarely reported in the literature. Although hypokalaemia often responds well to surgical treatment, some patients may continue to require antihypertensive therapy, albeit at lower doses postoperatively. Persistent hypertension after adrenalectomy has been associated with older age, elevated serum creatinine, use of multiple antihypertensive agents preoperatively, and longer duration of hypertension.¹⁰

In the present case, the patient's blood pressure and potassium levels normalised, and metabolic alkalosis resolved on the evening of surgery. This case is a rare example of Conn's adenoma presenting with hypokalaemic periodic paralysis, which responded well to robotic adrenalectomy.

Author contribution declaration: V.V. and P.T. diagnosed and managed the patient's electrolyte and endocrine abnormalities pre and post op. S.C.S, P.K and A.J. performed the robotic - assisted laparoscopic left adrenalectomy. S.C.S. and S.N.P. drafted the main manuscript and prepared Figure 1 (a, b, c and d). All authors reviewed and approved the final manuscript.

Conclusion

Although PHA due to Conn's adenoma is a rare cause of hypokalaemic paralysis, it should be considered in the differential diagnosis. Robotic-assisted adrenalectomy is a novel, effective, and minimally invasive approach to excise such tumours, offering improved ergonomics and favourable outcomes.

Shailesh Chandra Sahay, Pawan Kesarwani, Varun Verma, Priyamvada Tyagi, Abhijeet Jha, Shubhankar Powar. Robotic-Assisted Adrenalectomy: A Novel Approach to Manage Conn's Adenoma. MMJ. 2025, June. Vol 2 (2).

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Symptomatic Aortic Thrombosis in a Preterm Neonate: 1-Year Follow-Up

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Abstract:

Symptomatic aortic thrombosis, a devastating NICU complication, is increasingly diagnosed with bedside ultrasound. Early intervention mitigates adverse outcomes. In our case, a preterm, very low birth weight, growth-restricted baby developed aortic thrombosis with hypertensive emergency and later limb-threatening ischaemia — which usually requires thrombolysis. However, due to parents' reservations, he was given only therapeutic anticoagulation, with closely monitored activated partial thromboplastin time (APTT) targets, and this resulted in complete thrombus resolution. A multidisciplinary team approach was followed, and early detection with frequent monitoring led to a favourable outcome.

Key words: Neonatal Aortic Thrombosis, Thrombolysis, Heparin, Growth Restriction.

Introduction

Neonatal thrombosis is an emerging, rare complication of tertiary care neonatology with more remarkable survival of preterm babies. Timely diagnosis requires a high index of suspicion so that life-threatening complications can be pre-empted. Also, given the very limited experience with anticoagulants and fibrinolytics in this age group, and the high risk of bleeding, therapy must be carefully tailored in each case. Here, we report a case of spontaneous arterial thrombosis in a sick preterm that presented as a hypertensive emergency with multi-organ dysfunction, diagnosed by Doppler ultrasound and successfully managed with unfractionated heparin (UFH) infusion.

Case Report

A male baby conceived by in vitro fertilisation, weighing 1412 g, was delivered at 32 weeks' gestation via Caesarean section due to severe pregnancy-induced hypertension in the mother. The baby was the second of the dichorionic diamniotic twins and had features of foetal growth restriction. The mother had pregnancy-induced hypertension and intrahepatic cholestasis of pregnancy. There were no antenatal risk factors for sepsis. The baby cried immediately after birth but developed respiratory distress soon after, which was managed as per standard protocol after being shifted to the neonatal intensive care unit (NICU). The baby was started on orogastric feeds, which he did not tolerate, and had to be given fluids on Day 1 through a peripherally inserted central catheter (PICC) line. Initial investigations revealed

thrombocytopenia (120000 per μ L), polycythaemia (haematocrit 66.4%), and a negative sepsis screen. Repeat haematocrit at 12 hours of life had reduced to 60%.

On Day 2 of life, the baby had recurrent desaturations and was started on caffeine citrate. Dobutamine infusion was initiated in view of transitional circulation. A repeat sepsis screen was positive, prompting the initiation of broad-spectrum antibiotics (piperacillin-tazobactam and amikacin). By Day 3, the baby was off respiratory and inotropic support. Minimal enteral feeds were restarted and gradually increased.

After the initial improvement in respiratory parameters, the baby abruptly developed an increased fraction of inspired oxygen (FiO₂) requirement with poor perfusion and hypertension on Day 5. A repeat screen showed rising trend of C-reactive protein (CRP), leukopenia and worsening thrombocytopenia (platelet counts 61,000 per μ L). Blood cultures from twin 1 (sent on Day 1) grew *Klebsiella* (sensitive to meropenem and amikacin); accordingly, antibiotics in this infant were escalated. However, blood culture of this baby (twin 2) remained sterile.

Functional echocardiography demonstrated severe left ventricular dysfunction with mild eccentric mitral regurgitation; a single dose of intravenous furosemide was given, and the baby was started on labetalol infusion.

On Day 6 of life, renal function started deteriorating but urine output was maintained and ultrasound of the kidney, ureter, and bladder (KUB) was normal. Doppler ultrasound revealed partial thrombosis of abdominal aorta (Figure 1) extending into left renal artery. Anticoagulation was started with subcutaneous low molecular weight heparin (LMWH) at a dose of 1.5 mg every 12 hours.



Figure 1: Doppler ultrasound showing partial thrombosis of the abdominal aorta.

On Day 7 of life, clinical signs of right lower limb ischaemia were noted (Figure 2a), in the form of pallor and absent pulses. Review Doppler revealed dampened flow in the right external iliac (Figure 2b) and common femoral arteries, with echogenic thrombus in the renal and infrarenal abdominal aorta and narrowing of the left renal artery ostium. Paediatric cardiology and cardiovascular surgery teams were consulted. In view of thrombus progression despite subcutaneous LMWH and potential limb-threatening complications, thrombolysis was discussed with parents; the higher risk of bleeding complications after thrombolysis, compared to adults, was also explained. Following detailed and informed discussion, they gave a negative consent at this stage. They reserved their right to revisit this issue after a brief trial of alternate therapy.



Figure 2a: Ischaemic colour changes in the right lower limb on Day 7.



Figure 2b: Doppler showing dampened flow pattern in right external iliac artery.

As renal function was deranged and Factor Xa level monitoring was unavailable, LMWH was stopped, and UFH infusion was started via central line. Activated partial thromboplastin time (APTT) was monitored every six hours, targeting 2-2.5 times the control value. Limb inspection the next day showed some improvement in temperature and colour of the affected limb, but pulses were still palpable. Doppler showed no further thrombus extension; APTT-guided heparin infusion was continued.

Finally, by Day 10 of life, right lower limb perfusion was restored and Doppler showed normal flow in the right external iliac artery (Figure 3a). Skin colour changes resolved by Day 12 (Figure 3b). On Day 13 of life, labetalol infusion was stopped, and he was shifted to oral amlodipine. Feed intolerance continued until Day 14, after which he started tolerating feeds. Antibiotics were stopped on Day 14 of life. Cranial ultrasound done twice between Days 6 and 8 did not show any evidence of intraventricular haemorrhage.



Figure 3a: Renal Doppler showing normalisation of flow.



Figure 3b: Perfusion restored in the right lower limb on Day 12 of life.

Ultrasound on Day 16 revealed thin filaments of thrombus suggestive of resolving thrombi. Renal function had normalised; UFH was stopped and switched to LMWH, which was continued until the thrombophilia workup was complete.

Blood pressure normalised, and amlodipine was stopped on Day 20 of life. Review Doppler on Day 22 revealed marked resolution of thrombus in the abdominal aorta, left renal artery, and right external iliac artery, with only thin residual filamentous thrombi.

Intravenous fluids were gradually tapered, and the baby was on full feeds by Day 24 of life when the PICC line was removed. On Day 27 of life, no thrombus was visible (Figure 4), and flow in affected vessels was normal; enoxaparin was stopped.



Figure 4: Thrombus completely resolved on Day 27.

Investigations

Serial radiological tests and thrombophilia workup revealed a detailed thrombophilia workup was done, which revealed normal functional activity of protein C and S and antithrombin III. Genetic studies for the methylene tetrahydrofolate reductase gene, prothrombin gene 20210A, and Factor V Leiden mutation were negative.

Differential Diagnosis

Causes for hypertensive emergency in a newborn may include renovascular (e.g., renal artery stenosis, renal vein thrombosis,

acute kidney injury), cardiovascular, endocrine (e.g., congenital adrenal hyperplasia, hyperaldosteronism, hyperthyroidism), raised intracranial tension, or drugs (e.g., steroids, caffeine). Most of the aforementioned conditions were ruled out in our patient — although renal impairment did occur, it followed the hypertension rather than preceding it.

The baby had a few risk factors for neonatal thrombosis, including prematurity, intrauterine growth restriction, and a positive sepsis screen. However, these are more commonly associated with arterial thrombosis in the presence of underlying thrombophilic conditions — for which the baby tested negative. Moreover, in the absence of an umbilical artery catheter, arterial thrombosis manifesting as symptomatic aortic thrombosis was unexpected.

Treatment

A multidisciplinary team monitored the patient, and the baby's parents were involved in the decision-making process regarding anticoagulation versus thrombolysis at a crucial stage.

Outcome and Follow-Up

The baby was discharged on Day 28 of life on full breastfeeds, with adequate weight gain, a normal neurological examination, and a normal pre-discharge cranial ultrasound. Extensive thrombophilia workup was negative, and no antiplatelet or anticoagulant was prescribed at discharge. The baby remains under regular follow-up and is thriving. At 1 year of age, the child has no hypertension, no limb length discrepancy, and no functional deficit.

Discussion

Thrombosis incidence peaks in neonates compared to other pediatric ages.¹ Improved survival of sick and preterm infants has led to increased diagnosis in recent years. Arterial thromboses constitute nearly 50% of all neonatal thrombotic events, with an overall incidence of 5.1 per 100000 live births and 0.2% of NICU admissions. The largest study reported an incidence of 2.4 per 1000 admissions.²⁻⁴ However, symptomatic aortic thrombosis remains exceedingly rare (0.1 to 1.1 per 100000 live births).⁴

Neonates are vulnerable to hemorrhage and thrombosis due to immature coagulation pathways. This liability is due to reduced synthesis of various coagulation proteins, increased clearance of the coagulation factors, and altered function of certain factors and platelets.⁵

In some reports, the umbilical arterial catheter is the most critical risk factor for arterial thrombosis, with an incidence as high as 63%.⁶ Other known risk factors include sepsis, prematurity, asphyxia, dehydration, polycythaemia, and maternal diabetes. Less commonly, deficiencies of anti-thrombin III, protein C, protein S, as well as genetic defects like activated protein C resistance, Factor V Leiden mutation, hyperhomocysteinaemia, elevated lipoprotein (a), and the prothrombin gene G20210A mutations have been implicated. These genetic predispositions may have additive effects if other risk factors are present in a baby. In this case, the baby was growth-restricted, a factor that has also been proposed as a potential contributor to

thrombosis, particularly in those with underlying prothrombotic conditions.⁷ Another important aspect is the maternal presence of autoantibodies, such as antiphospholipid antibodies, which can also predispose neonates to thrombosis, suggesting a need to screen such babies for these antibodies during the neonatal period.⁸

Aortic thrombosis can present variably, ranging from asymptomatic to severe life-threatening complications, depending on the site and degree of occlusion by thrombus. This has been detected incidentally on autopsy of neonates who died due to some other reasons — especially in association with catheters. Initial presentation can include decreased distal pulsations and inability to withdraw blood from the catheter.⁹ Other signs can be colour change, peripheral gangrene, blood pressure difference between upper and lower limbs, renal failure, necrotising enterocolitis, congestive cardiac failure, and hypertension, to name a few.

The diagnostic approach to thrombosis varies. Angiography, although the gold standard for diagnosis of thrombosis in adults, is rarely used in neonates due to procedural difficulty. Ultrasound Doppler is the preferred modality whenever there is clinical suspicion of thrombosis; however, this may underdiagnose this condition. Echocardiography is indicated if cardiac dysfunction is suspected.

Symptomatic aortic thrombosis necessitates immediate triaging based on severity to determine the appropriate level of treatment to be initiated. It also depends on the centre's capabilities. The aim of the therapy in any case is to reduce further extension of the thrombus, restoration of blood flow to the affected organs, and reduce the risk of recurrence.¹⁰

LMWH is preferred in neonates due to its predictable pharmacokinetics, minimal monitoring, and reduced thrombocytopenia risk.¹¹ UFH is an alternative for anticoagulation, but it causes thrombocytopenia, requires frequent monitoring, has a short half-life, and may have partial resistance due to low antithrombin levels. In that case plasma transfusion is required to replete levels of antithrombin. These anticoagulants have equal efficacy in studies, and the decision is usually individualised.

Thrombolytic therapy includes agents like streptokinase, urokinase, and recombinant tissue plasminogen activator (tPA). However, the low plasminogen concentration in neonates may decrease the efficacy of these agents.¹¹ Conversely, immature cerebral vessels predispose to an increased risk of bleeding. Although systemic thrombolysis is a well-described treatment

option for symptomatic thrombosis, but data in neonates are very limited. In an old review, thrombolytic patency rates in neonates were reported to be 39% to 86%.¹² This was a combined study using all three agents. Recombinant tPA (alteplase) preferred thrombolytic agent in neonates due to its superior clot lysis, fibrin specificity, reduced allergic reactions, and shorter half-life. Prior administration of plasminogen through fresh frozen plasma (FFP) is recommended to augment its action.¹³ Thrombolysis is associated with haemorrhagic complications and distal limb ischaemia due to distal embolisation.

Surgical thrombectomy is an option in managing neonatal aortic thrombosis, but is rarely used owing to the surgical risks and limited data availability in the neonatal population. A case series by Payne *et al.*¹⁴ described aortic thrombosis in 12 neonates. Five of these patients were surgically treated with 100% survival. A Cochrane review comparing thrombolysis and surgical thrombectomy does not favour either approach in terms of limb salvage, amputation, or death and recommends that the choice between the two be individualised, balancing the risks of surgery against the potential complications of thrombolysis.¹⁵ An algorithmic approach has been suggested by Colburn *et al.*¹⁶ wherein all neonates with symptomatic aortic thrombosis should be given therapeutic anticoagulation. Further, if the neonate has absent distal pulses, then thrombolysis is initiated when there is no improvement in clot burden. Conversely, if the baby has gangrene or tissue loss features, thrombolysis is started immediately, and surgery is done if thrombolysis is unsuccessful. Upfront surgery is only suggested in neonates where thrombolysis is contraindicated. Constant Doppler monitoring is indicated to detect clot propagation for early escalation of care.

To conclude, symptomatic aortic thrombosis is a devastating complication rarely encountered in the NICU, even without an umbilical artery catheter. It needs a high index of suspicion for early detection and timely therapy. Anticoagulation remains the mainstay of treatment, with severe cases requiring thrombolysis or a surgical thrombectomy. Timely intervention can drastically improve outcomes in affected neonates.

Conclusion

Symptomatic aortic thrombosis is a rare complication in the NICU and requires a high index of suspicion, even in absence of umbilical catheter. Early detection and timely intervention can save babies from limb and life-threatening complications of aortic thrombosis. Early initiation of therapeutic anticoagulation appears safe and effective in neonates. Multidisciplinary evaluation and management, as well as shared decision-making involving the parents, contribute to better outcomes. Shared decision-making is critical due to limited experience, high bleeding risk, and potentially reduced efficacy of fibrinolytic therapy in newborns.

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Polymyxin B Therapy-Induced Respiratory Arrest in a Liver Donor: A Case Report

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Abstract:

Polymyxin B is a potent antibiotic used in multi-drug resistant (MDR) gram-negative infections. It is a known nephrotoxic and neurotoxic drug with serious side effects. Respiratory paralysis is very rarely seen with polymyxin B therapy, with only a few cases reported worldwide. We report a case of a young liver donor who developed respiratory arrest after receiving intravenous (IV) polymyxin B, required intubation, and mechanical ventilatory support. The patient regained full consciousness within an hour. After reviewing literature, we found that polymyxins can cause such side effects. Polymyxin B was discontinued, and she was extubated the following day. With the emergence of MDR organisms, the use of polymyxin B has increased tremendously. This case highlights the importance of closely monitoring patients who are administered such potent antibiotics.

Key words: Polymyxin B, Respiratory Arrest, Liver Donor.

Introduction

Polymyxin was first isolated in 1947 from the soil bacterium *Bacillus polymyxa*, which was later reclassified as *Paenibacillus polymyxa*.¹ Polymyxins are small lipopeptide molecules with polycationic peptide ring and a short protruding peptide attached to a fatty acid tail.² The clinically used polymyxins are polymyxin B and polymyxin E (colistin). They are used for multidrug-resistant (MDR) gram-negative bacterial infections.³ Their use declined in the 1980s because of nephrotoxicity concerns. However, due to increasing resistance to other antibiotics, the usage of polymyxins has now resurged.⁴ Polymyxin B is considered less nephrotoxic than colistin and is therefore more commonly used. Respiratory paralysis is an infrequent side effect, with only a few case reports documented globally.⁵⁻⁸

Case Report

We report a case involving a 35-year-old female liver donor who underwent a right liver lobe donor hepatectomy. She was previously healthy, with no comorbidities. The intraoperative period was uneventful. In the immediate postoperative period, the patient had an elevated total leucocyte count (TLC) of 20,500/ μ L, which progressively increased. We routinely administered cefoperazone-sulbactam and amikacin as antimicrobial prophylaxis, which was upgraded to meropenem on day 2. Her liver function tests and liver Doppler ultrasound

findings were normal. The patient complained of persistent severe abdominal pain despite adequate analgesia. Pancreatitis was suspected; pancreatic cultures, serum amylase, and lipase were ordered. There was a mild elevation of amylase and lipase consistent with pancreatitis. The patient's TLC increased further to 37,000/ μ L on day 4, along with fever spikes (Table 1). Given the recent occurrence of multiple MDR infections in the intensive care unit (ICU) and concerns for donor safety, the patient was started on polymyxin B. One hour after a loading dose of 15 lakh units infused over 1 hour, the donor complained of breathing difficulty and became apnoeic almost immediately. She was intubated and placed on mechanical ventilator support. The patient regained full consciousness within an hour of the event and responded well with minimal pressure support on the ventilator. After ruling out administration errors or unintended medications, her drug chart was carefully reviewed. Literature review confirmed that *polymyxin B* is associated with rare but serious adverse effects, including respiratory arrest, especially when combined with aminoglycosides. Our patient had been receiving amikacin until the day prior. *polymyxin B* was discontinued, meropenem was continued, and the patient was electively ventilated overnight. The patient was extubated the following day. All cultures were reported negative, her TLC gradually decreased, and she was discharged home on day 10.

Postoperative day	1	2	3	4	5	7	8
White blood count (WBC) / μ L	20,500	22,320	27,080	37,350	30,740	28,450	24,710
Total Bilirubin (mg/dL)	1.89	1.01	1.2	1.8	1.38		1.2
Direct Bilirubin (mg/dL)	0.8	0.6	0.8	1.16	0.8		0.7
Serum Glutamic-Oxaloacetic Transaminase (SGOT) (U/L)	471	370	239	148	101		82
Serum Glutamic-Pyruvic Transaminase (SGPT) (U/L)	270	223	168	130	82		65
Serum amylase (U/L)				279	125		
Serum lipase (U/L)				566	225		

Table 1: Postoperative laboratory trends.

Discussion

Although now widely used, polymyxin B is associated with serious side effects, including nephrotoxicity and neurotoxicity. The incidence of nephrotoxicity ranges from 20%-60%, and neurotoxicity occurs in approximately 7% of cases.⁴

Respiratory paralysis is a rare but potentially life-threatening side effect with only a few case reports. In 1968, Lindesmith *et al.* first reported 11 cases of polymyxin-induced respiratory paralysis.⁹ Neuromuscular blockade may occur at both pre- and post-synaptic sites. Presynaptic dysfunction occurs due to non-competitive blockade, which results in reduced acetylcholine release into the synapse.⁹ Other mechanisms include calcium depletion and prolonged depolarisation.¹⁰ This blockade is not reversed by cholinesterase inhibitors. The onset of

paralysis may range from 1 to 26 hours following polymyxin B administration. Risk factors for this adverse effect include renal failure, concurrent use of nephrotoxic medications, certain antibiotics (particularly aminoglycosides), higher doses of polymyxin B, and female gender.^{11,12}

Most reported cases involve elderly and sick individuals with some renal dysfunction.^{5-7,9}

However, our patient was a young, healthy donor with normal renal function. With the increase in home-care nursing facilities, potent antibiotics are routinely given at home. This case highlights the need to administer such potent antibiotics cautiously.

Conclusion

Although respiratory paralysis is a rare adverse effect of polymyxin B therapy, clinician awareness of such side effects is essential. With the increasing prevalence of MDR infections, the use of higher-end antibiotics has risen significantly, heightening the risk of such rare but serious events. This case underlines the importance of cautious use and close monitoring of such agents, even in otherwise healthy individuals.

D Navakanth, Sunita Verma, Vachaspati Kumar, Kshitij Sisodia, KR Vasudevan. Polymyxin B Therapy-Induced Respiratory Arrest in a Liver Donor: A Case Report. MMJ. 2025, June. Vol 2 (2).

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Therapeutic Plasma Exchange in Myelin Oligodendrocyte Glycoprotein-Related Optic Neuritis: Restoring Vision Through Early Intervention – A Case Report

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Abstract:

Myelin oligodendrocyte glycoprotein immunoglobulin G-associated optic neuritis (MOG-IgG ON) typically presents as severe, painful, and recurrent vision loss, often accompanied by optic disc oedema, which can result in significant visual morbidity. We report the case of a 27-year-old female of African ethnicity with a history of headache and bilateral gradual, progressive vision loss. Ophthalmic examination revealed no light perception and stage 3 papilloedema in both eyes. Magnetic resonance imaging (MRI) demonstrated bilateral optic neuritis, and anti-MOG-IgG was positive, confirming a diagnosis of MOG-IgG ON. The patient demonstrated notable visual improvement after the initiation of plasma exchange (PLEX) and high-dose corticosteroids within 53 hours of admission, followed by rituximab therapy. A total of seven sessions of PLEX were conducted, resulting in an improvement of ≥ 2 levels in the visual outcome scores by the end of the seventh session. Ultimately, a visual acuity of 6/6 in each eye was achieved after the administration of two doses of intravenous (IV) rituximab. This case study highlights the critical importance of early PLEX initiation to prevent irreversible optic nerve damage in MOG-IgG ON.

Key words: MOG-IgG-Associated Optic Neuritis, Plasma Exchange, High-Dose Corticosteroid, Rituximab.

Introduction

Optic neuritis (ON), a common cause of acute optic nerve injury in children and adults, is characterised by inflammation of the second cranial nerve.¹ It has an annual incidence of 3.9 per 100,000 population.² A strong female predominance has been observed among individuals who are seropositive for myelin oligodendrocyte glycoprotein immunoglobulin G (MOG-IgG) or anti-aquaporin-4 (AQP4) IgG.^{3,4} Vision loss due to MOG-IgG-associated ON (MOG-IgG ON) is typically severe, painful, recurrent, and associated with optic disc oedema.⁵

The efficacy of plasma exchange (PLEX) is attributed to the removal of circulating autoantibodies and other immunologically active substances (e.g., complement and cytokines) from the

blood.⁶ A trend toward increased usage of PLEX for severe demyelinating attacks, including ON, has been observed.^{7,8}

Early commencement of PLEX is crucial to the clinical outcomes in cases of severe ON.⁹ Early clinical recognition and initiation of treatment are beneficial for maximum visual recovery. This approach should be directed by early diagnosis of ON and its subtype, prompt administration of high-dose corticosteroids, and the addition of PLEX as second-line therapy. PLEX helps prevent the loss of high-contrast vision, enhances contrast sensitivity, and maintains colour vision and visual fields.¹

Improvement in visual function was assessed across ten levels, (Table 1) visual acuity (VA) improvement of ≥ 2 levels was selected as the outcome indicator for visual improvement.⁹

Level	Clinical Parameter
1	20/20
2	Scotoma, but better than 20/30
3	20/30 $\geq$ visual acuity $\geq$ 20/ 60
4	20/60 $\geq$ visual acuity $\geq$ 20/200
5	20/200 $\geq$ visual acuity $\geq$ 20/ 800
6	20/800 $\geq$ visual acuity $\geq$ 20/2000
7	Counting fingers
8	Hand movement
9	Light perception
10	No light perception

Table 1: Visual outcome score.

Case Report

Patient demographics and history: A 27-year-old woman of African ethnicity presented to our institute with complaints of headache localised to the left temporal region. The headache was gradual in onset, holocranial, and persistent throughout the day for the past two weeks. She subsequently developed gradual progressive bilateral vision loss, initially starting with decreased vision in her left eye over one week accompanied with pain on eye movement and blurring of vision, followed by complete loss of vision in both eyes over the subsequent week.

Initial presentation: Ophthalmic examination showed no light perception in either eye. The intraocular pressure was 16 mmHg. The anterior segments of both eyes were within normal limits. Posterior segments showed stage 3 papilloedema bilaterally. Ocular movements were full, and pupils were mid-sized and not reactive.

Investigations: A lumbar puncture was performed, following which transient improvement in vision was observed, which subsequently deteriorated in both eyes. The lumbar puncture and cerebrospinal fluid (CSF) reports were inconclusive.

Ocular coherent tomography (OCT) revealed complete obscuration of all disc margins, obliteration of the cup-to-disc ratio, and increased thickness of the superior and inferior quadrants of the retinal nerve fibre layer (RNFL).

Magnetic resonance imaging (MRI) of the whole brain revealed bilateral hyperintensities in the optic nerves with mild point contrast enhancement, along with mild scleral indentation, suggestive of bilateral optic neuritis with papilloedema (Figure 1).

Contrast-enhanced MRI of the whole spine revealed a subtle T2-weighted short tau inversion recovery (T2W/STIR) hyperintense signal at the cervicomedullary junction and along the anterior

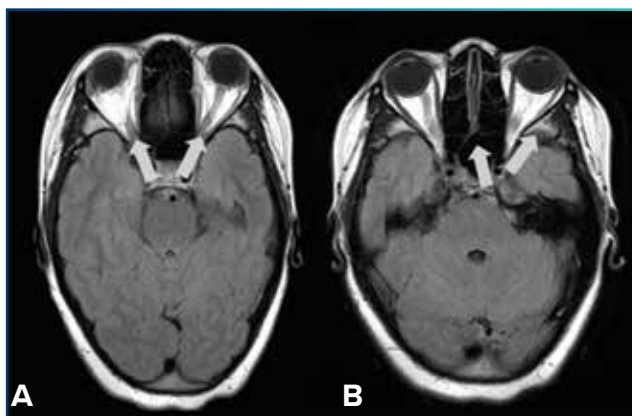


Figure 1 A and B: Magnetic resonance imaging (MRI) brain showing hyperintense signal intensity in the bilateral optic nerves with mild post contrast enhancement, along with mild indentation of sclera.

aspect of the cervical spinal cord from C2 to C7. No unusual enhancement was observed. Age-commensurate degenerative changes were observed in the rest of the spine (Figure 2).



Figure 2C: Magnetic resonance imaging (MRI) spine showing hyperintense signal at the cervicomedullary junction and along the anterior aspect of cervical spinal cord from C2 to C7 vertebral levels.

Serological tests showed anti-MOG positivity, and were negative for anti-neuromyelitis optica antibodies (NMO), antineutrophil cytoplasmic antibodies—cytoplasmic and perinuclear (c-ANCA and p-ANCA), and antinuclear antibodies by immunofluorescence (ANA-IF). Visual evoked potential (VEP) revealed prolonged P-100 latency in the right eye and non-recordable P-100 latency in the left.

Management

As per the American Society for Apheresis (ASFA) guideline, PLEX for acute and relapsing attacks is a category II, Grade 1B recommendation, and for maintenance therapy, a Category III, Grade 2C recommendation. For acute NO spectrum disorder, replacement doses of 1.5 plasma volumes are used, with a median of five sessions administered daily or on alternate days over a 10-day period.¹⁰ The

Type II category refers to disorders in which apheresis is considered an acceptable second-line therapy, either on its own or combined with other therapies. Meanwhile, Grade 1B indicates a strong recommendation supported by moderate quality evidence.

The patient was started with therapeutic PLEX on alternate days, accompanied by once-daily high dose intravenous (IV) methylprednisolone (IVMP) at 1 gm, within 53 hours of admission. A total of seven sessions of PLEX were performed using Spectra Optia® in which 1.5 times the total plasma volume was processed using a combination of albumin, fresh frozen plasma, and normal saline as the replacement fluid. Blood flow was aimed to reach 50-70 mL/kg. Anticoagulant citrate dextrose (ACD) was used as an extracorporeal anticoagulant in the ratio 1:12. Following this, the patient received two doses of 500 mg IV rituximab.

The patient experienced gradual improvement in visual acuity during the PLEX sessions, with improvement of ≥ 2 levels in the visual outcome scores by the end of the seventh session. Eventually, a best-corrected vision of 6/6 in both eyes was achieved after rituximab administration.

Discussion

PLEX is an emerging treatment modality for patients with neurological disorders. It has been effectively used for several decades and has evolved to become more practical, reliable, and associated with reduced complication rates. PLEX in patients with MOG-IgG ON is associated with better outcomes.^{5,11}

PLEX after IVMP is well tolerated. While IVMP remains first line, the combination of IVMP with PLEX can be used in steroid-refractory cases or recurrence of MOG-IgG ON in a previously affected eye, whereas immunosuppressants can be employed to prevent recurrence of MOG-IgG ON.¹

MOG-IgG seropositivity is associated with a relapsing course of inflammatory ON. Though most patients recover good visual function, predicting future attacks during remission remains an unanswered question.⁵ Hence, the most effective approach for optimising long-term visual outcome is the prevention of future attacks.⁸

Conclusion

MOG-IgG ON can lead to severe, painful, and recurrent vision loss. This case highlights the critical importance of early PLEX initiation to prevent irreversible optic nerve damage. The synergistic effect of combining PLEX with corticosteroids and immunotherapy accelerates recovery and preserves visual function, providing a possible treatment solution to achieve restoration of visual acuity.

Priyasha Prajapat, Rasika Dhawan Setia, Mitu Dogra, Rohit Bansil, Amena Ebadur Rahman, Vadad, Sonia Joseph, Dhriti Ghosh, Garima Katiyar. Therapeutic Plasma Exchange in Myelin Oligodendrocyte Glycoprotein-Related Optic Neuritis: Restoring Vision Through Early Intervention – A Case Report. MMJ. 2025, June. Vol 2 (2).

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Plantar Abscess: An Unusual Initial Presentation of Diabetes Mellitus

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Abstract:

A 56-year-old male presented with left heel pain, redness, swelling, without any fever, with a background history of hypertension. There was no history suggestive of diabetes or heart disease. Ultrasound imaging revealed a thickened plantar fascia with inflammatory changes and fat pad thickening. Magnetic resonance imaging (MRI) of the foot confirmed subcutaneous pus collection. Routine investigations revealed very markedly uncontrolled blood sugar levels. Drainage of pus with incision and debridement was carried out, and antibiotics, along with diabetic medications, were administered. Culture was suggestive of methicillin-resistant *Staphylococcus aureus* (MRSA), for which appropriate antibiotics were initiated, bringing the infection under control. The patient with high blood sugar presented with a plantar infection without any prior symptoms of diabetes mellitus. In this case, the first symptom of diabetes was an infection/abscess in the plantar fascia - a rare site of infection.

Key words: Plantar Abscess, Diabetes Mellitus, USG, MRI of foot.

Introduction

Diabetes mellitus is a chronic condition caused by either inadequate insulin production or by insulin resistance in the body, which leads to a long-term metabolic disorder. It is known to target approximately 537 million adults aged between 20-79 years globally. Further studies have predicted that by the year 2030, there will be 643 million people who will be affected.¹ India is known to be the epicentre of the global pandemic of diabetes mellitus. There is an increased prevalence seen mainly in the past four decades.² This is mainly due to an increase in development, demographic shifts, environmental factors, higher living standards, obesity, as well as the increased susceptibility observed in Indians due to genetic factors.³ The most commonly affected population in developing countries is aged between 45 and 64 years.⁴ Diabetes is a disease of individual cells, it is not just about hyperglycaemia and its complications – it causes multi-system involvement.

The most common diabetes-related cause of recurrent hospitalisation is foot wounds. Individuals with diabetes are known to have a tenfold increased risk of being hospitalised for soft tissue and bone infections of the foot compared to individuals without diabetes.⁵ The major microvascular complications seen are peripheral neuropathy, nephropathy, and retinopathy. Peripheral neuropathy is seen in almost 70% of

patients with diabetes and may be one of the presenting features in certain cases, thus causing foot wounds and infections.⁶

Evidence suggests that hyperglycaemia can accelerate non-enzymatic glycosylation and collagen deposition in abnormal periarticular regions of the connective tissues, which causes alterations in the structural matrix and mechanical properties of the tissues. This results in widespread arthrobrosis.⁷

Case Report

A 56-year-old male presented with a sudden onset, progressive left heel pain for two weeks, which was aggravated by walking. The pain gradually worsened during this period and was associated with redness, swelling, and blister formation over the plantar surface of the left foot. There was no known history of trauma or injury. He had a history of hypertension. He was afebrile, with a pulse rate of 112/min, respiratory rate of 18/min, blood pressure of 110/70 mmHg, and the peripheral oxygen saturation (SpO₂) of 98% on room air. Physical examination revealed localised tenderness over the calcaneum and the plantar aspect (sole) of the foot, with significant erythema and swelling. All his peripheral pulses were palpable, and sensory examination was normal.

Initial laboratory tests were suggestive of raised blood sugar level of 455 mg/dL and fasting blood sugar (FBS) of 174 mg/dL. His C-reactive protein (CRP) was elevated at haemoglobin was 12 g/dL, total leukocyte count (TLC) was 14,340/ μ L, and platelet count was 284000/ μ L. Serum creatinine was 0.7 mg/dL, and electrolytes were 134/4.5/99. Urinalysis was normal.

The patient was initially started on broad-spectrum antibiotics (piperacillin-tazobactam and linezolid). Ultrasound imaging revealed a thickened plantar fascia with inflammatory changes and fat pad thickening. Magnetic resonance imaging (MRI) confirmed subcutaneous pus collection, but there was no evidence of osteomyelitis. A multiloculated T2 hyperintense and T1 slightly hyperintense lesion was seen in the abductor hallucis longus muscle, measuring 1.4 x 5.3 x 1.2 cm (transverse x anteroposterior x craniocaudal), with surrounding muscle oedema and thin peripheral enhancement. A similar curvilinear and lobulated T2 hyperintense subcutaneous signal was noted in the plantar aspect of the hind foot medially extending over 2.7 x 5.8 x 2.6 cm, without significant enhancement on post-contrast images. These findings were concerning for cellulitis, with an evolving abscess or, less likely, areas of necrosis (Figure 1-4).



Figure 1: Axial T2 view with blue arrow localising the plantar abscess.



Figure 2: Axial T1 view with blue arrow localising the plantar abscess.



Figure 3: Post-contrast T1 axial view with blue arrow localising the plantar abscess.



Figure 4: Post-contrast T1 coronal view with blue arrow localising the plantar abscess.

The patient underwent prompt surgical incision and drainage of the abscess, along with debridement of necrotic tissue. Tissue cultures were suggestive of methicillin-resistant *Staphylococcus aureus* (MRSA). Linezolid injection was continued for the patient. Oral hypoglycaemic agents, along with insulin therapy, were initiated to control the hyperglycaemia. After achieving adequate control of the blood sugar levels with diabetic diet, diabetic medications, antibiotic therapy, and regular wound dressing, the patient started improving and was subsequently discharged.

Discussion

Plantar fasciitis is typically an inflammatory disease. In this case, it presented as a bacterial infection that further progressed to an abscess. Hyperglycaemia is likely to impair wound healing and immune function, making diabetic individuals more susceptible to infections, including plantar fasciitis complicated by abscess formation or deeper tissue involvement. There has been an increase in the incidence of early-onset diabetes mellitus recently and diabetes-related complications. Early detection of diabetes is essential, especially in the pre-diabetic stages, where lifestyle modifications can prevent the progression to full-fledged diabetes. A major step is controlling the glycaemic levels, thus preventing the complications. Appropriate oral hypoglycaemic agent use and, if necessary, the initiation of insulin should be done if required. Strict monitoring should be ensured to avoid the morbidity and mortality associated with diabetes.³

As per recently conducted studies, it has been observed that the prevalence of foot-related complications in diabetics is almost 25% throughout the average lifespan.⁸

In this case, the patient presented with a red, swollen, painful heel, which was, on further investigation, detected to be a plantar abscess. Raised blood glucose serves as an important nutrient

for underlying organisms, which started multiplying rapidly in the affected areas and led to abscess formation. In this case, the patient presented to us with a plantar abscess without any symptoms of diabetes like polyuria, polyphagia, polydipsia, or generalised weakness despite having very high sugar levels. The necessary surgical assistance with antibiotics and blood sugar medications was started, which led to prompt recovery.

Conclusion

Diabetes has been known as the “silent disease” for ages, without exhibiting any clinical features until it progresses to involve the target organs of the body.⁹ In many cases, it is observed that due to delayed or untimely diagnosis of diabetes mellitus in middle-aged and elderly individuals, patients tend to present to the hospital directly with various diabetes-related complications. Hence, early, active surveillance is a must. Conducting routine investigations/health checkups for diabetes is essential for preventing such complications. Patient education remains a cornerstone of diabetic foot management. This case highlights the need for regular foot care practices, such as daily inspections, proper footwear, and early intervention in case of minor injuries. Patients should self-monitor their blood sugar levels at regular intervals. They should also be informed regarding the various complications and risks associated with raised blood sugar levels.¹⁰

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An Unusual Presentation of Pulmonary Tuberculosis and Iron Deficiency Anaemia in a Case of Peutz – Jeghers Syndrome

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Abstract:

A 27-year-old male patient with Peutz – Jeghers syndrome (PJS), characterised by hyperpigmented lesions and the presence of intestinal polyps, was diagnosed on colonoscopy. The patient had a history of intussusception, which had been surgically treated in the past. He presented with severe iron deficiency anaemia and breathlessness at rest. Despite correction of haemoglobin, the breathlessness persisted, and he subsequently developed left-sided pleural effusion, which was diagnosed as tubercular. As pulmonary tuberculosis is common in India, any patient presenting with a unilateral pleural effusion should be suspected of having tuberculosis and managed accordingly.

Key words: Intestinal Polyposis, Pleural Effusion, Colonoscopy, USG-guided Pleural Tapping, Anti-tuberculosis Regimen.

Introduction

Peutz – Jeghers syndrome (PJS) is an inherited condition with an autosomal dominant pattern of inheritance.¹ Mutations in the STK11 gene, located on chromosome 19p13, are among the germline variants found in patients with PJS.² About 17% -50% of cases are solitary and have no associated family history.³

The syndrome is characteristically marked by flat, hyperpigmented, cutaneous lesions which are usually present on the eyelids, sclera, periorbital regions, lower lip, perioral regions and in the buccal mucosa. These skin lesions are mostly benign and do not pose a risk for malignant transformation. Multiple small and large polyps are found, which are hyperplastic, hamartomatous in nature. These polyps are located within the mucosal epithelium and consist of dendritic cells and contain smooth muscle fibre bundles from the muscularis mucosa—known as Peutz–Jeghers polyps.⁴

These polyps are most commonly found in the mucosa of the stomach, small intestine (particularly the jejunum), colon and rectum. Other common areas are the nasal passages, urinary tract and lungs.³ After recent research, it has been recognised that the hamartomas may possess malignant potential, and in some of them, adenomatous changes and

foci of adenocarcinoma may be seen.⁴ The first presentation of polyps occurs around the age of 11-13 years. During the first three decades, features of obstruction, intussusception, anaemia, and bleeding per rectum are commonly seen.⁵ Almost half of the patients with PJS suffer from small bowel intussusception throughout their lives.⁶ In the younger age group in patients without a family history, PJS is often diagnosed when they suffer from intestinal obstruction and need emergency care.⁷

Case Report

A 27-year-old male patient presented with complaints of low-grade fever, cough, breathlessness at rest, malaise, anorexia, and swelling of the limbs. On examination, he had a pulse rate of 124 beats per minute and a blood pressure of 90/60 mmHg. His temperature was 98°F, respiratory rate 28/min and an oxygen saturation of 98% on room air.

He had multiple hyperpigmented patches over the sclera and in the buccal mucosa (Figure 1), Grade II clubbing (Figure 2) pedal oedema, and scrotal swelling were noted (Figure 3). Overall, he appeared cachectic, with muscle wasting and pallor. On respiratory system examination, air entry was absent on the left side of the chest, and the trachea was deviated to the right. Vocal resonance was diminished on the left side, with no

added sounds. Other systemic examinations were found to be normal. He had a history of intussusception, for which he had undergone surgery in the past.



Figure 1: Hyperpigmented macules over buccal mucosa and sclera.



Figure 2: Digital clubbing.



Figure 3: Bilateral pedal pitting oedema.

Laboratory investigations revealed the following (Table 1):

Parameter	Value	Normal range
Haemoglobin	6.7 g/dL	13.5–17.5 g/dL
Total leucocyte count	11,250 / μ L	4,500–11,000 / μ L
Platelet count	327,000 / μ L	150,000–450,000 / μ L
Prothrombin time	11 sec	—
International normalised ratio (INR)	1.26	0.8–1.4
Serum creatinine	0.5 mg/dL	Up to 0.9 mg/dL
Serum sodium	130 mEq/L	135–145 mEq/L
Serum potassium	3.76 mEq/L	3.5–5 mEq/L
Serum chloride	101.2 mEq/L	98–107 mEq/L
Total protein	4.17 g/dL	6–8.3 g/dL
Serum albumin	1.1 g/dL	3.4–5.4 g/dL
Serum globulin	3 g/dL	2–3.5 g/dL
Serum glutamic oxaloacetic transaminase (SGOT)	49 U/L	7–56 U/L
Serum glutamic pyruvic transaminase (SGPT)	33.7 U/L	8–48 U/L
Alkaline phosphatase	145 U/L	45–115 U/L
Total bilirubin	0.13 mg/dL	0.1–1.2 mg/dL
Serum ferritin	21.9 ng/mL	30–300 ng/mL
Transferrin saturation	21.9%	20–50%
Total iron-binding capacity (TIBC)	271 μ g/dL	250–450 μ g/dL
Serum iron	7.51 μ g/dL	60–170 μ g/dL
Serum lactate dehydrogenase (LDH)	419 U/L	140–280 U/L

Table 1: Laboratory analysis of the patient.

Urine microscopy was normal, while stool occult blood tested positive. Chest X-ray showed left-sided pleural effusion (Figure 5). Lung ultrasonography (USG) confirmed a massive left-sided pleural effusion. Diagnostic and therapeutic pleural tapping was performed under ultrasound guidance. Pleural fluid analysis revealed—hazy appearance with clot formation. The fluid protein was 1.79 g/dL, and glucose was < 0.24 g/dL. The total nucleated cell count was 6476 cells/ μ L, 68% polymorphs, 32% lymphocytes. The adenosine deaminase (ADA) level was 70.4 U/L (Normal: < 40U/L). GeneXpert testing showed the presence of *Mycobacterium tuberculosis*. Lactate dehydrogenase (LDH) in the pleural fluid was 2610 U/L. Malignant cells were absent. Culture showed the presence of *Escherichia coli*, which was pan-sensitive.

An ultrasound of the abdomen was performed, revealing multiple jejunal polyps, following which a colonoscopy was ordered. On colonoscopy, numerous medium and large-sized polyps were observed (Figure 5), which were surgically managed with resection of affected areas.



Figure 4: Left-sided pleural effusion.



Figure 5: Colonoscopy suggestive of multiple intestinal polyps.

The patient was administered two units of packed red blood cells, an albumin infusion for 3 days and high-protein diet was advised, after which his oedema started reducing gradually. He was given an anti-tuberculosis regimen alongside antibiotics and other supportive management. Gradually, his symptoms started improving — absence of pedal oedema, absence of breathlessness, increased appetite, and absence

of fever. His vital parameters and laboratory values came back to normal, and he was then discharged after receiving adequate treatment.

Discussion

As per the World Health Organisation (WHO), PJS is diagnosed if any of the two following features are present:⁴

- Two or more histologically confirmed PJS-type hamartomatous polyps
- Family history of diagnosed PJS or similar clinical features
- Presence of hyperpigmented mucosal lentigos.

In this case, we see that two criteria are fulfilled. The patient had a positive history of multiple hamartomatous polyps with mucocutaneous pigmentation on the buccal mucosa and sclera. Most frequently observed complications of PJS are obstruction or intussusception of the intestinal lumen due to polyps. These polyps can lead to chronic blood loss, leading to anaemia.⁸ Up to 69% of patients with PJS experience intussusception. The risk of intussusception reaches 50% by age 20 in these patients.⁹

Our patient was breathless despite correcting haemoglobin by blood transfusion. Breathlessness was because of left-sided pleural effusion, which developed during admission. Bilateral pleural effusion would have been transudative. *Mycobacterium tuberculosis* is a well-known major public health issue and a leading cause of death globally.¹⁰

Patients with PJS are more prone to developing other systemic illnesses and should be promptly investigated in such cases so that the appropriate treatment may be started.

The deranged iron profile was suggestive of iron deficiency anaemia. The patient was then immediately started on treatment with the anti-tuberculosis regimen, which was not multidrug-resistant. The patient started showing signs of improvement and was then discharged.

Conclusion

As patients of PJS are susceptible to different malignancies of the gastrointestinal tract, oesophagus, uterus, ovaries, breast, pancreas, lung, testis, surveillance should be done at regular intervals to enable early diagnosis.⁴ Currently surveillance of the large bowel by colonoscopy or flexible sigmoidoscopy with the use of barium enema is usually recommended every 2-3 years starting from adulthood. Upper gastrointestinal endoscopy should be done every 2-3 years.³

Patients and relatives should be informed about the possible complications and risks of developing other systemic comorbid illnesses like tuberculosis, especially in areas which have high prevalence. Early surveillance facilitates prompt diagnosis and treatment.

Nitin Rathod, Andrea Janice Fonseca, Mohammed Amin Hamidani, Snehal Sadanandan. An Unusual Presentation of Pulmonary Tuberculosis and Iron Deficiency Anaemia in a Case of Peutz–Jeghers Syndrome. *MMJ*. 2025, June. Vol 2 (2).

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An Unusual Case of Gonadal Venous Thrombosis Presenting as Fever of Unknown Origin

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Abstract:

Gonadal vein thrombosis (GVT) is an uncommon clinical entity typically associated with postpartum or postoperative states. Its occurrence in the context of systemic autoimmune diseases is rare and diagnostically challenging, particularly when presenting as fever of unknown origin (FUO).

We report the case of a 39-year-old woman presenting with a six-month history of painful red discoloration of the fingertips, right lower quadrant abdominal pain, and five months' history of persistent low-grade fever. Initial evaluation revealed systemic symptoms including significant fatigue, weight loss, dry cough, and alopecia. Physical examination showed cervical lymphadenopathy, painful oral ulcers, malar rash, and bilateral lower limb oedema. Laboratory investigations revealed leukopenia, elevated inflammatory markers, hypoalbuminemia with nephrotic-range proteinuria, positive antinuclear antibody (ANA) with high titres, and hypocomplementemia. Imaging identified a right gonadal vein thrombosis and multiple fluorodeoxyglucose (FDG)-avid lymph nodes on positron emission tomography - computed tomography (PET-CT). The clinical picture, combined with serological findings, was consistent with a diagnosis of mixed connective tissue disease (MCTD) with features overlapping systemic lupus erythematosus (SLE) and polymyositis. A secondary antiphospholipid syndrome (APS) was considered likely in the context of thrombosis and positive beta-2 glycoprotein antibodies and anti-cardiolipin antibodies.

This case underscores the importance of considering systemic autoimmune diseases in the differential diagnosis of FUO and thrombosis at unusual sites. GVT, though rare, may be the first manifestation of an underlying connective tissue disease or APS, and warrants comprehensive immunological and haematological evaluation.

Key words: FUO, Gonadal Venous thrombosis, Mixed Connective Tissue Disease, APS.

Introduction

Gonadal vein thrombosis (GVT) is a rare vascular condition most commonly observed in the postpartum period or following pelvic surgery. It is infrequently encountered in non-obstetric settings and seldom reported as a primary manifestation of systemic autoimmune or connective tissue diseases. The clinical presentation of GVT can be subtle and often mimics other causes of abdominal pain, making diagnosis challenging. When accompanied by systemic features such as fever of unknown origin (FUO), generalised lymphadenopathy, and

mucocutaneous involvement, the differential diagnosis broadens significantly, requiring consideration of inflammatory, infectious, and malignant aetiologies.¹

Systemic autoimmune diseases such as systemic lupus erythematosus (SLE), Sjögren's syndrome, systemic sclerosis, and polymyositis are known to present with protean manifestations that may mimic infection or malignancy.² Vascular complications, particularly thrombosis in unusual locations, may be the initial

or sole manifestation of underlying antiphospholipid antibody syndrome (APS), which can be either primary or secondary to a systemic autoimmune condition.

We present an unusual case of GVT in a previously healthy woman, presenting with FUO and multisystem involvement, ultimately diagnosed as mixed connective tissue disease (MCTD) with overlapping features of SLE and polymyositis. This case highlights the diagnostic complexity of GVT in the autoimmune context and underscores the need for a high index of suspicion for systemic diseases in patients presenting with FUO and atypical thrombotic events.

Case Report

A 39-year-old woman from Rajasthan, India, presented to the internal medicine outpatient department with a constellation of symptoms that had evolved over the previous six months. Her primary complaints included episodic painful red discoloration of the fingers, persistent right lower quadrant abdominal pain, and low-grade fever.

The digital symptoms began six months prior and were characterised by sudden-onset, intermittent, painful erythema localised to the distal palmar aspect of all fingers. The episodes were non-progressive and relieved transiently by immersion in cold water. There were no features suggestive of gangrene, colour changes extending to the hands, or associated temperature fluctuations. The pain was severe enough to impair fine motor function.

Simultaneously, she developed right lower quadrant abdominal pain, initially dull and intermittent but progressively intensifying over time to a continuous, stabbing quality, rated as 10/10 in severity. The pain was non-radiating, unresponsive to oral paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs), and eventually required intravenous (IV) analgesics during hospitalisation. There was no diurnal variation or known precipitating factors.

Five months prior to presentation, she began experiencing persistent low-grade fever (100–101°F) without chills or rigors. The fever was insidious in onset and recurred after the effect of antipyretics waned. It was associated with severe fatigue and myalgia, significantly limiting her activities of daily living. Systemic review revealed additional symptoms, including a dry, non-productive cough of four months' duration without diurnal or positional variation; approximately 10 kg of unintentional weight loss over six months; progressive fatigue, diffuse scalp hair thinning with visible patchy hair loss; and proximal muscle weakness, manifesting as difficulty rising from a chair or lifting her arms above her head.

There was no history of photosensitivity, oral or genital ulcers prior to this episode, Raynaud's phenomenon, joint pain, sicca symptoms, dysphagia, chest pain, dyspnoea, palpitations, urinary symptoms, or mood disturbances. She denied any recent infections, travel, allergen exposures, or occupational risk factors. There was no personal or family history of autoimmune, thrombotic, or malignant conditions.

Her menstrual history was unremarkable, with regular cycles and no abnormal bleeding or dysmenorrhoea. Obstetric history included two full-term deliveries without complications. She was not on any medications prior to the onset of symptoms and had no known drug or food allergies.

Examination

On presentation, the patient was lying comfortably in bed, alert, and well-oriented to time, place, and person. Her gait was normal.

General examination

- **Pallor:** Present
- **Icterus, cyanosis, clubbing:** Absent
- **Lymphadenopathy:** A single, non-matted, non-tender cervical lymph node measuring approximately 8 × 6 cm was palpable in the right posterior triangle, supraclavicular in location (2 cm above the clavicle). It was soft to firm in consistency, not fixed to overlying skin or underlying structures. There was no erythema, fistula, sinus formation, or discharge associated with it. No other lymph nodes were appreciable.
- **Oedema:** Bilateral grade 3 pitting oedema was noted in the lower limbs, extending from both feet up to the knees. There was no skin induration.

Oral examination

- Multiple small, painful, round-to-oval ulcers measuring 1–2 cm were noted over the oral mucosa. These ulcers had a red base with a pale border and were diffusely distributed without evidence of discharge or induration at the base. The patient exhibited difficulty opening the mouth, with opening limited to two finger breadths.

Neck and thyroid examination

- The thyroid gland was not enlarged and was non-tender. It moved with deglutition and protrusion of the tongue and was freely mobile. However, diffuse hardening of the right thyroid cartilage was appreciated. No overlying erythema was present.

Systemic examination

- **Cardiovascular system (CVS):** S1 and S2 heart sounds were normal. No murmurs were heard.
- **Central nervous system (CNS):** Higher mental functions, cranial nerves, motor and sensory systems, reflexes, gait, and autonomic function were all intact. There were no signs of meningeal irritation.
- **Respiratory system:** Bilateral air entry was equal with no added sounds (e.g., crepitations, wheeze).
- **Abdomen:** Soft, non-tender, non-distended. No organomegaly or palpable masses were noted.

Local examination (skin and extremities)

- A non-pruritic, non-tender macular rash was observed bilaterally over the malar prominences as shown in Figure 1. The rash spared the nasolabial folds and was not associated with puffiness or change in skin temperature.
- Erythema was present over the distal interphalangeal joints of all fingers in both hands as shown in Figure 2, consistent with the patient's complaint of painful, red fingers.



Figure 1: Malar rash.



Figure 2: Painful erythema over digits.

Investigations

Laboratory investigations

1. Her baseline lab investigations are shown in Table 1.

Haemoglobin (MCV/MCH)	10.2 g/dL (84 fL/28 pg)
TLC (N/L/M)	2900 cells/ μ L (83%/ 12%/2.9%)
Platelet Count	330 x 10 ³ / μ L
Creatinine	0.6 mg/dL
EGFR	116 mL/min/1.73 m ²
Urea	15 mg/dL
Sodium/Potassium	136 mmol/L/4.5 mmol/L
Calcium /HCO₃	8.2 mg/dL/19 mmol/L
Bilirubin (Total)	0.3 mg/dL
AST/ALT	101 U/L/56 U/L
ALP/GGT	101 U/L/81 U/L
Protein (Albumin/Globulin)	6.9 g/dL (2.5 g/dL/4.4g/dL)
CRP	14 mg/dL
ESR	120 mm/hr
APTT	44 seconds
PT INR	11.4 seconds/0.93
Peripheral Blood Smear	Normocytic normochromic anaemia with leukopenia
UACR	3874 mg/g
24 hour Total Protein	1283 mg/day
C3/C4	40/8 mg/dL
Rheumatoid Factor/ CCP	9.5 IU/mL/ 0.4 U/mL
Ferritin	1969 ng/mL
Beta 2 Glycoprotein IgA	8.1 U/mL
dRVVT – Lupus Anti-Coagulant Ratio	1.96 (Lupus like anti-coagulant present)
D-Dimer	1026 ng/mL FEU

Table 1: Baseline laboratory investigations.

Abbreviations : ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; APTT: Activated partial thromboplastin time; AST: Aspartate aminotransferase; CCP: Cyclic citrullinated peptide; CRP: C-reactive protein; C3: Complement component 3; C4: Complement component 4; D-dimer: Fibrin degradation product; DRVVT: Dilute Russell viper venom time; EGFR: Estimated glomerular filtration rate; ESR: Erythrocyte sedimentation rate; FEU: Fibrinogen equivalent units; GGT: Gamma-glutamyl transferase; HCO₃: Bicarbonate; IgA: Immunoglobulin A; INR: International normalised ratio; MCH: Mean corpuscular haemoglobin; MCV: Mean corpuscular volume; N: Neutrophil; L: Lymphocyte; M: Monocyte; PT: Prothrombin time; RF: Rheumatoid factor; TLC: Total leucocyte count; UACR: Urine albumin-to-creatinine ratio.

2. Connective tissue disease (CTD) profile – Her CTD Profile for autoimmune work up is shown in Table 2.

ANA	> 1:2560 +
Antinucleosome	16
Anti DS–DNA	17
Antihistone	24
Anti SSA/60 KD	57
Anti SSA/52 KD	64
Anti SSB	60
Anti CENP- A/B	10
Anti M2 recombinant	7
C–ANCA & P–ANCA	Negative (0.2 & 0.2)

Table 2: Connective tissue disease (CTD) profile.

Abbreviations : ANA: Antinuclear antibody; Anti-CENP-A/B: Anti-centromere protein A/B antibodies; Anti-dsDNA: Anti-double-stranded DNA antibody; Anti-M2 recombinant: Anti-mitochondrial M2 recombinant antibody; Anti-SSA/52 kD: Anti-Sjögren's-syndrome-related antigen A, 52 kilodalton; Anti-SSA/60 kD: Anti-Sjögren's-syndrome-related antigen A, 60 kilodalton; Anti-SSB: Anti-Sjögren's-syndrome-related antigen B antibody; C-ANCA: Cytoplasmic anti-neutrophil cytoplasmic antibody; P-ANCA: Perinuclear anti-neutrophil cytoplasmic antibody.

Radiological investigations

- All the radiological investigations done are shown in Table 3.

USG W/A (16/4/25)	- Right gonadal venous thrombosis - Uterine adenomyosis
CECT CHEST (16/4/25)	- Few centrilobular pulmonary nodules in inferior lingular segment of left upper lobe – likely infective aetiology - Small fibrotic bands in medial segment of right middle lobe
CECT ABDOMEN (16/4/25)-	- Right ovary = bulky in size - Expansion of right ovarian vein with presence of intra luminal hypodense partial to near complete lumen occluding thrombus not reaching up to IVC as shown in Figure 3.
PET CT (21/4/25)	FDG avid heterogeneously enhancing right posterior cervical, mediastinal, axillary, abdominal/retroperitoneal lymph nodes seen.

Table 3: Radiological investigations done for patient.

Abbreviations : CECT: Contrast-enhanced computed tomography; FDG: Fluorodeoxyglucose; IVC: Inferior vena cava; PET-CT: Positron emission tomography–computed tomography; USG W/A: Ultrasonography of whole abdomen.



Figure 3: Right ovarian venous thrombosis.

Histopathological diagnosis:

- Biopsy from right cervical lymph node (Figure 4):** Showing non-granulomatous necrotising lymphadenitis.

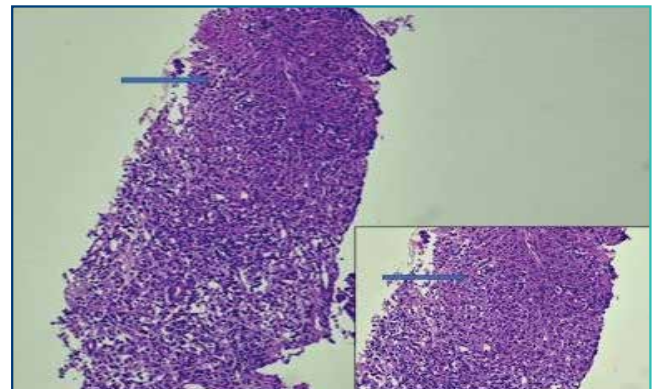


Figure 4: Right cervical lymph node biopsy.

- Renal biopsy (Figure 5):** All glomeruli showed diffuse thickening of glomerular basement membrane with sub-epithelial spikes and pinholes.

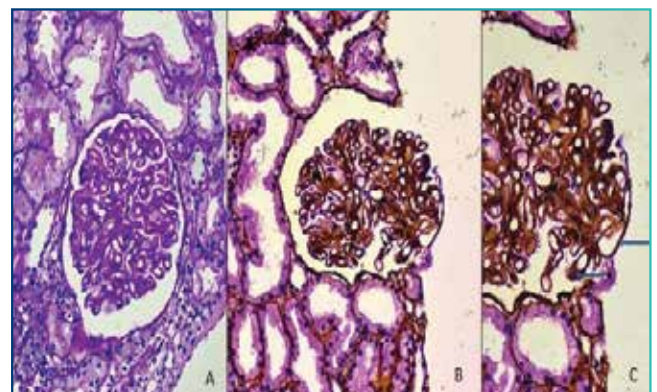


Figure 5: Renal biopsy: a) PAS stain (20X), b) Silver stain (20X), c) Silver stain (40X).

- **Renal biopsy with direct immunofluorescence (Figure 6):** Showing peripheral and mesangial deposits with “Full House effect”.

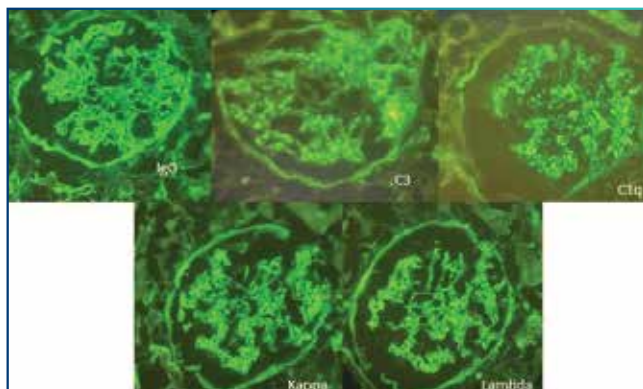


Figure 6: Renal biopsy with direct immunofluorescence.

Diagnosis

Based on the clinical presentation, laboratory investigations, immunological profile, and radiological findings, the patient was diagnosed with:

1. MCTD with features overlapping:
 - o SLE: Positive ANA (> 1:2560), anti-dsDNA, anti-nucleosome, anti-SSA/SSB antibodies, oral ulcers, malar rash, leukopenia, and nephrotic-range proteinuria with hypocomplementemia (low C3 and C4)
 - o Polymyositis: Proximal muscle weakness with mildly elevated creatine kinase (CK)
2. Right GVT, confirmed on ultrasound and contrast-enhanced computed tomography (CT) abdomen secondary to APS, supported by vascular thrombosis and positive beta-2 glycoprotein antibody
3. Lupus nephritis Grade 5 with “Full house” effect – histopathologically confirmed.

Discussion

GVT represents an exceedingly rare but potentially serious vascular complication that can present diagnostic challenges due to its nonspecific clinical manifestations. In this case, the patient's persistent fever for five months without an identifiable cause initially classified her condition as FUO, which eventually led to the discovery of right GVT in the setting of MCTD with features of secondary APS.

GVT is an uncommon clinical entity with a reported incidence of approximately 0.08% in studies utilising CT imaging for diagnosis.¹

Traditionally, GVT has been most frequently associated with the postpartum period, following hysterectomy, or after lymphadenectomy for gynaecological malignancies, with up to 80% of cases occurring in these settings.¹ The predominance of right-sided involvement (59% of cases in one study) has been attributed to anatomical factors including

the longer length of the right gonadal vein compared to the left, and an increased absence of competent valves in the right gonadal vein.¹ However, GVT occurring in the context of autoimmune disorders, particularly MCTD, represents an unusual presentation that warrants attention.

The hypercoagulable state observed in autoimmune disorders provides a mechanistic explanation for thrombotic events such as GVT in our patient. Active inflammation, a hallmark of connective tissue diseases, creates a prothrombotic environment characterized by upregulation of tumour necrosis factor- α (TNF- α) and activation of endothelial cells.² This inflammatory milieu increases tissue factor expression (a natural procoagulant) while simultaneously downregulating protein C (a natural anticoagulant).² Additionally, endothelial activation promotes platelet aggregation, further contributing to thrombus formation.

The risk of venous thromboembolism is particularly elevated during periods of increased disease activity, with studies suggesting that the highest risk occurs within the first year of disease onset.² This temporal relationship aligns with our patient's presentation, as her thrombotic complication manifested during the active phase of her newly diagnosed MCTD.

MCTD, first described by Sharp *et al.* in 1972, represents an autoimmune disorder with overlapping features of systemic sclerosis, SLE, and polymyositis.³ With an estimated annual incidence of 1.9-2.1 cases per 100,000 adults and a female predominance (female-to-male ratio of 3.3:1), MCTD remains a relatively rare condition.³

While once perceived as a mild and treatable condition, MCTD can pose significant morbidity and mortality risks, particularly when complicated by vascular events.³ The thrombotic risk in MCTD appears to be mediated through multiple mechanisms, including endothelial dysfunction, inflammation-induced hypercoagulability, and the possible presence of antiphospholipid antibodies, as observed in our patient.

APS may occur as a primary disorder or secondary to systemic autoimmune diseases, particularly SLE and MCTD. Antiphospholipid antibodies are frequently detected in patients with SLE, with lupus anticoagulant found in approximately one-third of cases and anti-beta 2 glycoprotein-1 antibodies in about 20%. These antibodies demonstrate a strong association with thromboembolic events in patients with connective tissue diseases.

In our case, the patient exhibited clinical and laboratory features consistent with secondary APS (elevated beta-2 glycoprotein IgA levels and significantly elevated D-dimer), which likely contributed to the development of GVT. The recognition of APS in this setting has significant therapeutic implications, as it influences the choice of anticoagulant therapy. Vitamin K antagonists are generally preferred over direct oral anticoagulants for secondary thromboprophylaxis in patients with APS.

FUO, defined as a temperature exceeding 38.3°C (101.0°F) persisting for at least three weeks without an established aetiology after thorough clinical evaluation, represents a diagnostic conundrum that requires systematic investigation. When FUO occurs in the context of autoimmune disorders, the diagnostic complexity increases due to the multisystemic nature of these conditions and the variable manifestations of disease activity.

In our patient, the prolonged fever initially dominated the clinical picture, obscuring the underlying GVT. This case underscores the importance of comprehensive vascular imaging in patients with persistent unexplained fever, particularly those with clinical features suggestive of autoimmune disease. The combination of ultrasonography, contrast-enhanced CT, and positron emission tomography proved instrumental in establishing the diagnosis of GVT and characterising the extent of systemic involvement.

The management of GVT in the setting of MCTD with secondary APS involves a multifaceted approach addressing both the thrombotic complication and the underlying autoimmune disorder. Anticoagulation therapy forms the cornerstone of GVT management, typically administered for a duration of three to six months.¹ However, in patients with persistent antiphospholipid antibody positivity, extended or indefinite anticoagulation may be necessary to prevent recurrent thrombosis.

For the underlying MCTD, treatment typically includes immunomodulatory agents such as corticosteroids, hydroxychloroquine, and other disease-modifying antirheumatic drugs tailored to the specific clinical manifestations. The management of secondary APS requires particular attention to anticoagulation strategies, with vitamin K antagonists generally preferred over direct oral anticoagulants due to superior efficacy in preventing recurrent thrombosis in this patient population.

According to the Kidney Disease: Improving Global Outcomes (KDIGO) 2024 guidelines, a renal biopsy is essential in patients with SLE presenting with proteinuria ≥ 500 mg/day or unexplained rise in serum creatinine to classify lupus nephritis (LN) and guide therapy. However, in practice—especially in resource-limited settings or unstable patients—empirical treatment may be initiated when classical serological and clinical features are present.⁴

The updated KDIGO 2024 and American College of Rheumatology (ACR) 2024 guidelines recommend a “triple therapy” approach for active Class III/IV LN.^{4,5}

- Glucocorticoids (preferably initiated with (IV) pulse methylprednisolone and tapered to ≤ 5 mg/day over 6 months)
- Mycophenolate mofetil (MMF)
- Belimumab or a calcineurin inhibitor (such as voclosporin).

Hydroxychloroquine is universally advised for all patients with (LN), unless contraindicated, due to its reno protective and immunomodulatory benefits.

From an Indian perspective, several randomised controlled trials have demonstrated comparable efficacy of low-dose cyclophosphamide and MMF as induction therapies for LN. A landmark Indian study by Bharati *et al.* 2019 compared two steroid regimens and demonstrated improved outcomes with a lower steroid burden, aligning with the KDIGO emphasis on minimising long-term glucocorticoid exposure.⁶

For the management of APS in this patient, vitamin K antagonists (VKAs) such as warfarin are preferred over direct oral anticoagulants (DOACs), particularly in those with arterial thrombosis or high-risk antibody profiles.

This case highlights several important clinical lessons. First, it illustrates the need for heightened awareness of thrombotic complications in patients with MCTD, even in the absence of traditional risk factors for venous thromboembolism. Second, it emphasises the value of comprehensive vascular imaging in the evaluation of FUO, particularly when associated with localised abdominal pain. Finally, it underscores the importance of screening for antiphospholipid antibodies in patients with connective tissue diseases who develop thrombotic events, as this has significant implications for management.

Future research directions should focus on elucidating the precise mechanisms underlying the thrombotic risk in MCTD, developing risk stratification tools to identify patients most susceptible to vascular complications, and optimising anticoagulation strategies for this unique patient population.

Conclusion

This case represents an unusual presentation of GVT manifesting as FUO origin in a patient with newly diagnosed MCTD and features of secondary APS. It highlights the complex interplay between autoimmunity, inflammation, and thrombosis, while emphasising the importance of comprehensive evaluation in patients with prolonged unexplained fever. Recognition of this rare association can facilitate prompt diagnosis and appropriate management, potentially preventing serious complications of untreated venous thromboembolism in this vulnerable patient population.

Aryan Arora, Prateek Bhanu, Sandeep Budhiraja, Anisha Manocha. An Unusual Case of Gonadal Venous Thrombosis Presenting as Fever of Unknown Origin. MMJ. 2025, June. Vol 2 (2).

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Kikuchi Disease in a Male: A Rare Case Report

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Abstract:

Kikuchi-Fujimoto Disease (KFD) is a rare, benign, self-limiting cervical lymphadenitis of unknown aetiology, with a worldwide distribution and a higher prevalence among Japanese and other Asiatic individuals. It predominantly affects young adults under the age of 30, predominantly women. It can closely mimic infective and immunological disorders and is often reported as a cause of prolonged fever of unknown origin. Although the clinical course is typically benign, KFD has been often misdiagnosed as malignancy or infection. In this case report, we present a case of a 20-year-old male, a known case of hypothyroidism, who presented with high-grade fever with chills for one month and multiple swellings over the neck. He was evaluated and diagnosed as a case of KFD on an excisional biopsy of a left cervical lymph node and was treated with steroids and other symptomatic measures.

Key words: Kikuchi-Fujimoto Disease (KFD), Histiocytic Necrotising Lymphadenitis, Excision Biopsy.

Introduction

Kikuchi-Fujimoto disease (KFD), also known as Kikuchi's disease or histiocytic necrotising lymphadenitis, is a rare, benign and a self-limiting syndrome, characterised by painful or painless lymph node enlargement, usually accompanied by fever, night sweats, weight loss, severe headache, arthralgia, myalgia, rash and hepatosplenomegaly.^{1,2}

Although benign, KFD is often mislabelled as an infection or malignancy.³ It was originally described in 1972 in Japan by Dr. Masahiro Kikuchi and Y. Fujimoto.^{4,5} The exact pathophysiology remains unclear, but the disease is thought to be triggered by an autoimmune condition, infection, or a physical injury, leading to an inflammatory cascade.^{4,5} The disease onset is generally acute or subacute, evolving over a period of 2-3 weeks. Generalised lymphadenopathy is rare, although cervical lymphadenopathy is almost always present. The lymph nodes are typically mobile, solitary, and painful, with sizes ranging from 0.5 cm to 4 cm, and rarely exceeding 6 cm. The most commonly involved lymph nodes are located in the posterior and anterior cervical triangles, but may also occur in the axillary, supraclavicular, mediastinal, inguinal, peritoneal, or retroperitoneal regions.

Kikuchi's disease is extremely rare, and its exact incidence remains uncertain. It can affect individuals of all age groups but is most commonly seen in individuals under 30 years of age.³ Kikuchi's disease, is most frequently observed in Asian populations, with rare sporadic cases reported in the United States and Europe.

Case Report

A 20-year-old male, resident of North India, a known case of hypothyroidism, presented with multiple neck swellings and high-grade fever with chills, persisting for one month. No other localising symptoms or signs were elicited. There was no prior history of tuberculosis.

On clinical examination, multiple enlarged lymph nodes were noted in the left axilla and cervical region. They were soft in consistency, mobile, painless, and measured approximately 3 x 2.5 cm. Lymph nodes were not palpable in other parts of the body. Systemic examination findings were within normal limits. Laboratory investigations including complete blood count (CBC), liver function tests (LFT), kidney function tests (KFT), peripheral smear, procalcitonin, and urine routine analysis were within normal limits. Peripheral smear for malaria parasites (performed

in another hospital) was negative. Tests for Widal, scrub typhus, and viral markers-Human Immunodeficiency Virus types 1 and 2 (HIV-1 and HIV-2), Hepatitis C Virus (HCV) and Hepatitis B surface Antigen (HBsAg)—were negative. Paired urine and blood cultures were sterile. Transthoracic echocardiography (TTE) showed no evidence of vegetations, clots, or pulmonary embolism.

The erythrocyte sedimentation rate (ESR) was mildly raised at 41 mm in the first hour, and C-reactive protein (CRP) was 1.7. Serum ferritin (430 ng/mL) and lactate dehydrogenase (LDH) (384 U/L) were also mildly raised.

Tests for Mantoux, Monospot, serum angiotensin-converting enzyme (ACE) Levels, antinuclear antibodies (ANA) by indirect immunofluorescence assay (IFA) and screening profile, anti-streptolysin O (ASO) titre, coronavirus disease 2019 reverse transcription polymerase chain reaction (COVID 19 RT-PCR), influenza RT-PCR, Brucella immunoglobulin M (IgM) and immunoglobulin G (IgG), cytomegalovirus (CMV) IgM, Epstein-Barr Virus viral capsid antigen (EBV VCA) IgM, and Toxoplasma serology were all negative.

Contrast-enhanced computed tomography (CECT) chest showed multiple enlarged, homogenous axillary lymph nodes, as shown in Figure 1



Figure 1: Contrast-enhanced computed tomography (CECT) chest (performed externally) showed at least three enlarged homogenous axillary lymph nodes, largest measuring 3.8 X 2.7 cm.

Ultrasound (USG) of the axilla performed in another hospital, showed multiple enlarged left axillary lymph nodes (2.1 x 1.4 cm) with necrosis. A USG-guided fine needle aspiration cytology (FNAC) of the cervical lymph node was performed, along with immunohistochemistry (IHC) studies, followed by an excision biopsy of the lymph node.

FNAC of the cervical lymph node showed moderate cellularity comprising a polymorphous population of lymphoid cells, with the presence of macrophages and occasional immunoblasts. The background showed necrotic areas; however, no well-formed granulomas were identified.

Subsequent excision biopsy of the lymph node showed a distorted nodal architecture (Figure 2). Pale areas were noted within the lymph node, composed of eosinophilic, granular material, and karyorrhectic debris (Figure 3), interspersed with lymphocytes and histiocytes. These areas notably lacked neutrophils and giant cells. Other areas showed primary and secondary lymphoid follicles. No granulomas were identified, and no acid-fast bacilli (AFB) were seen on Ziehl-Neelsen stain.

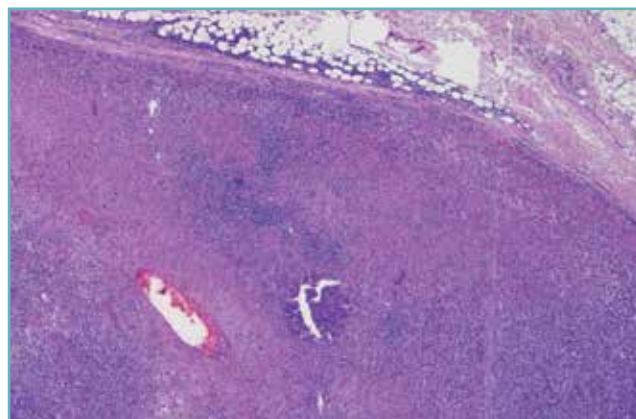


Figure 2: Lymph node with distorted architecture and pale necrotic areas.

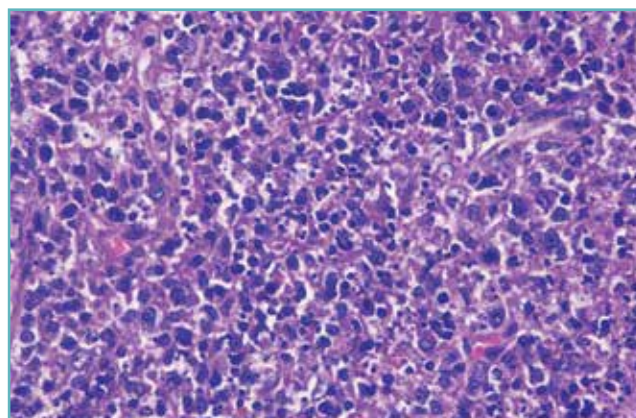


Figure 3: Lymph node exhibiting karyorrhectic debris devoid of neutrophils. Immunohistochemical stains, including Cluster of Differentiation (CD)3, CD20, CD15, CD30, Paired Box Protein 5 (PAX5), Epstein-Barr Virus Latent Membrane Protein (EBV-LMP), B-cell lymphoma 2 (Bcl2), terminal deoxynucleotidyl transferase (Tdt), and Ki67 proliferation index were done, and the possibility of a lymphoproliferative disorder was completely excluded. Based on the morphological findings and IHC results, a diagnosis of necrotising lymphadenitis suggestive of KFD was rendered.

The patient was started on oral steroids, showed signs of improvement, and was discharged from hospital on oral steroids with advice for follow-up through the outpatient department (OPD).

Discussion

When evaluating a patient for KFD, it is essential to initiate an infectious work-up guided by the patient's medical history. This should include recent infectious illness, travel history, exposure to animals or tuberculosis, and current or recent antibiotic use. The most common presentation of KFD includes localised or generalised lymphadenopathy, fever, fatigue, weight loss, hepatosplenomegaly, and rash. A definitive diagnosis requires excisional lymph node biopsy, as IHC analysis is necessary.^{5,6} The exact aetiology of KFD is not known, although infectious agents such as EBV, HIV, Herpes Simplex Virus (HSV), dengue virus, Human T-lymphotropic Virus type 1 (HTLV 1), parvovirus B19, *Toxoplasma gondii*, *Yersinia enterocolitica*, *Bartonella* spp., and *Brucella* spp. may have a role.

Serological testing for various viral and bacterial causes of lymphadenitis, along with an autoimmune work-up including family history, should be considered based on the exposure history and clinical presentation. For suspected tuberculous lymphadenitis, Mantoux test, or interferon-gamma release assay (IGRA) should be performed.

Peripheral flow cytometry may be contemplated in cases with a suspicion of malignancy. Histological and immunohistochemical analysis are important for excluding malignancy.

Diagnosing KFD necessitates an excisional biopsy of an enlarged lymph node, with IHC playing a crucial role in excluding other differential diagnoses.⁷ KFD is characterised by three histological stages—proliferative, necrotising, and xanthomatous.

A notable absence of neutrophils or eosinophils is evident across all these stages, and serves as a crucial distinguishing feature between KFD and infectious aetiologies.^{6,8} Furthermore, microscopic examination and culture studies typically yield negative results.

Laboratory investigations may reveal raised CRP, ESR, ferritin, aminotransferases, and LDH. Leukopenia occurs in 20%-58% of cases.

Characteristic histopathologic findings of KFD include irregular paracortical areas of coagulative necrosis with abundant karyorrhectic debris, distortion of nodal architecture, and large number of different types of histiocytes at the margin of necrotic areas.

Neutrophils are characteristically absent, and plasma cells are either absent or scarce. Atypia in the reactive immunoblastic component may mimic lymphoma. The immunophenotype shows a predominance of T cells with few B cells.⁹

Differential Diagnosis

Distinguishing KFD from lymphomas and infectious aetiologies is critical, and additional support for the histologic diagnosis can be obtained through cultures and serological testing. Although systemic lupus erythematosus (SLE) lymphadenitis may resemble KFD histologically, the presence of haematoxylin bodies in SLE lymphadenitis aids differentiate it from KFD.¹⁰

Infectious diseases

- **Viral:** EBV, CMV, Infectious hepatitis, HSV, human herpesvirus-6 (HHV-6), varicella-zoster virus (VZV), rubella, measles, HIV, and human herpesvirus-8 (HHV-8)
- **Bacterial:** Streptococci, staphylococci, tuberculosis, brucellosis, plague, and chancroid
- **Fungal:** Histoplasmosis, coccidioidomycosis, and paracoccidioidomycosis
- **Chlamydial:** Lymphogranuloma venereum (LGV), and trachoma
- **Parasitic:** Toxoplasmosis, leishmaniasis, trypanosomiasis, and filariasis
- **Rickettsial:** Scrub typhus, rickettsial pox, and Q fever

Immunologic diseases

Rheumatoid arthritis (RA), juvenile RA, mixed connective tissue disease (MCTD), SLE, dermatomyositis, and Sjögren's syndrome.

Malignant diseases

Hodgkin's lymphoma, non-Hodgkin lymphoma (NHL), hairy cell leukaemia (HCL), malignant histiocytosis, and amyloidosis.

Lipid storage diseases

Gaucher's disease, Niemann-Pick disease, Fabry disease, and Tangier disease.

Endocrine diseases

Hyperthyroidism.

Other disorders

Castleman's disease (a rare disorder that affects lymph nodes and organs), sarcoidosis, severe hypertriglyceridaemia, Kawasaki disease, histiocytosis X, and lymphomatoid granulomatosis.⁸

Management

No specific treatment exists for KFD. It follows a self-limiting course, typically resolving spontaneously within 1-6 months, and has an excellent prognosis.

Supportive management is the mainstay of treatment. Corticosteroids and immunosuppressants may be considered for severe extranodal or generalised KFD or recurrent cases.

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Conclusion

Although KFD is rare, it should be considered in the differential diagnosis of a young patient presenting with fever and cervical lymphadenopathy. While it is historically more common in females, recent studies suggest a nearly equal incidence among males and females. Due to its characteristic overlap with conditions like tuberculous lymphadenitis and lymphoma, KFD remains an arduous diagnosis for physicians. Therefore, clinicians must remain vigilant and consider KFD as a potential diagnosis to prevent mismanagement. Histological studies are essential to exclude other possible causes of lymphadenopathy.⁸ Early recognition of disease is important to prevent complications.

Vinay Labroo, Sharique Ahmed, Sayani Bera, Madhura More. Kikuchi Disease in a Male: A Rare Case Report. MMJ. 2025, June. Vol 2 (2).

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Robotic-Assisted Excision of a Giant Presacral Mass Presenting as Urinary Retention

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Abstract:

Although presacral masses are uncommon, surgical resection is advised if they are identified, particularly in symptomatic patients. Additionally, there is a chance that the tumour could be malignant. Numerous surgical techniques, such as posterior, anterior, and combined abdominosacral approaches, have been documented for the resection of presacral tumours. Laparoscopic or robotic methods for resecting presacral masses are becoming increasingly common with the advent of minimally invasive techniques. Here, we present a unique case of a large presacral mass presenting with urinary retention and constipation. The mass was excised with robotic assistance. It was removed successfully without any concomitant injury to urinary bladder or rectum. The patient's urinary and bowel obstructive symptoms resolved immediately following surgery. Robotic-assisted excision of a presacral mass offers advantages, including enhanced magnified vision and improved instrument articulation.

Key words: Presacral Mass, Mature Teratoma, Urinary Retention.

Introduction

The majority of documented series on presacral masses and tumours are case reports, as these lesions are uncommon. Owing to the presence of various embryological remnants and distinct tissue types in the presacral region, a wide spectrum of tumour forms can develop. Presacral tumours are categorised into five groups based on their origin: congenital, inflammatory, neurogenic, osseous, and miscellaneous.¹ These tumours can be benign or malignant.² On magnetic resonance imaging (MRI), solid lesions indicate malignant characteristics.³ Most presacral tumours are discovered incidentally and do not exhibit any specific symptoms.⁴ Due to the possibility of growth or malignant change, surgical excision is advised upon diagnosis, in both symptomatic and asymptomatic patients.⁵

Numerous surgical techniques have been documented for the resection of presacral tumours. While posterior, anterior, and combined abdominosacral approaches are frequently used, transvaginal and transrectal techniques have also been used to resect presacral malignancies.

With the advent of minimally invasive surgery, laparoscopic and robotic methods for resecting presacral tumours are increasingly

being adopted for presacral tumour resection. Here, we describe a case of a presacral mass that was successfully excised using a robotic anterior approach.

Case Report

A 55-year-old woman presented to her physician with acute urinary retention. She was catheterised and underwent imaging. Ultrasound (USG) followed by computed tomography (CT) showed a 285-cc sized hypodense collection with enhancing wall in the presacral region, along with air foci within the collection (Figure 1A). The patient was planned for robotic excision of the pelvic mass via an anterior approach.

Initially, during dissection posterior to the rectum, the cyst could not be localised. A Romson 24-French abdominal drain tube was therefore inserted rectally to help demarcate the rectum and cyst boundaries. Once localised, the dissection planes became much clearer. The rectum and mesorectum were preserved during medial dissection (Figure 1B), and the presacral venous plexus was preserved posteriorly. Laterally, care was taken to avoid injury to the ureter and autonomic nerves. The distal dissection proved most challenging, as the uterus and other pelvic viscera, including the rectal wall, limited

visualisation of the dissection plane. To facilitate the procedure, the cyst was decompressed and its contents aspirated. Careful traction and counter-traction of the surgical plane was essential for achieving a successful bloodless dissection. The specimen was extracted through the right lower quadrant trocar site after extending the incision by about 3 cm (Figure 1C). The robotic resection was completed without significant intraoperative events. Histopathology confirmed the diagnosis of a mature cystic teratoma (Figure 1D). The patient was discharged home on postoperative day 3 without any complications.

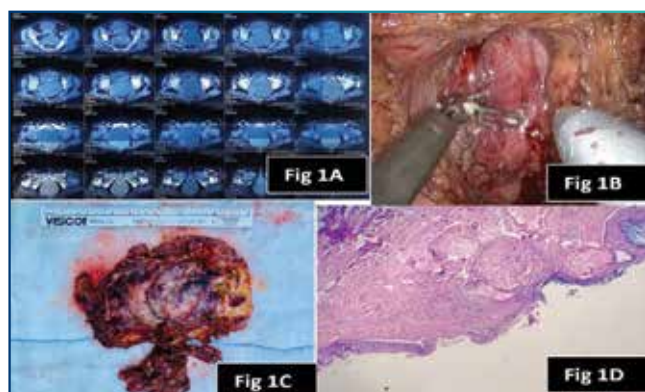


Figure 1A: Computed tomography (CT) images showing solid cystic mass in presacral region pushing the urinary bladder and rectum anteriorly. **Figure 1B:** Intraoperative picture showing the glistening anterior surface of the cyst wall. Rectum is seen pushed on left side. **Figure 1C:** Gross specimen showing the collapsed cyst with variegated consistency. **Figure 1D:** Histopathology with haematoxylin and eosin-stained sections, showing a cyst wall lined by stratified squamous and ciliated columnar epithelium, with the presence of skin adnexal structures, mature adipose tissue, and smooth muscle.

Discussion

A traditional technique that offered a short path of entry into the presacral area and adequate surgical access was the posterior approach, also known as the Kraske trans-sacral approach. However, division of the pelvic floor muscles and coccygectomy or sacrectomy could result in postoperative discomfort and a potential risk of faecal incontinence.⁶ For larger tumours extending downward to as low as S4 and upward as far as the sacral promontory, an abdominosacral approach is advised. When there is no nerve involvement and the tumour's inferior margin lies above S4, the anterior or abdominal approach is recommended.⁷ This approach allows excellent exposure of the ureters, pelvic autonomic nerves, and iliac arteries.⁸

Although the anterior approach often necessitates a long midline incision, the advent of minimally invasive techniques has enabled resection of presacral tumours using anterior robotic or laparoscopic techniques.⁹ Given the potential for malignant transformation, it is crucial to achieve complete resection of presacral masses.¹⁰ In summary, a laparoscopic anterior approach is both feasible and safe for the resection of presacral tumours. Care should be taken to avoid injury to vascular and neurological structures, visceral organs, or inadvertent perforation of the cystic lesion.¹¹ In this case, we employed the anterior robotic technique to successfully excise the presacral tumour.

Conclusion

The robotic anterior approach is a safe and viable option for the resection of presacral masses. It is important to avoid injury to vascular, neurological, and visceral organs. Presacral masses rarely present with urinary retention and constipation. This case was unique in that the patient presented with acute urinary retention. The robotic approach enabled superior delineation of the surrounding pelvic anatomy, thereby facilitating a precise and effective surgical resection.

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Extracorporeal Irradiation (ECI): An Overview

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Abstract:

Extracorporeal irradiation (ECI) of the bone is used in the management of malignant bone tumour (MBT). It consists of surgical removal of the tumour-bearing bone segment from the body followed by removal of the tumour and soft tissue from the bone followed by high dose irradiation of the bone and re-implantation of the sterile bone back into the body. Since radiation is delivered to the bone segment outside the body, the usual radiation-related side effects do not occur, resulting in better compliance. We report a case of ECI in the management of a malignant bone tumour and provide an overview of the ECI technique. Based on our study, ECI provides a viable alternative to amputation, enabling patients to preserve their limbs and maintain a good quality of life. Overall, ECI is a valuable treatment option for orthopaedic and radiation oncologists for managing primary MBTs with good functional outcomes and short-term survival rates.

Key words: ECI, Limbs Preservation Surgery, Autografts, Malignant Bone Tumour, Osteosarcoma.

Introduction

Radiation given outside the body to kill the tumour cells in the bone is called extracorporeal radiotherapy (ECRT).^{1,3} It is a method that is used in the management of malignant bone tumours (MBT). It was first reported by Spira *et al.* in 1968, where ECRT was used for the first time in management of MBT.^{1,2} Extracorporeal irradiation (ECI) consists of en-block resection of tumour bearing bone segment, removal of tumour from the bone, irradiation and reimplantation back into the body. Malignant bone tumours can be treated either with limb salvage surgery or by surgical amputation. Limb salvage surgery is a procedure that helps to preserve the limb by removing the part of bone involved with the tumour and the surrounding tissues. In the majority of cases treated with limb salvage surgery, biological methods of reconstruction are used, where the patient's own bone can be saved after irradiating it.

Material & Methods

MBT patients were studied, and patients with histopathological proof of malignancy and no evidence of distant metastases were considered suitable for limb preservation therapy (LPT). A clinical examination was done in detail by an orthopaedic surgeon, medical oncologist and radiation oncologist. All investigations such as haematological tests (e.g., liver function tests [LFTs], kidney function tests [KFT]), x-rays, computed

tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) scan were done according to a standardised protocol to assess the local extent of the disease and distant metastases.

During a single session of ECI, a dose of, 50 Gray (Gy) was delivered using 6 megavolt (MV) photon energy. Two parallel opposed antero-posterior fields were used. The radiation field size was chosen to ensure adequate coverage of the bone segment. The radiation duration was approximately 25-30 minutes.

Parameters defining the ECI treatment are:

Field size: X=8, Y=22.7

Gantry angle: 0° & 180°

Collimator angle: 0

Dose rate: 600 cGy/min

Monitor units (MU): 2446 MU

Energy: 6 MV Photon

Techniques of ECI

Limb preservation surgery was planned about four weeks after completion of the neoadjuvant chemotherapy. The size of the tumour was marked, and the amount of bone to be removed

was planned. Intraoperatively, the affected bone segment was removed, and frozen sections were taken from the proximal and distal ends of the bone. The resected specimen was then transferred to a separate sterile trolley under all aseptic precautions. The bone specimen was then washed with pulse lavage to remove all the soft tissues from the bone. Afterwards, tibia tumour bone was packed with vancomycin-soaked mops to reduce the risk of infection (Figure 1). The bone segment was tightly wrapped in multiple layers of drapes to avoid air gaps that would affect homogenous radiation dose delivery. The bone segment was sent to the radiotherapy department in a sterile condition.



Figure 1: Packing of the bone segment with vancomycin-soaked mops, wrapped in multiple layers in a sterile condition.

A dose of 50 Gy radiation was given during a 30-minute duration using 6 MV photons with parallel opposing fields to kill all the tumour cells (Figure 2). The segmented bone was transferred back to the operation theatre (OT) under sterile conditions. The bone was then reimplanted with fixation devices, with or without a vascularised autologous bone graft. The advantages of re-fixation with the same bone is that it provides an exact match to the resected bone which is now tumour-free.



Figure 2: The resected bone irradiated with 50 Gy for a duration of 25-30 minutes.

Discussion

MBTs are relatively rare but occur more frequently in children and adolescents because of their active skeletal growth.^{2,3} Due to recent advances in imaging, pathological, surgical techniques, chemotherapy and radiation therapy, management in most cases now favour limb preservation therapy (LPT) over amputation. The main aim of LPT is to completely resect the tumour and to maintain limb function. This involves reconstructive procedures by using either bone grafts or prosthesis.² ECI is a convenient and a cost-effective way of LPT.²⁻⁶ ECI involves *en bloc* removal of the tumour-affected bone segment, irradiation of the bone segment and reimplantation of the tumour free bone segment back in the body. This allows the delivery of very high doses of radiation to the tumour bed, which would otherwise not be possible. This high dose, ranging from 50-300 Gy is not only lethal to all tumour cells, but also diminishes the chances of recurrence.^{2,5-7} The other advantages of ECI include the ability to deploy an anatomically size-matched graft for reconstruction. It has a psychological advantage as the patient feels that their own bone is being used as prosthesis. It is also more cost-effective. ECI is now being used to treat primary malignant bone tumours like osteosarcomas — aggressive tumours that affect the metaphysis of long bones. In such cases ECI proves to be beneficial, especially when complete surgical resection of the disease cannot be done.^{8,9}

We had a histopathological proven case of MBT without any evidence of distant metastasis. The case was discussed in tumour board and planned for limb preservation treatment i.e., neoadjuvant chemotherapy followed by surgery along with ECI. The patient received a single high dose of 50 Gy of extracorporeal radiation by using 6 MV photon energy. The patient was followed for a period of five months, after which the metals plates were removed (Figure 3).



Figure 3: Postoperative follow-up after duration of five months and removal of metal plate.

Conclusion

ECRT is a new limb salvaging procedure that is increasingly being used. ECI has several advantages, including a precise anatomical fit of reimplanted bone segment, preservation of joint mobility, no issues of allograft rejection, less or no risk of disease transmission or immunological reaction, and ready availability of bone.⁶⁻⁸ Limitations of ECRT includes its unsuitability for bones that are structurally weak or have pathological fractures. Additionally, the overall duration of the surgery is increased. ECI is technically feasible in the management of MBT and provides decent local control and short-term survival rates. ECI is a convenient alternative to prosthesis from a health economic point of view. Further studies with larger sample sizes and longer follow-up periods are needed to improve our understanding of outcomes such as graft rejection rates, infection rates (including comparisons between ECI and prosthetic reconstruction), limb length discrepancies, and the patient's overall quality of life.¹⁰

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Emergency Pancreaticoduodenectomy in a Non-Trauma Setting: A Rare Procedure with Rare Indications – Case Report and Review of Literature

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Abstract:

Pancreaticoduodenectomy (PD) is a major procedure with high morbidity even in elective settings. Emergency pancreaticoduodenectomy (EPD) is a rare procedure, reported mostly for traumatic injury to pancreas, duodenum, or surrounding structures. It is an extremely rare procedure performed in a non-trauma setting, constituting 0.3%-3% of total PDs. EPD carries significant morbidity and mortality, thus presenting a major challenge for the surgeon and patient. The patients are in a compromised condition due to associated conditions such as sepsis, bleeding, malignancy, etc. Very few cases have been reported in the literature where EPD has been performed in these scenarios, with different methods of management and varying outcomes. We report one such case that was managed as a two-stage procedure and the patient recovered very smoothly.

Key words: Emergency Pancreaticoduodenectomy, Non-Traumatic, Staged Reconstruction.

Introduction

Pancreaticoduodenectomy (PD) is a technically complex procedure. The morbidity and mortality of the elective procedure has decreased in recent years, especially due to appropriate preoperative management, although morbidity rates remain high (30%-50%). Mortality has decreased considerably in elective settings (< 5%) due to good preoperative preparation and planning.^{1,2} Reported morbidity and mortality for emergency pancreaticoduodenectomy (EPD) are 50%-80% and 0%-40% respectively.³⁻⁶ The lack of such preoperative preparation makes EPD even more demanding and challenging. The technical complexity of EPD is amplified by other underlying factors, such as malignancies, local infection, blood loss, coagulation disorders, and a severely altered general condition.⁷ In this article, we present a case and discuss the indications and outcome of EPD in non-traumatic settings.

Case Report

A 50-year-old male presented with jaundice of recent onset to Max Super Speciality Hospital, Mohali. Evaluation revealed a mass in the ampullary region on contrast-enhanced computed tomography (CECT) of the abdomen (Figure 1). Side-viewing endoscopy revealed a large ulceroproliferative lesion at the ampulla (Figure 2). A biopsy was taken from the lesion. Post-procedure, the patient developed hypotension with passage of blood in the stool. Relook endoscopy revealed bleeding from the lesion. Endoscopic and interventional radiology control of bleeding were attempted but failed. The patient's condition continued to deteriorate despite adequate blood transfusion and being on triple inotropic support.



Figure 1: Contrast-enhanced computed tomography (CECT) of the abdomen showing ampullary mass.



Figure 2: Endoscopy showing a proliferative lesion at ampulla with stent in situ.

The only option left to control bleeding was surgery, which entailed PD. As the patient was very sick, with haemoglobin of 3 gm% and on triple inotropes, surgery itself was extremely high risk. After counselling relatives and obtaining informed consent, the patient was taken up for surgery.

EPD was performed. As the patient was sick and there was considerable bowel wall oedema due to resuscitative efforts, it was decided to perform reconstruction as a staged procedure. The common bile duct (CBD) and pancreatic duct were cannulated and exteriorised. The stomach was closed with a stapler. The abdomen was left open as a laparostomy and covered with sterile dressings. The patient was shifted back to the intensive care unit (ICU) on a ventilator and stabilised by infusing blood products. He was taken up for reconstruction on postoperative day 3 after he had remained stable for a continuous 24 hours without inotropes.

Reconstruction was done by duct-to-mucosa pancreaticojejunostomy (PJ), end-to-side hepaticojejunostomy, and end-to-side gastrojejunostomy. A feeding jejunostomy was performed to start feeding as soon as possible after surgery. The abdomen was closed. He recovered well after reconstructive surgery and was extubated after 2 days. Jejunojejunal (JJ) feed was started from day 1 after surgery, and oral diet was started on day 3. He made a very good recovery without any complications except for a wound infection, which was managed with local dressings. He was discharged from the hospital on day 7 after reconstructive surgery. Biopsy revealed villous adenoma with low-grade dysplasia.

Discussion

EPD in non-traumatic settings is rare, and very few cases, either as isolated case reports or small case series, have been reported. EPD in non-traumatic settings has been reported in 0.3%-3% of total PD series.⁴

EPD is usually classified as either traumatic or non-traumatic in origin. Non-traumatic causes are further classified as uncontrolled bleeding, perforation, ischaemia, and iatrogenic injuries. Uncontrolled bleeding seems to be the most common cause for EPD, followed by perforation due to endoscopy, surgery, or tumour.⁴ Morbidity and mortality for EPD in non-traumatic settings has been reported to be around 50%-80% and 0%-40% respectively.³⁻⁶ This increased morbidity and mortality has been attributed to a lack of preoperative preparation and the sick general condition of the patient at the time of surgery. The technical complexity of EPD is amplified by other underlying factors, such as malignancies, local infection, blood loss, coagulation disorders, and a severely altered general condition.⁷ Postoperative pancreatic fistula (POPF) has been reported as the main cause of morbidity in elective PD. POPF and sepsis remains the main cause of morbidity and mortality in EPD. In the analysis of a 66-patient cohort, Poca *et al.* found a morbidity rate of 62%, POPF rate of 21.21%, blood loss of 800 mL, and a length of hospital stay of 27 days for EPD.^{8,9} It has also been reported that morbidity and mortality are affected by the indication for EPD. Patients suffering from perforation undergoing EPDs had a significantly higher association with surgical mortality than those suffering from bleeding.⁴

There are differences of opinion regarding the management of the pancreatic stump. A two-stage PD with delayed fashioning of PJ has been advocated to bridge severely ill patients in emergency settings and avoid POPF development.³ However, a study has shown that there is no difference in mortality between one-stage and two-stage EPD for haemodynamically unstable trauma patients.¹⁰ Few studies have advocated pancreaticogastrostomy to drain a soft pancreas with a non-dilated duct where the jejunum is unsuitable for anastomosis due to oedema, making PJ anastomosis technically demanding.^{6,7} Other methods of managing the pancreatic stump include primary closure of the stump or tube drainage of the pancreatic duct, thus forming an external pancreatostomy. These procedures were done in unfavourable circumstances.^{8,9}

Although there is increased morbidity and mortality, EPD is still justified in desperate, life-threatening situations to save a patient's life. The involvement of experienced hepatopancreatobiliary (HBP) surgeons, the indication for operation, and timely surgery are important for optimal surgical outcomes. Long-term survival is possible if complications and POPF can be successfully managed in the early postoperative period.

Conclusion

EPD is a formidable, lifesaving operation reserved for pancreaticoduodenal trauma, perforations, and bleeding not manageable by a less invasive approach. It is a rare operation that carries a higher morbidity and mortality than elective PD. It is performed in desperate, life-threatening situations and can be a life-saving measure in most cases, as shown in the literature.

Manmohan Singh Bedi, Amrit Suman. Emergency Pancreaticoduodenectomy in a Non-Trauma Setting: A Rare Procedure with Rare Indications – Case Report and Review of Literature. MMJ. 2025, June. Vol 2 (2).

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Unilateral Biportal Endoscopy: A Modern Shift in Endoscopic Spine Surgery Techniques

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Abstract:

Minimally invasive spine surgery (MISS) has undergone a paradigm shift with the advent of unilateral biportal endoscopy (UBE), a technique that marries the principles of conventional open spine surgery with modern endoscopic innovation. At our centre, we recently initiated a UBE spine surgery programme to expand our minimally invasive capabilities. In our initial experience, ten patients underwent successful UBE procedures, including discectomy, unilateral laminectomy for bilateral decompression (ULBD), and transforaminal lumbar interbody fusion (TLIF). Patients demonstrated excellent clinical outcomes, with minimal blood loss, early mobilisation, and short hospital stays. Two illustrative cases highlight the efficacy of UBE in both elective and emergency settings. The first involved a patient with degenerative disc disease managed with UBE-TLIF, while the second showcased urgent decompression for cauda equina syndrome due to a large disc herniation. Our early results affirm the safety, versatility, and effectiveness of the UBE technique in managing diverse lumbar pathologies with minimal morbidity and rapid recovery.

Key words: Unilateral Biportal Endoscopy, Discectomy, Transforaminal Lumbar Interbody Fusion, Radiculopathy, Endoscopic Discectomy.

Introduction

Endoscopic spine surgery is evolving rapidly, offering patients less invasive options with faster recovery and excellent outcomes.¹⁻⁴ In recent years, unilateral biportal endoscopy (UBE) has emerged as a prominent technique in addressing lumbar degenerative diseases and other spinal pathologies. It is widely acknowledged for its advantages, including a wide surgical field, greater operative flexibility, minimal tissue damage, efficient neural decompression, and faster postoperative recovery.⁵⁻¹⁰ At our centre, we have recently embraced this cutting-edge technique by initiating our endoscopic spine surgery program, with a focus on UBE spine surgery.

Within a short span, we have successfully performed ten endoscopic spine procedures, showcasing our growing proficiency and commitment to minimally invasive solutions (Table 1).

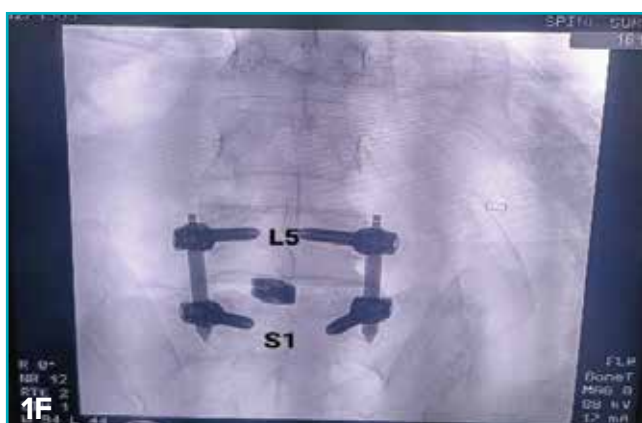
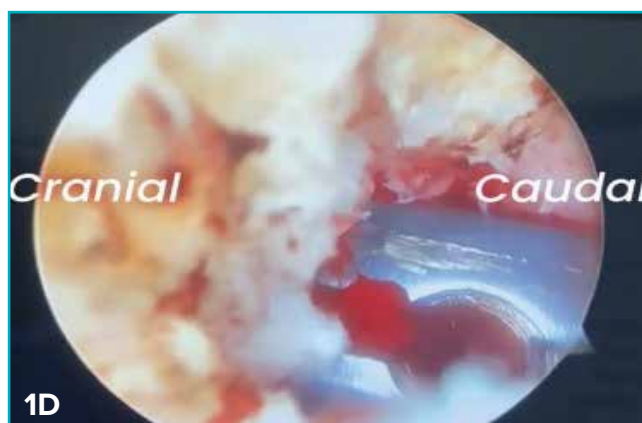
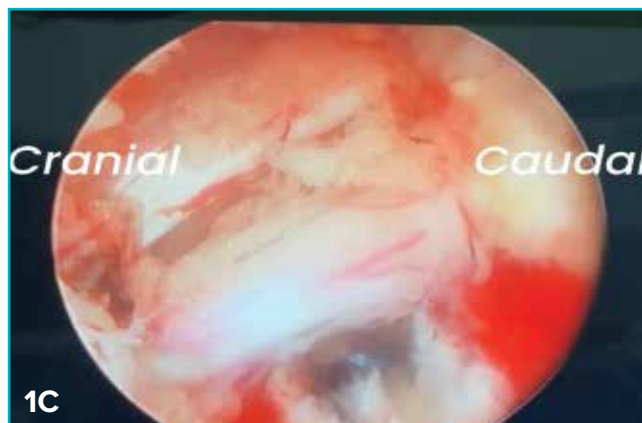
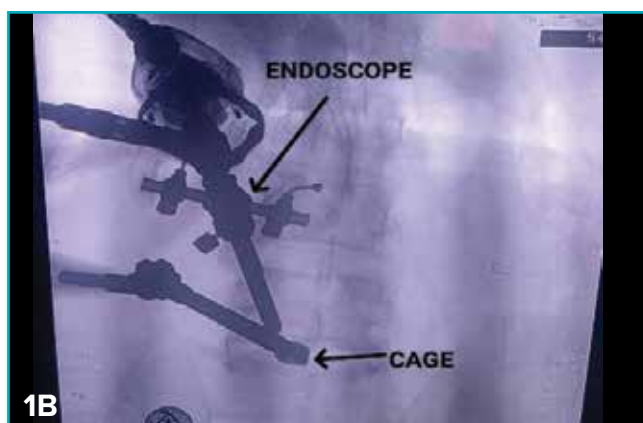
Unilateral biportal endoscopy (UBE) - Procedures	Number of cases
UBE-Transforaminal lumbar interbody fusion (TLIF)	1
UBE-Discectomy	6
UBE-Unilateral laminectomy for bilateral decompression (ULBD)	3
Total	10

Table 1: Overview of unilateral biportal endoscopy (UBE) procedures performed.

All patients experienced smooth post-operative recovery, with minimal blood loss, early mobilisation, and excellent clinical outcomes. This success reflects the promising future of UBE as a safe, effective, and patient-friendly technique for managing various spinal pathologies.

Case Report: 1

A 47-year-old male presented to our spine department with complaints of severe lower back pain for the past several months. The pain was progressive, aggravated by activity, and unrelieved by conservative measures such as physiotherapy, analgesics, and rest. Neurological examination was intact, with no motor or sensory deficits. The straight leg raise test was negative bilaterally. There were no signs of bladder or bowel involvement. Magnetic resonance imaging (MRI) of the lumbosacral spine revealed degenerative disc disease at the L5-S1 level with Modic changes, reduced disc height, and endplate irregularity. A UBE-transforaminal lumbar interbody fusion (TLIF) was planned and successfully performed at L5-S1 (Figure 1A-G). The patient was mobilised on the same day of surgery. He reported immediate relief from pre-operative back pain, and there were no neurological deficits post-operatively. Blood loss was minimal, and there were no intraoperative complications. The patient was discharged the next day in a stable condition, with appropriate pain management and post-operative instructions.



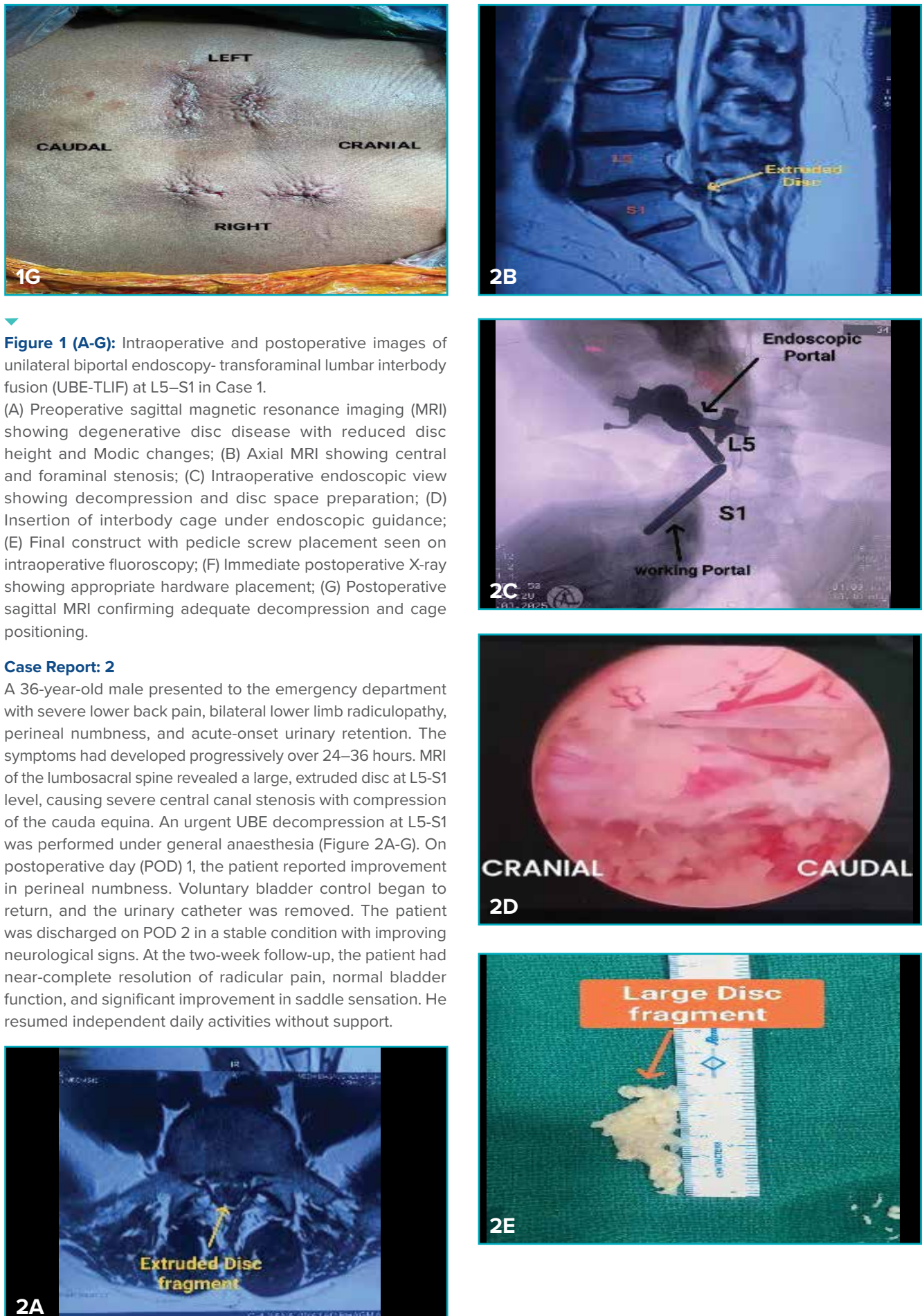




Figure 2 (A-G): Imaging and intraoperative visuals of emergency unilateral biportal endoscopy (UBE) decompression in Case 2 with cauda equina syndrome.

(A) Preoperative sagittal magnetic resonance imaging (MRI) showing a large extruded L5–S1 disc causing severe central canal stenosis; (B) Axial MRI highlighting nerve root compression and cauda equina crowding; (C) Endoscopic image showing herniated disc fragment; (D) Removal of disc material under direct visualisation; (E) Decompressed thecal sac and nerve roots visible endoscopically; (F) Postoperative axial MRI demonstrating relieved compression; (G) Postoperative sagittal MRI confirming decompression of the thecal sac.

Discussion

Our initial experience with UBE spine surgery at a single centre has shown promising results across a variety of lumbar pathologies. In our series of ten cases—including UBE discectomy, ULBD, and TLIF—patients demonstrated excellent clinical outcomes, minimal post-operative pain, early mobilisation, and short hospital stays. The UBE technique provided clear visualisation, effective decompression, and preservation of surrounding anatomical structures, supporting its role as a safe, versatile, and minimally invasive alternative to conventional spine surgery (Table 2).¹¹⁻¹⁶ With continued experience and refinement, UBE is poised to become an integral part of modern spinal care. As we continue to expand our expertise, we believe UBE will play a central role in transforming the landscape of spine surgery (Figure 3A-C)

Key Advantages of UBE Spine Surgery

1	Minimally invasive	Smaller incisions and minimal tissue disruption reduce post-operative pain and hospital stay.
2	Wider field of view	The biportal technique offers excellent visualisation of neural structures
3	Faster recovery	Patients mobilise early and return to routine activities sooner than with conventional surgery.
4	Versatile applications	Suitable for discectomy, decompression, and selected fusion procedures.
5	Preservation of anatomy	Less trauma to muscle and bone compared to open surgery, preserving spinal integrity

Table 2: Five key advantages of unilateral biportal endoscopy (UBE) endoscopic spine surgery.





◀ **Figure 3 (A-C):** Schematic representation of key advantages of unilateral biportal endoscopy (UBE).

(A) Minimal invasiveness with small incisions and muscle-sparing approach; (B) Enhanced visualisation due to dual portal technique allowing better access to pathology; (C) Versatile application enabling discectomy, decompression, and fusion with faster recovery and preservation of spinal anatomy

Conclusion

UBE signifies a modern leap in minimally invasive spine surgery. By combining the familiarity of open surgical instruments with the precision of endoscopic visualisation, UBE offers a versatile, muscle-sparing, and effective method for treating a wide range of spinal disorders. Its cost-effectiveness and adaptability make it particularly valuable in resource-limited settings, offering high-quality care without prohibitive expenses. UBE is set to define the future of spinal decompression and possibly fusion techniques. Structured training and ongoing research will be essential to realise its full potential and refine its scope of application.

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A Rare Case of Female Urethral Carcinoma Treated with an In-house Developed Intra-Vaginal Brachytherapy Cylinder

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Abstract:

Primary tumours of the female urethra are rare and account for less than 0.02% of malignant diseases in women. Management varies depending on the clinical stage and location of the lesion. Currently, there are no randomised studies to guide treatment of this disease. The purpose of this study is to report a case of squamous cell carcinoma (SCC) of the distal urethra (cT3N0M0) in a female, treated using an in-house developed, reusable, six channel vaginal brachytherapy cylinder. A 11 x 12 x 8 mm tumour, involving the anterior vagina and posterior urethral wall at the level of the external urethral meatus, was treated with 45 Gray (Gy) in 25 fractions to the gross disease and regional lymph nodes using external beam radiotherapy (EBRT), followed by intra-vaginal brachytherapy (IVBT) as a minimally invasive procedure. An IVBT planning scan was performed with a Foley catheter in situ, and contrast was instilled into the bladder to displace the anterior urethral wall and bladder away from the target. An in-house developed six-channel applicator was used to deliver a targeted brachytherapy dose of 3 Gy per fraction (to a depth of 1.3 cm) for six fractions. The patient tolerated the procedure well, without significant side effects. Response assessment, conducted two months post-treatment using contrast-enhanced magnetic resonance imaging (CE-MRI), showed complete resolution of disease. The peripheral needle placement allowed for asymmetric dose shaping to adequately cover the target while minimising exposure to organs at risk. The use of commercially available multi-channel applicators is often limited by cost. However, our low-cost, in-house developed, multi-channel vaginal cylinder is reusable and can be applied across various clinical cases.

Key words: Brachytherapy, Multichannel Brachytherapy, Intra-Vaginal Cylinder, Carcinoma Urethra.

Introduction

Primary urethral carcinomas are exceedingly rare, more prevalent among men than in women, and account for less than 1% of all genitourinary malignancies.¹ Among neoplasms of the female urethra, the majority (38%-46.7%) are adenocarcinomas. Less common histological types include squamous cell carcinoma (SCC; 25.4%-28%), urothelial carcinoma (24.9%-28%) and other variants (6%).²

Clinical management varies depending on the clinical stage and location of the lesion. To date, no prospective randomised studies exist to guide treatment. Both surgery and radiotherapy (RT) have been advocated as effective treatment modalities for early-stage urethral cancers. Tumours arising from the distal urethra are generally diagnosed at an early stage and have high cure rates. However, knowledge about this rare disease

remains limited, and most available data derive from individual case reports. We therefore present our case of female urethral carcinoma treated with RT.

Case Report

A 72-year-old woman presented with dysuria and a burning sensation in the urethra. Clinical examination revealed a nodular lesion at the posterior aspect of the urethral meatus. The mass was palpable both at the urethral meatus and in the distal urethra on vaginal examination. Suspicion of anterior vaginal wall involvement was noted, but no palpable inguinal lymphadenopathy was present (Figure 1). A contrast-enhanced magnetic resonance imaging (CE-MRI) scan of the pelvis showed a small, well-defined, T2 hyperintense cystic lesion (measuring 11 x 12 x 8 mm) in the left anterolateral aspect of the vagina, located below the level of pubic symphysis and at the level of the

external urethral meatus. The lesion showed internal diffusion restriction and thin peripheral post-contrast enhancement (Figure 2). A biopsy was performed, and histopathology was suggestive of SCC. A whole body 18-fluorodeoxy-glucose (FDG) positron emission tomography-computed tomography (PET-CT) scan was done to rule out metastatic disease. It showed FDG-avid, mildly ill-defined thickening with a maximum standardised uptake value (SUVmax) of 8.1 in the distal vaginal canal, with no other abnormal hypermetabolic foci elsewhere in the body. The tumour was clinically staged as cT3N0M0,



Figure 1: Pre-treatment clinical image of the urethral meatus (lesion visible in posterior wall).

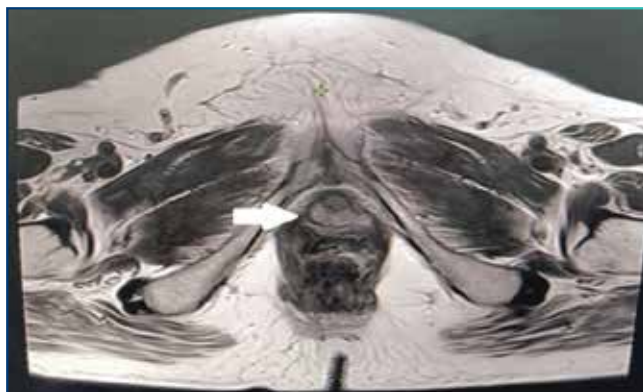


Figure 2: Pre-treatment axial section of T2-weighted magnetic resonance image of lesion (marked with arrow) in posterior urethra.

The case was discussed by a tumour board, and in view of the patient's age and tumour stage, the consensus recommendation was to proceed with definitive RT. The patient received external beam radiotherapy (EBRT) to the gross tumour and regional lymph nodes with a total dose of 45 Gy delivered in 25 fractions (1.8 Gy per fraction) using image-guided intensity modulated radiation therapy (IGRT).

This was followed by intra-vaginal brachytherapy (IVBT). For optimal organ sparing, a planning scan was performed with a Foley catheter in situ and contrast introduced

into the bladder to visualise and displace the anterior urethral wall and bladder away from the treatment field (Figure 3). A custom-designed, in-house developed six-channel applicator was used to deliver a targeted brachytherapy dose of 3 Gray (Gy) per fraction to a depth of 1.3 cm, delivered twice daily, at least 6 hours apart for a total of six fractions over three days. This applicator enabled differential dosing to the target volume while minimising exposure to the rectum and posterior vaginal wall (Figure 3). The patient tolerated the procedure well, without any significant side effects. The dose received by 2 cc volumes of the bladder and rectum was 0.7 Gy and 1.5 Gy per fraction, respectively. A total of 95% of the clinical target volume received 97% of the prescribed dose.

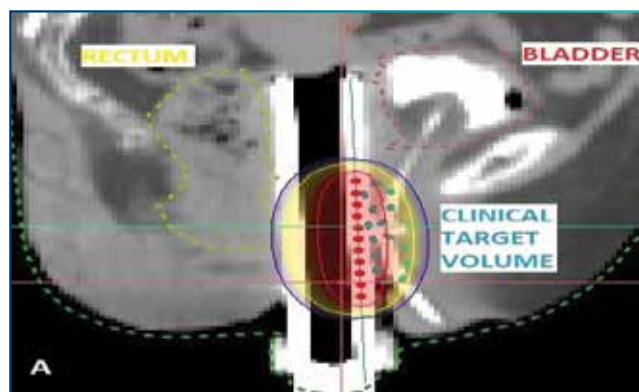


Figure 3: (A) Planned treatment isodose lines (75% – dark blue, 100% – yellow, 200% – red) covering the clinical target volume (dotted blue line) and sparing of the rectum (dotted yellow) and bladder (dotted red); (B and C) In-house developed six-channel intravaginal brachytherapy cylinder (B) Individual components; (C) Assembled cylinder.

Two months post-treatment, CE-MRI (Figure 4) showed a significant response to therapy, with no diffusion restriction noted in the urethral region, indicating a complete response. On clinical examination, no lesion was visible or palpable at the urethral meatus (Figure 5).

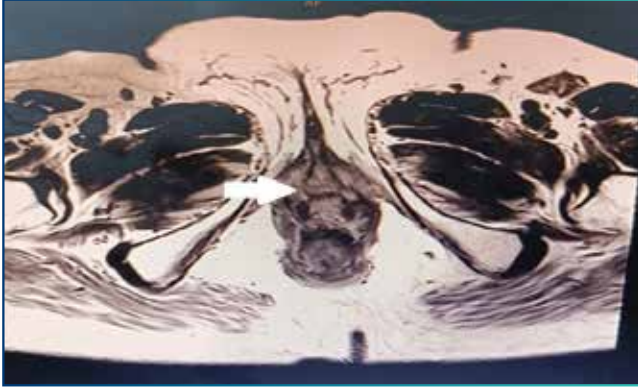


Figure 4: Post-treatment axial section of T2-weighted magnetic resonance image showing complete resolution of lesion (arrow marking pre-treatment disease location).



Figure 5: Post-treatment clinical image of the posterior urethral meatus (no visible lesion).

Discussion

The primary urethral carcinoma in females is a rare disease, with adenocarcinoma being the most common histological type, followed by SCC.² Symptoms of female urethral carcinoma are varied, and the carcinoma initially spreads by local invasion into the periurethral tissue, vagina, vulva, and proximally to the bladder neck.³ Lymphatic drainage from the proximal urethra is to the obturator and internal iliac group of lymph nodes, while drainage from the distal urethra is to the inguinal group of lymph nodes. Up to 30% of patients have clinically palpable lymph nodes, and over 90% of these are metastatic. Distant metastasis is uncommon.³ Biopsy may be performed cystoscopically or transvaginally with a needle.

MRI is commonly used for staging, and treatment is determined by the stage at initial presentation. Bracken *et al.* observed 81 cases of female urethral carcinoma and found that patients with large tumours (> 4 cm) had a lower 5-year survival rate (13%) compared to patients with small tumours (< 2 cm, 60%).⁴ Given the poor prognosis associated with this cancer, knowledge of prognostic factors is essential.

Due to its rarity, establishing a definitive treatment strategy is challenging. A multimodal therapy approach which includes definitive surgery plus chemotherapy and RT is generally recommended. However, RT is an alternative to surgery in locally advanced disease, with comparable survival rates⁵ as shown in a large retrospective, registry-based study. The authors support the use of definitive RT (with or without chemotherapy) as a treatment option for organ preservation in well-selected patients.⁶ The addition of brachytherapy (BT) to RT reduces the risk of local recurrence,⁷ and in our case, the use of a six-channel IVBT cylinder allowed for differential dose distribution. This allowed for dose escalation to the target area while minimising radiation to the adjacent organs, as compared to a standard single-channel applicator.

Conclusion

Although female urethral carcinoma is a rare disease entity, clinicians should maintain a high index of suspicion for malignancy in patients with relevant symptoms to make an accurate diagnosis. Careful clinical examination and imaging studies are helpful for confirming the diagnosis. Although there is no established standard therapy, RT combined with BT may be considered as an effective organ-preserving treatment option.

Rashi Agrawal, Nelesh Aggarwal, Balasubramanian S, Deepak Arora. A Rare Case of Female Urethral Carcinoma Treated with an In-house Developed Intra-Vaginal Brachytherapy Cylinder. MMJ. 2025, June.

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Unmasking a Silent Giant: Complicated Resection of a Retroperitoneal Ganglioneuroma

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Abstract:

Ganglioneuromas are rare benign tumors arising from sympathetic neural crest cells, typically detected incidentally or due to compressive symptoms. Proximity to retroperitoneal vasculature complicates management.

A 28-year-old female presented with progressive abdominal pain, fullness, and backache. Imaging revealed a large retroperitoneal lobulated lesion around the coeliac axis extending into the right suprarenal region, encasing the hepatic artery. Biopsy confirmed a ganglioneuroma. After being denied surgery initially due to operative risks, she underwent successful surgical excision at a tertiary centre. The mass was dissected from the hepatic artery, coeliac axis, portal vein, pancreas, and IVC via midline laparotomy with Kocherization.

Complete resection of retroperitoneal ganglioneuroma, though surgically challenging due to vascular encasement, is feasible and curative with meticulous dissection and multidisciplinary expertise.

Key words: Ganglioneuroma, Sympathetic Neural Crest Cells, Retroperitoneal.

Introduction

Ganglioneuromas (GN) are benign, differentiated tumours arising from sympathetic ganglion cells and Schwann cells. Representing the benign end of the neuroblastic tumour spectrum, they are most commonly located in the posterior mediastinum and retroperitoneum. Due to their slow growth, symptoms typically present late when the mass becomes sizable or causes compression of adjacent structures.

Surgical excision remains the gold standard for treatment. However, involvement of major vascular structures such as the hepatic artery, portal vein, or inferior vena cava can increase surgical complexity and risk.¹

This report describes a case of a large retroperitoneal GN encasing the hepatic artery in a young adult female, managed successfully through complex surgery.

Case Report

A 28-year-old female presented to a government hospital with a six-month history of progressive abdominal pain, upper abdominal fullness, and dull backache. She had no significant medical history or systemic complaints. Physical examination was unremarkable apart from upper abdominal tenderness. Routine laboratory parameters were within normal limits. Computed tomography (CT) scan of the abdomen revealed a large, lobulated lesion measuring 116 x 53 x 97 mm with enhancing septations and calcific foci, situated in the right suprarenal region. The lesion encased the hepatic artery anteriorly and displaced adjacent vascular and visceral structures, including the coeliac axis, portal vein, pancreas, and inferior vena cava (Figure 1).

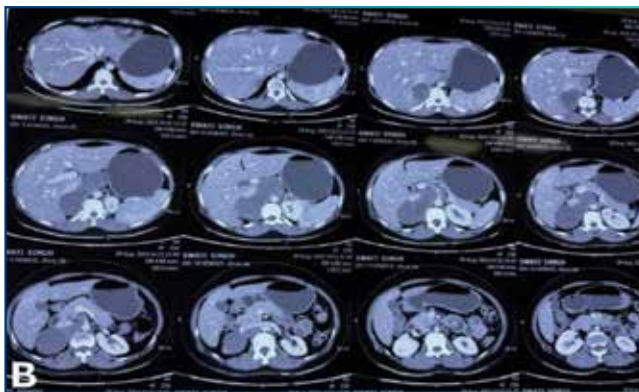
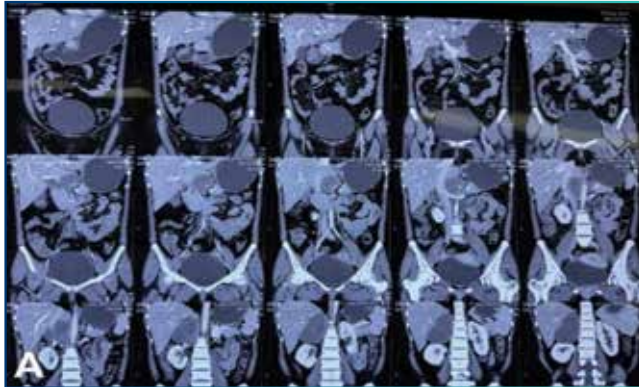


Figure 1: Contrast-enhanced CT showing a lobulated retroperitoneal mass encasing the hepatic artery. (A) Coronal view. (B) Axial view.

An image-guided core needle biopsy was performed, and histopathology revealed mature ganglion cells within a Schwannian stroma, confirming the diagnosis of GN. Due to extensive vascular involvement and the risk of intraoperative haemorrhage, the patient was denied surgical treatment at the initial government facility.

Seeking further management, she presented to Max Super Specialty Hospital, Lucknow, where a multidisciplinary tumour board recommended surgical excision.

Surgical Procedure

A midline laparotomy with full Kocherisation was performed. Intraoperatively, the mass was found arising near the coeliac axis, extending laterally below the pancreas and portal vein, and reaching below the inferior vena cava. It was noted to encase the hepatic artery anteriorly (Figure 2A).



Figure 2A: Intraoperative image showing the lobulated retroperitoneal mass.

Key surgical steps followed were:

1. Dissection of the portal structures and hepatic artery up to the coeliac axis.
2. Mobilisation between the mass and superior border of the pancreas and the superior mesenteric artery.
3. Dissection of the mass away from the lesser sac and retro-pancreatic space.
4. Mobilisation of the remaining mass from the inferior vena cava.

The surgery lasted four hours with an estimated blood loss of 150 mL.

Histopathology

Gross examination of the excised specimen showed a lobulated, firm, grey-white mass (Figure 2B).



Figure 2B: Resected lobulated, grey, firm mass.

Microscopy revealed well-circumscribed tumor tissue with Schwann cells and scattered ganglion cells. Schwann cells displayed spindle-shaped morphology with elongated, bland nuclei and loose, fibrillary, homogenous, eosinophilic cytoplasm. Ganglion cells, on the other hand, were mature, exhibiting a single eccentric round nucleus, a prominent nucleolus, and compact, granular, eosinophilic cytoplasm, with some showing occasional pigment deposition. No naked neuropil, neuroblastic foci, atypia, or mitoses were present (Figure 3). Final diagnosis: Maturing ganglioneuroma (Schwannian stroma-predominant).

The patient had an uneventful postoperative recovery and was discharged on the ninth postoperative day.

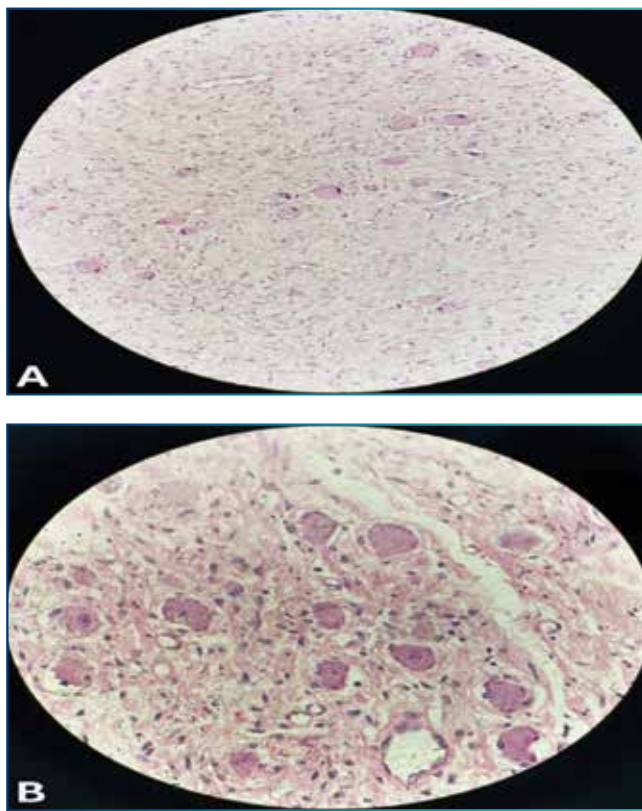


Figure 3: Mature ganglion cells and Schwannian stroma consistent with ganglioneuroma. (A) Tissue section (H & E x20). (B) Tissue section (H & E x40).

Discussion

Neuroblastic tumours (NTs) are the most common solid neoplasms of childhood, arising from primordial neural crest cells located in the sympathetic ganglia and adrenal medulla. The vast majority of them are sporadic. NTs are divided into three categories: neuroblastomas, ganglioneuroblastomas, and GN. GNs typically present in the fourth or fifth decade of life. They are most commonly found in the retroperitoneal space (32%-52%) and the posterior mediastinum (39%-43%), with less frequent occurrences in the cervical region (8%-9%).² Unlike other neuroblastic tumours, GNs are generally hormonally silent and are often diagnosed incidentally on radiography, or present as a large mass with symptoms of compression.^{3,4} According to the International Neuroblastoma Pathology Classification (INPC), GNs are subtyped into GN, maturing and GN, mature.⁵ The GN, maturing subtype was formerly classified as “stroma-rich, well-differentiated NT” in the original Shimada classification. GN, mature subtype is the prototypic GN of traditional classification schemes. Less than 30% of these tumours occur in the adrenal glands and are usually asymptomatic. The remainder develops in the posterior compartment of the mediastinum, retroperitoneum, and other sites. Rarely, they can be associated with hypertension, watery diarrhoea, and hypokalaemia or masculinisation.⁶

CT and magnetic resonance imaging (MRI) play pivotal roles in preoperative assessment, delineating the extent of vascular involvement, which critically influences surgical planning. Characteristically, these tumours appear as well-defined, lobulated masses with homogeneous or heterogeneous enhancement and may contain calcifications.^{4,7}

Histopathological confirmation is mandatory, with biopsy demonstrating mature ganglion cells within a Schwannian stroma and absence of immature neuroblastic elements.^{1,5,8}

Surgical excision remains the cornerstone of treatment. Cases involving major vascular encasement require advanced surgical expertise and careful intraoperative dissection to prevent catastrophic bleeding and preserve vital vascular anatomy.¹

This case underscores the feasibility of complete excision even in complex presentations with vascular involvement, highlighting the role of multidisciplinary care in achieving optimal outcomes.

Chakradhar Singh, Shashank Chaudhary, Anju Shukla. Unmasking a Silent Giant: Complicated Resection of a Retroperitoneal Ganglioneuroma. MMJ. 2025, June. Vol 2 (2).

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Rituximab for Thrombotic Thrombocytopenic Purpura: A Case Report

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Abstract:

Thrombotic thrombocytopenic purpura (TTP) is a rare thrombotic microangiopathy (TMA). The diagnosis is difficult and can be easily missed. TTP is an emergency condition, and its treatment must not be delayed once a diagnosis is established. Delays in treatment may result in significant morbidity and mortality. There has been a significant reduction in the mortality rate following the emergence of plasma exchange therapy. However, a high rate of recurrence has been noted in those who have achieved remission. Patients who fail to respond to plasma exchange therapy may respond to various other drugs. One such drug is rituximab, which is an anti-CD20 antibody that depletes B cells.

We present a case of a 38-year-old man with anaemia, thrombocytopenia, elevated creatinine, increased lactate dehydrogenase (LDH), seizures, and schistocytes in the peripheral smear, which favoured TTP. The absence of a disintegrin and metalloproteinase with thrombospondin motifs 13 (ADAMTS13) levels confirmed TTP. The patient responded to rituximab therapy and was cured of TTP.

TTP is a relatively uncommon condition with the potential to develop serious consequences leading to mortality. Early diagnosis and treatment are essential to avoid this. In our case, due to the early diagnosis and therapy, the patient was cured of the dreadful disease.

Key words: Thrombotic Thrombocytopenic Purpura (TTP), ADAMTS13 Deficiency, Rituximab, Plasma Exchange Therapy, Microangiopathic Haemolytic Anaemia (MAHA), PLASMIC Score.

Introduction

Thrombotic thrombocytopenic purpura (TTP) is a rare thrombotic microangiopathy (TMA) characterised by von Willebrand factor (VWF)-platelet-rich hyaline thrombi that develop in the arterioles and capillaries of the affected individual. It is a relatively uncommon condition with the potential to develop serious consequences affecting the brain, pancreas, kidney, and heart, amongst other organs.¹ The diagnosis of TTP is confirmed when the patient presents with at least three of the following symptoms: microangiopathic haemolytic anaemia (MAHA), thrombocytopenia, neurological phenomena (stroke or seizures), fever, and end-organ damage.^{2,3} The most common triggers for TTP include viral or bacterial infections, malignancy, and autoimmune diseases.⁴ Complications arising from cardiac or neurological abnormalities are the most common cause of mortality in these patients. The mortality rate from TTP has decreased drastically from > 90% to < 10%-30% after the emergence of plasma exchange therapy.⁵ However, a high rate of recurrence has been noted in those who have

achieved remission.^{6,7} A few patients may even present with multiple relapses requiring numerous sessions of plasma exchange therapy, which can be costly and may even lead to complications such as thrombosis, infections, and other reactions to transfusion.

A few patients fail to respond and achieve remission on plasma exchange therapy. These patients may show a response to corticosteroids, cyclophosphamide, azathioprine, vincristine, high-dose intravenous immunoglobulin, staphylococcal protein A immunoadsorption, cyclosporine A, and/or splenectomy.⁸⁻¹¹

TTP results from the inhibition of the VWF-cleaving protease, a disintegrin and metalloproteinase with thrombospondin motifs 13 (ADAMTS13), a member of a family of proteases with a disintegrin-like and metalloproteinase with thrombospondin type 1 motifs.¹²

Studies in the past have reported an association between the subset of thrombotic MAHA with the deficiency of ADAMTS13. The pathogenesis of TTP may involve a deficiency of ADAMTS13.¹³⁻¹⁶ In adults, immunoglobulin (Ig) autoantibody against the ADAMTS13 enzyme is usually the cause of ADAMTS13 deficiency.^{15,16} Immunosuppressive therapy may be useful in these cases due to this autoimmune cause.

Rituximab is an anti-CD20 antibody that depletes B cells in the lymphoid tissue as well as in the circulation. It is known to be effective in the treatment of numerous antibody-mediated autoimmune diseases, including autoimmune thrombocytopenia.^{17,18}

Case Report

A 38-year-old man presented with fatigue, lethargy, and headache. A detailed blood work-up revealed very low vitamin B12 levels of < 50 ng/mL. He was prescribed intramuscular injections of vitamin B12 1000 mcg on alternate days. After the 3rd injection, he developed a haematoma at the injection site. His injections were immediately stopped, and he was started on sublingual vitamin B12. After 4 months, he presented with a severe headache for the last 10-15 days. While he was being evaluated for a headache, after 2 weeks, he had an episode of recurrent vomiting associated with weakness over the left half of his body with motor power of 3/5. His blood reports revealed a low platelet count of 11,000/mm³, elevated serum creatinine of 1.8 mg/dL, and low haemoglobin of 9 gm/dL. He refused a magnetic resonance imaging (MRI) of the brain because of severe claustrophobia. The haematologist advised a change in treatment strategy in view of anaemia, thrombocytopenia, elevated creatinine, increased lactate dehydrogenase (LDH), seizures, and schistocytes in the peripheral smear, which favoured TTP. The absence of ADAMTS13 levels confirmed TTP. The high-risk nature of the disease was explained to the relatives. The patient underwent three plasmapheresis sessions on alternate days along with intravenous methylprednisolone and rituximab. The patient responded with a satisfactory complete blood count (CBC) and no further requirement of packed cells and platelet transfusion. The patient was extubated and discharged in a very stable condition with normal laboratory tests. He was given two more doses of rituximab and steroids weekly. TTP is a dreadful disease with a poor outcome, but if diagnosed and treated early, it can also be cured.

Discussion

The incidence of TTP is estimated to be around 2 per million per year.¹⁹ The most commonly affected age group is the fourth decade of life, and women are more likely to be affected compared to men.²⁰ TTP usually occurs in its secondary form in association with various predisposing factors, including malignancy, infection (e.g. human immunodeficiency virus [HIV]), autoimmune diseases (e.g. systemic lupus erythematosus), certain drugs, and pregnancy. Primary TTP without any predisposing factors is usually rare, which makes it extremely difficult to diagnose.

Diagnosis of TTP

TTP must be suspected in any patient who presents with MAHA and thrombocytopenia, as these are the hallmarks of TTP.^{19,21} This is a form of haemolytic anaemia that presents with schistocytes or red blood cell fragments on peripheral blood smear. In healthy individuals, schistocytes are reported within the range of 2 to 3 per 1000 red blood cells.^{22,23} The mechanical shearing of these red blood cells while they traverse through microvascular thrombi results in the formation of these schistocytes in patients with TTP. Thus, the presence of schistocytes is most suggestive of TTP when they are present as the dominant abnormality on red blood cell smear.²⁴ Patients with TTP report a higher percentage of schistocytes on average compared to other forms of TMAs (4% to 8% schistocytes in TTP vs 0.2% to 2% schistocytes in transplant-associated TMA, preeclampsia, and haemolytic-uremic syndrome).^{22,23} Previous studies demonstrate that signs and symptoms of abnormal bleeding, such as petechiae, ecchymoses, and menorrhagia have been reported in about 46% of cases.²⁵ A high platelet count of > 30 × 10⁹/L is usually suggestive of other forms of TMA but does not rule out TTP.

The nervous system is usually the most affected organ, involved in 40% to 80% of TTP cases, with symptoms ranging from minor headache to severe seizure, stroke, or coma.^{19,21} A nine-fold increase in mortality was noted in patients with a Glasgow Coma Scale (GCS) score of 14 or less compared to those with a normal GCS score.²⁶ Another organ commonly affected in cases with TTP is the gastrointestinal tract (35% to 40% of cases). They may present with symptoms such as abdominal pain, nausea, vomiting, or diarrhoea. The kidneys may also be affected, with a median creatinine at presentation being 0.9 to 1.4 mg/dL. Only about 4% to 15% of the patients present with acute renal failure requiring dialysis, and renal dysfunction is more common in the older age group.²⁷

With regards to the evaluation of a patient with TMA, the primary goal of a physician is to promptly initiate plasma exchange therapy in those who may have TTP. This decision is, however, extremely challenging due to the rarity of TTP and the variations and overlap in clinical presentation with other TMAs. Laboratory detection of ADAMTS13 activity is of immense help in these cases, but due to their unavailability at most centres, clinical prediction scores have been developed.²⁸ The most recently developed is the PLASMIC score, which has proved to be robust and cost-effective.²⁹⁻³² The PLASMIC score categorises patients into low-risk, intermediate-risk, and high-risk. Immediate plasma exchange therapy is suggested in high-probability PLASMIC scores, while in cases with a low-probability PLASMIC score, plasma exchange therapy may be withheld, and the physician must search for an alternative diagnosis.³³

The presence of ADAMTS13 deficiency on laboratory testing strongly supports the diagnosis with high specificity and sensitivity. Severe deficiency (< 10%) of ADAMTS13 activity further confirms the diagnosis. Thus, diagnosing a patient with TTP is a multistep process involving careful interpretation of the clinical presentation, clinical prediction scores, and laboratory findings.

Treatment of TTP

TTP is an emergency condition, and its treatment must not be delayed after a diagnosis is established. Delay in treatment may result in significant morbidity and mortality. A severe deficiency of the ADAMTS13 activity is required to confirm the diagnosis, but one must not wait for the report before initiating therapy.

The first-line treatment for TTP is therapeutic plasma exchange (TPE).⁵ The therapy must be continued until a clinical response has been obtained and maintained for an additional two days. Glucocorticoids are also used along with TPE from the time of initiation of the therapy. Most standard practices recommend the use of oral prednisone (dose 1 mg/kg/day) daily until a clinical response has been achieved.³⁴ These may later be tapered off over a period of 3-4 weeks.

In our case, the use of rituximab proved to be highly effective in treating the patient. Rituximab is usually prescribed within the first few days of hospitalisation in cases of acute TTP. A prospective phase 2 trial has proved the efficacy of rituximab when used in conjunction with the standard therapy in acute TTP.³⁵ Trials conducted in the past have also demonstrated that rituximab given in cases of acute TTP results in fewer relapses.^{19,35-38} A recent meta-analysis has also proved that administration of rituximab in the acute stage further reduces the mortality rate.³⁹ A few previous studies have also demonstrated the efficacy of rituximab in cases of refractory TTP as well as in cases non-responsive to TPE.^{37,38,40}

Declaration

The author certifies that he has obtained appropriate patient consent form. In the form, the patient has given his consent for his clinical information to be reported in the journal. The patient understands that name and initials will not be published, and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

Conclusion

TTP is a rare condition which can be easily missed by the primary physician. However, it is an emergency and requires immediate management. Thus, it is important to be on the lookout for this condition and initiate therapy immediately. TPE and corticosteroids are the first-line therapies. Rituximab has proven to be highly effective in both acute as well as refractory TTP.

Ashutosh Shukla. Rituximab for Thrombotic Thrombocytopenic Purpura: A Case
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THE IMAGES

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Cytotoxic Lesions of the Corpus Callosum: A Neuroradiological Stroke Mimic

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Abstract:

Cytotoxic lesions of the corpus callosum (CLOCCs) represent a distinct radiological entity that can mimic ischaemic stroke on neuroimaging. We present a case of a 36-year-old male with persistent headaches and altered sensorium whose magnetic resonance imaging (MRI) revealed hyperintense lesions on diffusion-weighted imaging with corresponding hypointensity on apparent diffusion coefficient maps in the splenium of the corpus callosum. The patient had no identifiable vascular risk factors, suggesting an alternative aetiology to stroke. CLOCCs can be associated with various conditions including infections, metabolic disorders, and drug toxicity. Recognition of this entity can prevent misdiagnosis as ischaemic stroke and guide appropriate management. Follow-up imaging confirmed the typically transient nature of these lesions, with complete resolution observed at four weeks.

Key words: Cytotoxic Lesions, Corpus Callosum, MRI, Headaches, Altered Sensorium, Stroke Mimic.

Introduction

The corpus callosum, the largest white matter tract in the brain connecting the cerebral hemispheres, can be affected by various pathological processes. Cytotoxic lesions of the corpus callosum (CLOCCs) represent a distinct radiological entity characterised by transient lesions with restricted diffusion on magnetic resonance imaging (MRI).¹ These lesions predominantly affect the splenium of the corpus callosum and have been associated with numerous aetiologies, including infectious diseases, metabolic disturbances, drug toxicity, and other systemic conditions.⁴

CLOCCs are often misdiagnosed as acute ischaemic stroke due to their appearance on diffusion-weighted imaging (DWI), potentially leading to inappropriate management strategies. Despite their alarming radiological appearance, these lesions typically resolve completely within weeks to months without specific treatment.² Understanding the characteristic imaging features and clinical contexts in which CLOCCs occur is crucial for accurate diagnosis and management.

This case report describes a patient presenting with persistent headaches and altered sensorium who was found to have CLOCCs on neuroimaging. We discuss the clinical presentation, diagnostic approach, pathophysiological

mechanisms, and management considerations for this radiological entity.

Case Report

A 36-year-old male presented to our emergency department with complaints of persistent, moderate to severe headache for three days and progressive altered sensorium over the preceding 24 hours. The headache was described as diffuse, non-pulsatile, and unresponsive to over-the-counter analgesics. There was no history of fever, recent infections, trauma, or substance abuse. The patient had no known comorbidities and was not on any regular medications.

On examination, the patient was afebrile with stable vital signs. Neurological examination revealed a Glasgow Coma Scale score of 13/15 (E3V4M6), with the patient being disoriented to time and place. There were no focal neurological deficits, meningeal signs, or papilloedema. Routine laboratory investigations, including complete blood count, renal function tests, liver function tests, and serum electrolytes, were within normal limits. Cerebrospinal fluid analysis was unremarkable.

Brain MRI was performed, which revealed oval-shaped lesions in the splenium of the corpus callosum characterised

by hyperintensity on DWI and hypointensity on T1-weighted images. The lesions showed restricted diffusion with corresponding hypointensity on apparent diffusion coefficient (ADC) maps and hyperintensity on T2-FLAIR sequences. There was no gadolinium enhancement or mass effect (Figure 1). Magnetic resonance angiography was normal with no evidence of vascular occlusion.

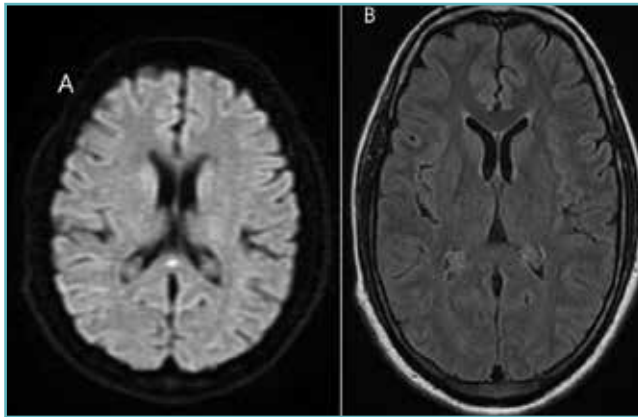


Figure 1: Magnetic resonance imaging (MRI) findings showing cytotoxic lesions in the splenium of the corpus callosum, characterised by restricted diffusion and hyperintensity on T2-FLAIR images.

Based on the clinical presentation and characteristic MRI findings, a diagnosis of CLOCCs was made. The patient was managed conservatively with intravenous fluids and symptomatic treatment for headache. His sensorium gradually improved over the next 48 hours, and he was discharged after five days of hospitalisation. Follow-up MRI performed four weeks later showed complete resolution of the lesions, confirming the transient nature of CLOCCs.

Discussion

CLOCCs represent a distinct radiological entity characterised by transient lesions with restricted diffusion on MRI. These lesions predominantly affect the splenium of the corpus callosum, as observed in our patient. The term "cytotoxic" refers to the pathophysiological mechanism involving intracellular oedema due to dysfunction of cellular fluid homeostasis.⁵

Pathophysiology

The pathophysiology of CLOCCs is not fully understood but is thought to involve excitotoxicity due to elevated glutamate levels, leading to cytotoxic oedema. This process results in water influx into neurons and glial cells, causing cell swelling and restricted diffusion seen on MRI.¹ The splenium of the corpus callosum may be particularly vulnerable due to its high density of glutamate receptors and specific cellular architecture that makes it susceptible to excitotoxic injury.⁶

Alternative mechanisms proposed include intramyelinic oedema due to separation of myelin layers, inflammatory infiltrates, and oxidative stress. The transient nature of these lesions suggests that the underlying pathology is reversible, unlike the permanent damage typically seen in ischaemic stroke.³

Aetiology

CLOCCs have been associated with numerous conditions, broadly categorised as:

1. **Infections:** Viral encephalitis (particularly influenza, rotavirus, adenovirus), coronavirus disease 2019 (COVID-19), Epstein-Barr virus, and other infectious processes.
2. **Metabolic disorders:** Hypoglycaemia, hypernatraemia, hyponatraemia, and hepatic encephalopathy.
3. **Drug-related:** Antiepileptic medications (particularly carbamazepine, oxcarbazepine), metronidazole, 5-fluorouracil, and immunosuppressants.
4. **Others:** High-altitude cerebral oedema, malignancy, eclampsia, and systemic inflammatory conditions.⁴

In our patient, the absence of identifiable risk factors suggests either an undiagnosed viral infection or an idiopathic aetiology, which has been reported in approximately 15%-20% of cases.²

Clinical Presentation

The clinical presentation of patients with CLOCCs varies widely, ranging from asymptomatic cases discovered incidentally to severe encephalopathy. Common symptoms include altered mental status, seizures, headache, and ataxia. The severity of symptoms does not necessarily correlate with the extent of lesions on imaging.¹

Our patient presented with persistent headache and altered sensorium, which are consistent with previous reports. The absence of focal neurological deficits, despite the presence of restricted diffusion on MRI, is a key clinical feature that helps differentiate CLOCCs from acute ischaemic stroke.

Imaging Characteristics

The radiological hallmark of CLOCCs is the presence of oval or round lesions in the splenium of the corpus callosum with restricted diffusion on MRI. These lesions are hyperintense on DWI and hypointense on ADC maps, similar to acute ischaemic stroke. However, unlike stroke, CLOCCs typically do not conform to a vascular territory and often resolve completely on follow-up imaging.⁵

Based on morphology, CLOCCs can be classified into two patterns:

- **Type 1:** Small, oval lesion in the centre of the splenium
- **Type 2:** Larger, more extensive lesion involving most of the corpus callosum

Our patient exhibited the more common Type 1 pattern. The absence of gadolinium enhancement and mass effect further supports the diagnosis of CLOCCs rather than a neoplastic or inflammatory process.

Management and Prognosis

Management of CLOCCs is primarily supportive and directed at the underlying aetiology when identified. In most cases, the lesions resolve spontaneously within weeks to months

without specific treatment. Follow-up imaging is recommended to confirm resolution and exclude alternative diagnoses if symptoms persist.³

The prognosis for patients with CLOCCs is generally favourable, with complete clinical and radiological recovery in most cases. However, the underlying aetiology may influence the outcome, with poorer outcomes reported in cases associated with severe metabolic derangements or encephalitis.²

Conclusion

CLOCCs represent an important differential diagnosis for patients presenting with neurological symptoms and restricted diffusion on MRI. Recognition of this entity can prevent misdiagnosis as ischaemic stroke and avoid unnecessary interventions such as thrombolysis. The case presented highlights the characteristic imaging features and clinical course of CLOCCs, emphasising their typically benign and reversible nature.

Clinicians should maintain a high index of suspicion for CLOCCs when encountering lesions with restricted diffusion in the corpus callosum, particularly in patients with a clinical presentation inconsistent with ischaemic stroke. A thorough evaluation for potential underlying aetiologies and follow-up imaging are warranted to confirm resolution of the lesions.

Further research is needed to elucidate the exact pathophysiological mechanisms underlying CLOCCs and to develop targeted therapeutic strategies for cases with persistent symptoms or incomplete resolution.

Abhishek Dixit, Man Mohan Mehndiratta, Tanzeel Wani, Deepinder Kaur Maini. Cytotoxic Lesions of the Corpus Callosum: A Neuroradiological Stroke Mimic. MMJ. 2025, June. Vol 2 (2).

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Robotic Surgery for a Congenital Branchial Cleft Cyst Presenting in a Young Adult

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Abstract:

Robotic surgery has recently evolved and is rapidly augmenting both endoscopic and conventional open surgeries. Robotic surgery is currently used for thyroid surgeries for both benign and malignant conditions offering less invasive surgical options, better cosmesis, faster recovery, and reduced morbidity. Its use has also been reported in congenital conditions presenting as neck swellings, such as thyroglossal cysts, branchial cysts, and cystic hygromas. Robotic surgery provides excellent visualisation and ergonomically favourable access to deep-seated neck masses, while preserving aesthetic integrity by avoiding open cervical incisions. With careful patient selection and appropriate surgical expertise, it ensures a safe, effective, and cosmetically superior alternative to traditional open surgery.

Key words: Neck Masses, Thyroid, Branchial Cleft Cyst, Thyroglossal Cyst.

Introduction

Congenital neck masses are present at birth and can result from developmental anomalies such as branchial cleft cysts, thyroglossal duct cysts, and cystic hygromas. These masses typically present in childhood but can persist into adulthood if left untreated. Other congenital causes include dermoid cysts, teratomas, and vascular anomalies like haemangiomas and lymphangiomas.

Branchial cleft anomalies form due to incomplete involution of branchial cleft structures. Around the fourth week of gestation, neural crest cells migrate into the future head and neck region, where six pairs of branchial arches begin to develop. The mesoderm is covered externally by ectoderm and internally by endoderm. Although there are six pharyngeal arches, in humans, the fifth pharyngeal arch exists only transiently during embryogenesis.

The five pharyngeal arches are separated by depressions known as clefts on the ectodermal surface, and corresponding pouches on the endodermal surface, yielding four pharyngeal clefts. The ventral part of the first cleft obliterates, whereas the dorsal part gives rise to the external acoustic meatus and pinna. Normally, the second to the fourth clefts obliterate due to overgrowth of the second pharyngeal arch.¹

Branchial cleft cysts are the second most common congenital anomalies of the head and neck, following thyroglossal duct anomalies.² They result from the incomplete fusion of a pharyngeal cleft.

The second pharyngeal cleft is the source of the most prevalent type of branchial cyst; abnormalities originating from the first, third, and fourth clefts are less common.³

Congenital anomalies exist from birth, even if they might not be noticeable or symptomatic right away. Most lesions manifest as a cutaneous punctum in childhood, although they can also appear as cysts or neck lumps.^{4,5} Anomalies involving branchial cysts can manifest as cysts, sinuses, or fistulae.^{6,7}

According to the Bailey-Proctor classification (Figure 1),⁸ second branchial cysts are divided into four types:

- Type-I cysts are located along the anterior border of the sternocleidomastoid muscle, beneath the superficial cervical fascia.^{9,10}
- Type-II cysts are the most common and are located just laterally to great vessels beneath enveloping fascia of the neck.^{11,12}
- Type-III cysts pass between the internal and external carotid arteries.

- Type-IV cysts are located in the pharyngeal mucosal space, just deep to the palatine tonsil and medial to great neck vessels, often extending upward towards the skull base.^{13,14}

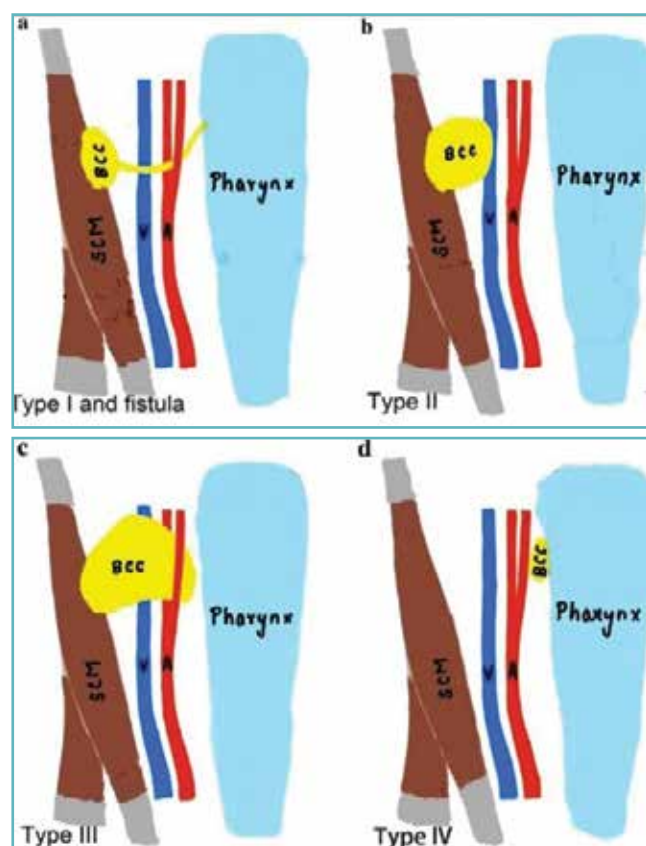


Figure 1: Bailey-Proctor classification.

Case Report

A 29-year-old female presented to the outpatient department (OPD) with a chief complaint of swelling in the left submandibular region for the last six months and pain in the swelling for the last three days, associated with high-grade fever. There was no history of trauma or any other event that could be suspected of contributing to the onset of the swelling. The patient denied history of dysphagia, dyspnoea, dysphonia, or any other symptoms of nerve involvement. The swelling was initially small in size and gradually progressed to its current size. It was not associated with any pain until the last three days.

On clinical examination, a solitary swelling measuring 10 cm x 8 cm was noted in the left submandibular region (Figure 2), extending from the angle of the mandible posteriorly (not crossing the sternocleidomastoid muscle) till the submental region anteriorly, crossing the midline, with superior extension to the mesenteric region. There was associated erythema of the overlying skin. The pinchable overlying skin was warm and tender to palpation, with a soft consistency. The swelling was immobile in either direction. There was no limitation in mouth opening.



Figure 2: Showing a large swelling in the submandibular region (Preoperative)

The patient was admitted to the surgical ward for further evaluation. Baseline investigations revealed leucocytosis (total leucocyte count: 14,000/mm³), while the rest of the routine laboratory investigations were within normal limits. To better delineate the extent of the swelling, an magnetic resonance imaging (MRI) of the neck was performed, which revealed a large well defined, smooth walled septate cystic lesion in the left submandibular region, located below the level of the mylohyoid muscle. The lesion was bulging superomedially, medial to the mandibular body and extended laterally to reach the skin surface, with associated dilatation of the Wharton's duct (Figure 3).



Figure 3: T2-weighted magnetic resonance imaging (MRI) images: (A) Coronal view, (B) Sagittal view of head and neck region.

A CT angiography was also done to confirm the diagnosis and assess if there was any vessel involvement. The CT angiography confirmed that the external carotid artery was not encased by the cyst, supporting a robotic excision approach. The robotic technique was chosen due to its precision in an extremely sensitive anatomical region, aiming to avoid complications. Its binocular 3D high-definition vision and precise ergonomic movements enables surgeons to perform complex surgeries in deep and narrow areas with better precision.

Despite the cyst's large size (approximately 10 cm × 8 cm), robotic excision allowed for complete removal and safe dissection from the surrounding vascular structures and the submandibular gland. This was achieved without complications and with minimal scarring, a significant advantage over traditional open surgery. The patient benefited from improved cosmetic outcomes.

Ethical Approval

This case report has been reported in line with the Surgical CAse REport (SCARE) criteria.

Sources of Funding

None.

Conflict of Interest Disclosure

The authors declare that they have no financial conflicts of interest in relation to the content of this report.

Conclusion

Recent advances in minimal invasive surgery, particularly using robotic techniques, are gaining popularity. The scope of robotic surgery continues to expand rapidly. This case report highlights the importance of imaging for an accurate diagnosis and the clinical and cosmetic advantages of robotic excision of a branchial cleft cyst.

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Polyarteritis Nodosa Masquerading as Fever

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Abstract:

Polyarteritis nodosa (PAN) is a rare, necrotising medium-vessel vasculitis characterised by multisystem involvement and the absence of anti-neutrophil cytoplasmic antibodies (ANCA), with an estimated prevalence of 3–4 cases per million annually. Early recognition is critical to prevent life-threatening vascular complications. A 68-year-old male with known coronary artery disease presented with one week of high-grade fever, dry cough, dyspnoea on exertion, lower-extremity oedema, transient chest rash, anorexia, and weight loss. Initial laboratory evaluation revealed leukocytosis, markedly elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), hyponatraemia, mild renal and hepatic dysfunction, and elevated N-terminal pro b-type natriuretic peptide (NT-proBNP) and ferritin. Imaging showed hepatosplenomegaly and perinephric fat stranding. Despite broad-spectrum antibiotics and corticosteroids, inflammatory markers remained elevated. Autoimmune serology was antinuclear antibody (ANA)-negative but positive for myositis antibodies (Mi-2, Ku, Ro-60) with low complement levels; ANCA were negative. On hospital Day 10, the patient developed sudden left flank pain, hypotension, lactic acidosis, and worsening renal function. Computed tomography (CT) angiography demonstrated multiple microaneurysms in renal, hepatic, splenic, and mesenteric vessels with active bleeding from a left renal artery aneurysm and a large perinephric haematoma. Emergent coil embolisation and drainage were performed. Skin biopsy confirmed transmural fibrinoid necrotising vasculitis; nerve conduction studies revealed sensorimotor neuropathy. A diagnosis of PAN was established. The patient received high-dose intravenous (IV) methylprednisolone followed by oral steroids and azathioprine. Clinical and laboratory parameters improved rapidly, and he was discharged on maintenance immunosuppression in stable condition. This case is unique for its initial presentation mimicking sepsis and heart failure, the absence of ANCA, and life-threatening rupture of a renal artery aneurysm — an uncommon but recognised complication of PAN. In patients with fever of unknown origin and multisystem involvement unresponsive to antimicrobial therapy, medium-vessel vasculitis must be considered. Prompt angiographic evaluation and histopathologic confirmation facilitate early immunosuppressive treatment, reducing morbidity and improving survival in PAN.

Key words: Polyarteritis Nodosa, Fever, Vasculitis, Renal Artery Aneurysm, Perinephric Haematoma.

Introduction

Polyarteritis nodosa (PAN) is a rare necrotising medium-vessel vasculitis which affects multiple organs such as the nerves, kidneys, and gastrointestinal system. Data for PAN in India are limited. Initial case reports from the All India Institute of Medical Sciences (AIIMS), New Delhi, and the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh described a range of clinical features, including constitutional symptoms, mononeuritis multiplex, hypertension, and gastrointestinal complications. Mononeuritis multiplex has persistently been established as the most common neurological manifestation, found in up to 83% of Indian patients.¹ Diagnosis of PAN may be difficult because of its nonspecific clinical presentation and the lack of characteristic serological markers like antineutrophil cytoplasmic antibodies (ANCA). A negative skin biopsy is not conclusive for excluding PAN.² Spontaneous perirenal haematoma due to ruptured microaneurysm is a rare but dangerous complication of PAN.³ In this article, we report the case of an elderly man who had spontaneous perirenal haematoma and was later diagnosed to have PAN.

Case Report

A 68-year-old male with a history of coronary artery disease (CAD) presented with high-grade fever, cough with minimal whitish sputum, exertional dyspnoea, bilateral pedal oedema, along with erythematous rash over the chest for a duration of one week. Over the last one month, he had a loss of appetite and weight.

There was no history of joint pain, oral ulcers, photosensitivity, or hair loss. He had no prior diagnosis of autoimmune disease or hepatitis. On examination, he was conscious and oriented with bilateral episcleritis, grade 2 pedal oedema. His blood pressure was 110/76 mmHg and pulse was 90/min. Systemic examination revealed bilateral infrascapular fine crepitations with decreased breath sound intensity, mild hepatosplenomegaly, and mild left flank tenderness. There was no lymphadenopathy, or focal neurological deficit noted.

Initial investigations are mentioned in Table 1.

Parameter	Value
Haemoglobin	10.7 g/dL
Total leukocyte count (TLC)	13,600/mm ³
Neutrophils	88%
Platelet count	1.5 lakh/mm ³
Erythrocyte sedimentation rate (ESR)	84 mm/h
C-reactive protein (CRP)	325 mg/L
Procalcitonin	34 ng/mL
Serum creatinine	1.9 mg/dL
Serum sodium	124 mEq/L
Serum potassium	4.5 mEq/L
Total bilirubin	2.6 mg/dL
N-terminal pro b-type natriuretic peptide (NT-proBNP)	10,200 pg/mL
Serum ferritin	1224 ng/mL



Table 1: Initial laboratory investigations.

Urinalysis was normal.

Regular fever workup was negative for infectious disease aetiology, including blood and urine cultures. Chest X-ray showed bilateral pneumonitis. Computed tomography (CT) of the chest revealed interlobular septal thickening, pleural effusions, and cardiomegaly. CT of the abdomen showed bilateral perinephric stranding, hepatosplenomegaly, and cholelithiasis without cholecystitis.

Empiric antibiotics and steroids temporarily suppressed fever, but inflammatory markers remained elevated. Autoimmune screening revealed antinuclear antibody (ANA) immunofluorescence negative but ANA line immunoassay (ANA-LIA) panel positive for Mi-2, Ku, and Ro-60. Complement component 3 (C3) and complement component 4 (C4) levels were decreased. Cytoplasmic ANCA (C-ANCA) was indeterminate and perinuclear ANCA (P-ANCA) was negative.

On Day 10, the patient presented with acute-onset abdominal pain with hypotension (blood pressure 60/40 mmHg), elevated lactate (4.7 mmol/L), and deteriorating renal parameters.

CT angiography was performed and revealed multiple small and medium-sized artery aneurysms of both kidneys, hepatic and splenic branches, and the superior mesenteric artery, as well as an actively bleeding left upper pole artery aneurysm causing a large perinephric haematoma (Figure 1).

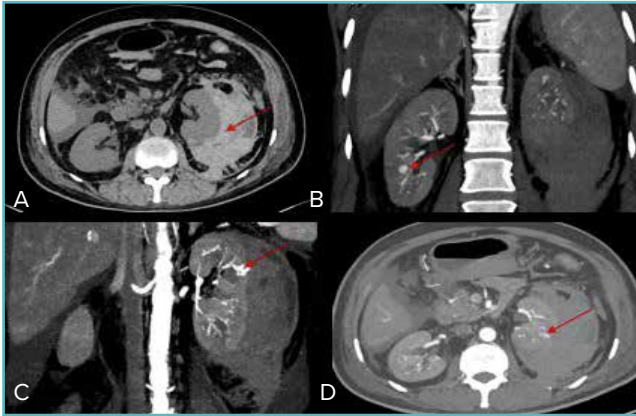


Figure 1: A: Non-contrast computed tomography (CT) image showing perinephric collection of blood around the left kidney; B: Contrast-enhanced CT image of the right kidney showing aneurysm; C and D: Contrast-enhanced CT images showing "culprit" bleeding aneurysm.

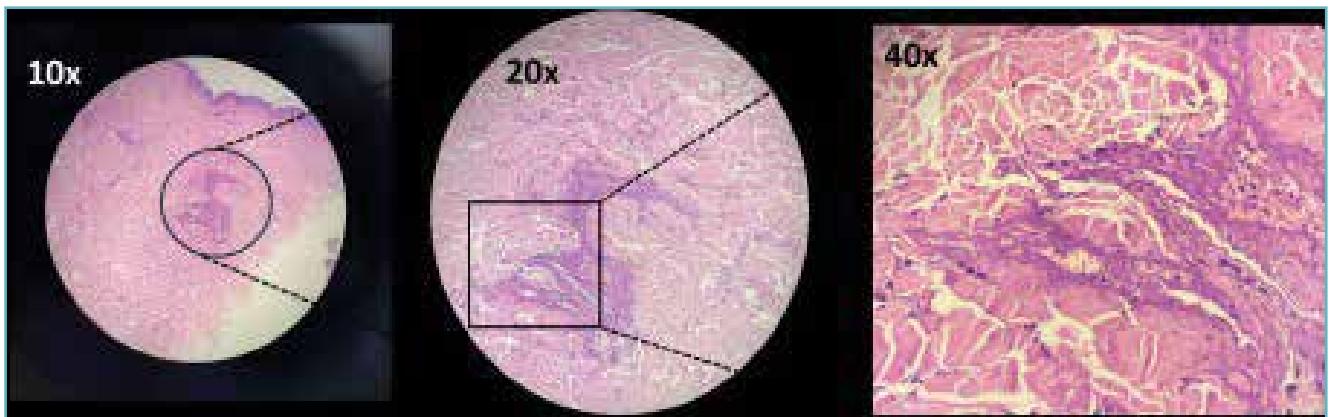


Figure 2: Fibrinoid necrosis of the vessel wall with perivascular inflammation.

Nerve conduction studies showed mixed axonal and demyelinating neuropathy in all four limbs. Hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (anti-HCV) antibodies were negative. The patient showed clinical improvement. Renal function and laboratory parameters stabilised, and he was discharged on azathioprine and low-dose steroids. He remained stable on follow-up with no recurrence of fever or abdominal symptoms.

Discussion

PAN, initially described by Kussmaul and Meier, was characterised by the 1994 Chapel Hill Consensus Conference (CHCC) as a necrotising arteritis of medium- and small-sized arteries, without glomerulonephritis. The 2012 CHCC revision additionally defined PAN as an ANCA-negative vasculitis and introduced new categories, such as single-organ vasculitis and hepatitis B virus (HBV)-associated vasculitis, while distinguishing it from idiopathic PAN. To improve diagnostic consistency, the European Medicines Agency (EMA) subsequently developed

Emergency angioembolisation of the left renal artery was performed, and a pigtail catheter was placed to drain the haematoma.

A diagnosis of PAN was made. He was treated with intravenous (IV) methylprednisolone pulse doses.

A skin biopsy from an erythematous rash over the abdomen revealed fibrinoid necrosis of the vessel wall with perivascular inflammation, consistent with vasculitis as shown in Figure 2.

a stepwise classification algorithm based on CHCC definitions and the American College of Rheumatology (ACR) criteria.⁴ A multicentric study by Joshi and Mittal, conducted across major Indian cities, compiled 1064 cases of vasculitis, of which 8.83% were PAN and 1.22% were cutaneous PAN. Conversely, Henoch–Schönlein purpura (21.8%), Takayasu arteritis (20.2%), and Wegener's granulomatosis (13.8%) were most commonly reported vasculitis types. Microscopic polyangiitis (MPA), which PAN is easily mistaken for other conditions and was observed in 3.94% of cases. The results reflect the relative infrequency of PAN in the Indian population.¹

Diagnosis of PAN remains challenging due to its protean clinical manifestations and the absence of a definitive diagnostic test. It may present with nonspecific symptoms (e.g., fever, weight loss, myalgia, neuropathy) or mimic infections, malignancies, or autoimmune diseases. Unlike other vasculitides, PAN tends to be ANCA-negative and typically does not involve arterioles, capillaries, or glomeruli, resulting in delayed diagnosis. The

diagnosis of PAN in our patient was supported by the ACR 1990 classification criteria. These criteria, derived from a comparison of 118 PAN cases and 689 controls with other vasculitides, include ten clinical, laboratory, radiologic, and histopathologic features. The presence of at least three of the following — weight loss ≥ 4 kg, livedo reticularis, testicular pain, myalgias, mononeuropathy or polyneuropathy, diastolic blood pressure > 90 mmHg, elevated serum creatinine or blood urea nitrogen, HBsAg positivity, angiographic abnormalities, and biopsy-proven arterial inflammation — confers a sensitivity of 82.2% and specificity of 86.6% for PAN classification.⁵

In our case, the diagnosis of PAN was initially obscured by overlapping features of sepsis with heart failure. The occurrence of a spontaneous perinephric haematoma from aneurysmal rupture, multisystemic involvement of peripheral neuropathy, acute kidney injury, episcleritis, and aggressive clinical course despite empiric antibiotics, all pointed in the direction of systemic vasculitis. This uncommon but characteristic angiographic feature, along with skin biopsy showing leukocytoclastic vasculitis, established the diagnosis of PAN. This case underscores the importance of considering PAN in patients with fever of unknown origin and progressive multisystem involvement particularly with poor clinical response to infection-directed therapy. It also highlights the need to integrate clinical findings, radiologic evidence and histopathology rather than relying solely on serologic markers or autoantibody panels, which are potentially non-specific or misleading in ANCA-negative vasculitides such as PAN.⁶

The differential diagnosis includes infections and other vasculitides. The most important infectious mimics are infective endocarditis, human immunodeficiency virus (HIV)-associated vasculitis, and mycotic aneurysms. The non-infectious mimics are ANCA-associated vasculitides — granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) — as well as immunoglobulin A (IgA) vasculitis, cryoglobulinaemic vasculitis, and drug-induced vasculitis. Key distinguishing features include ANCA status, organ involvement, and histology.⁷

In patients with PAN linked to HBV or hepatitis C virus (HCV) infection, the primary emphasis of therapy is the administration of antiviral drugs for treatment of the underlying viral disease.⁸ Single-organ PAN is typically monophasic and non-recurrent. Isolated single-organ PAN is generally diagnosed histologically from surgical specimens, and treatment beyond surgical excision is typically not required.⁸ Mild cutaneous PAN, presenting with subcutaneous nodules and livedo reticularis, may respond to nonsteroidal anti-inflammatory drugs (NSAIDs), rest, and elevation of limb(s).⁹ In cases of severe active PAN, usual therapy consists of high-dose glucocorticoids combined with cyclophosphamide. IV methylprednisolone is generally administered in the dose range of 7-15 mg/kg (maximum of 1 g/day) over three consecutive days, followed by oral prednisone at 1 mg/kg/day for two to four weeks with tapering over time according to response.¹⁰ Cyclophosphamide may be given orally at 2 mg/kg/day or intravenously at 15 mg/kg at Weeks 0, 2, and 4, and subsequently every three weeks until remission.¹¹ Following cyclophosphamide induction, patients are switched to a maintenance immunosuppressive drug like azathioprine (2 mg/kg/day) or methotrexate (20-25 mg weekly), with the overall duration of immunosuppressive therapy — induction and maintenance — usually lasting to 18 months. Relapsing patients can be treated with a more extended course.¹² In our patient, cyclophosphamide was deferred because of ongoing haematuria and a recent vascular intervention. Immunosuppression was initiated with IV glucocorticoids, followed by azathioprine, once appropriate thiopurine methyltransferase (TPMT) activity was confirmed.

With prompt and appropriate immunosuppressive therapy, the five-year survival in PAN can be greater than 80%.¹³ However, delays in diagnosis or therapy can result in catastrophic complications, including life-threatening phenomena like spontaneous aneurysmal rupture, as in our case where the patient presented with a perinephric haematoma secondary to renal artery bleeding. This uncommon but dangerous presentation reinforce the importance of prompt recognition of vasculitic features, particularly in patients presenting with unexplained systemic symptoms and organ involvement.

Vishal Kharb, Faizal Mohammed M, MRJ Qureshi, P Garg, Vivek Saxena, Abhishek Rajendra Agarwal, Monica Mahajan. Polyarteritis Nodosa Masquerading as Fever. MMJ. 2025, June. Vol 2 (2).

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Research Methodology and Biostatistics

Series VI - Observational Studies

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Abstract:

Studies on antecedent-outcome relationships in naturally occurring events are called observational studies. Hazardous 'interventions', such as smoking and anaemia, are particularly suitable for observational studies because these cannot be intentionally introduced but occur naturally.

In a prospective observational study, subjects with specific antecedents or exposure are followed up for the occurrence of the outcome. This design yields more valid results because the subjects are monitored over time. A retrospective study starts with the outcome — for example, individuals with and without a disease — and investigates previously occurring events that might have led to the disease in some and not in others. This type of study can be completed more quickly but may involve biased assessment of the antecedents. A cross-sectional study requires a carefully chosen, adequately representative sample and gives valid results when both antecedents and outcomes are properly assessed at the same time. The merits and demerits of these designs are discussed in this article.

This article also describes some other observational study designs such as case-control, nested case-control, and retrospective cohort studies, which are sometimes misunderstood.

Key words: Prospective Studies, Retrospective Studies, Cross-Sectional Studies, Analytical Studies, Case-Control Studies, Retrospective Cohort Studies, Nested Case-Control Studies.

What is an Observational Study?

In clinical trials, we intentionally administer an intervention to human subjects and study how it affects them. Thus, this forms a stimulus-response experimental setup in human beings. Such studies typically offer good control over the selection of subjects, allocation between the case and the control groups, and blinding — thus providing credible evidence for or against a cause-effect relationship, or at least a stimulus-response relationship.

However, in many situations, feasibility, cost, or ethical considerations prevent us from conducting a trial. Smoking is a well-known example. We cannot ethically ask people to smoke for 10 years to study its effect on pulmonary functions. Instead, we assess the pulmonary functions of people who already smoke, across various durations and intensities. Similarly,

we cannot ask pregnant women to become anaemic to study how different grades of anaemia affect birth outcomes such as gestational age, intrauterine growth retardation, or birth weight. Instead, we observe naturally occurring cases of anaemia in antenatal women to study its effects on birth outcomes.

When the 'intervention' is a naturally occurring factor that is already present in some individuals but not in others, and we simply observe the outcomes, the study is referred to as an observational study. While observational studies are a natural choice for investigating the effect of adverse factors, they are sometimes preferred for beneficial interventions too, due to convenience, cost and speed. For example, in studying dietary supplementation, we may observe outcomes such as liver and kidney functions in those already taking specific supplements

for a defined period and compare these with individuals not taking the supplementation. This strategy could be more efficient than conducting a trial in which some participants are asked to take supplements while equivalent controls are asked not to. However, in observational studies, several other factors, such as age, nutritional status, and comorbidities can play spoil sport as confounders. Confounders are factors whose effects are so closely intertwined that their individual effect cannot be separated. They typically affect both the antecedents and the outcomes of interest, thereby contaminating the results.

The term 'observational study' associated with the study of antecedent-outcome relationships. While the underlying question may relate to cause and effect, observational studies rarely meet the strict conditions required to meet causality.¹ These conditions are numerous and beyond the scope of this article. Therefore, observational studies can only confirm or refute associations, not causality — unless those strict conditions are met.

To understand observational studies, it is necessary to understand the terms 'antecedents' and 'outcomes.' Antecedents are factors that are precursors and contribute to the outcome of interest. These may include risk factors (e.g., metabolic syndrome for cardiovascular diseases), exposures (e.g., radiation leading to illness), or protective factors (e.g., a healthy diet reducing risk of certain cancers). Outcomes are the consequences of interest, such as the onset of a disease, survival duration, or improvement in the condition. In the smoking–pulmonary function example, smoking is the antecedent and pulmonary function is the outcome. In the anaemia–birth outcome example, anaemia is the antecedent and birth characteristics are the outcomes. A factor may be an antecedent in one study and outcome in another; for example, obesity is an antecedent for diabetes but an outcome for sedentary behaviour.

Since the aim is to assess the antecedent-outcome relationship, an observational study is an analytical study as explained in an earlier article.² If the aim is not to examine this relationship but to merely describe characteristics of the population or estimate exposure levels, the study is descriptive rather than analytical. Such descriptive studies, sometimes referred to as prevalence studies, might focus on the proportion of subjects who are non-smokers, mild, moderate, or heavy smokers, or assess smoking intensity using indices, or describe demographics such as age, sex, socio-economic status, and stress levels.

Observational studies can be carried out using different designs. One design is the ecological study, in which population-level rather than individual-level data are used. For example, Moreira-Soto *et al.*³ analysed the relationship between severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) laboratory testing capacity and socio-economic factors across 109 countries in 2020-21 to identify potential determinants of global disparities in testing capacity, without using individual-level data.

More commonly, observational studies involve individual-level data and can be prospective, retrospective, or cross-sectional. Note that these classifications apply only to analytical studies (which assess antecedent-outcome relationships) and not to

descriptive studies. Some researchers mistakenly refer to descriptive studies as observational studies. For example, Maposse *et al.*⁴ studied the prevalence of cell phone use while driving and erroneously called it an observational study instead of a descriptive study.

Prospective, Retrospective, and Cross-Sectional Studies

The natural design of an observational study follows a direction from antecedent to outcome. This requires selecting subjects with and without the antecedent of interest and following them up for the occurrence or non-occurrence of outcomes. The two groups — those with and without the antecedent — must otherwise be equivalent at baseline. A study evaluating the use of a cemented dual mobility cup for primary total hip arthroplasty in terms of quality of life⁵ will yield valid results only if the patients receiving the cemented cup have the same clinical condition at baseline as those treated with alternative procedures.

The essential feature of a prospective design is follow-up. This can be short, lasting a few hours or days, or long, spanning several years. For instance, a study investigating anaemia in pregnant women and birth outcomes is prospective if women with different grades of anaemia (none, mild, moderate, and serious) are enrolled and followed up for outcomes such as birth weight. It becomes retrospective if researchers examine the records of mothers of newborns with different weights (low, normal, high) to determine their haemoglobin (Hb) levels during the antenatal period, say in the first trimester. In this case, this investigation moves from outcome (birth weight) to antecedent (Hb level).

The anaemia-birth outcome study becomes cross-sectional when all births within a specified period are included, and Hb levels of the mothers and the birth weights of the infants are recorded at a single point in time.

Variations of Observational Studies

Colloquially, the prospective-retrospective classification is based on the time frame. A study is considered retrospective if based on records of cases no longer available, and prospective if based on subjects enrolled from a specified date moving forward. However, this time-based classification does not align with the correct scientific usage, which classifies studies based on the direction of enquiry: from antecedent to outcome (prospective), or from outcome to antecedent (retrospective), regardless of the time frame.

For more clarity on the time aspect, consider a study on mortality among COVID-19 patients admitted to the intensive care unit (ICU)⁶ The study was based on records, but the direction of investigation was from antecedent (ICU admission) to outcome (mortality). Therefore, despite using retrospective data, it qualifies as a prospective study in terms of design. Nevertheless, the authors referred to it as a "retrospective cohort study."

This brings us to the term 'cohort study'. A cohort is a group of people with defined, shared characteristics. There may be a cohort of specific cases to be admitted over the next year (a

prospective cohort) or cases admitted over the past 3 years (a retrospective cohort). However, the term "retrospective cohort" does not automatically imply a retrospective study. The direction of the investigation in a cohort study, whether prospective or retrospective, is typically from antecedent to outcome, such as from the admission to discharge.

However, Li *et al.* retrieved records of patients with coronary heart disease (CHD), categorised them into mild, moderate, and severe stenosis groups using Gensini score, and analysed the role of remnant cholesterol (RC) in predicting stenosis severity.⁷ Here, the direction of investigation was from outcome (severity of stenosis) to antecedent (RC), which is a retrospective design. Yet, the authors referred to it as a "retrospective cohort study." Such variations in usage are common in the literature, although scientifically, a cohort study should ideally follow a prospective direction from antecedent to outcome. A prospective study may also be longitudinal, where subjects are observed at several time points rather than at just the endpoint.

A case-control study, in which the case group comprises individuals with a disease (or another outcome) and the control group includes those without it, is also retrospective in design. It begins with subjects who have (case group) and do not have (control group) the outcome and investigates the antecedents. This design provides valid results only if the case and control groups are equivalent at baseline apart from the antecedents under study. Otherwise, differing antecedents may act as confounders and bias the results. In the anaemia-birth weight example, potential confounders include parental weight, calorie intake, and intake of nutritional supplements. If the case group has specific comorbidities that the control group does not, the results may be invalid because of baseline inequivalence. A type of observational study is the nested case-control study, in which cases and controls are drawn from a cohort already being investigated for another purpose. Wu *et al.*⁸ reported such a study, selecting cases with gestational diabetes mellitus (GDM) and controls without GDM from a birth cohort. They studied the role of maternal plasma concentrations of trimethylamine N-oxide and its precursors — choline, betaine, and carnitine — in the risk of developing GDM.

Merits and Demerits of the Different Types of Observational Studies

An in-depth consideration of the various designs within the observational study paradigm reveals that each design has advantages in some situations and disadvantages in others. Since individuals with outcomes are already identified and the investigation looks backwards to assess antecedents, retrospective studies can be completed quickly and require fewer resources. Multiple antecedents can be investigated simultaneously. These studies can begin with an adequate number of cases and controls, and there is minimal risk of dropouts. However, the demerits include the potential for recall lapse, especially when subjects are asked to recall past events — milder events are often forgotten, while severe ones are more easily remembered. Some participants may intentionally withhold information, leading to biased results. This design cannot assess risk directly, as risk has future implications; instead, odds ratios are calculated. Establishing a cause-effect relationship is more difficult in a retrospective design because the temporal sequence of events can be ignored easily.

Conversely, these precisely are the merits of a prospective design. A prospective observational study can assess risk, and both negative and positive predictive values of the antecedents for an outcome can be calculated. This design can come closer to establishing a cause-effect relationship. These are the two major strengths of prospective studies. They provide greater confidence in the results because all events are observed in real-time as they occur. However, if the outcome of interest is rare, the final number of cases may be low, which reduces the statistical power to detect an effect. Moreover, prospective studies are expensive due to the need for follow-up. Dropouts can occur, and some subjects may change their status during the follow-up period, introducing a potential bias.

Cross-sectional studies can provide credible results when the chosen sample adequately represents a full spectrum of the target population, and both antecedents and outcomes are properly assessed. This design has minimal risk of recall bias or similar errors, as data collection occurs at a single point in time. In conclusion, the choice of study design in observational research should be guided by a careful consideration of the various merits and demerits discussed in this article.

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Student Interviews

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In Pursuit of Excellence:

Dr. Nikita's Path from India to the National Health Service (NHS)



Dr. Nikita Goel

- 1. So, could you tell us something about yourself? What made you interested in medicine? What is your current designation?**

I'm currently working as a Rheumatology Registrar at London Northwest University Hospital. My interest in medicine began early, sparked by a combination of personal experiences and a fascination with science. Over time, through academic study and clinical exposure, the initial curiosity evolved into a deep commitment. I am particularly drawn to how medicine challenges you to be both analytical and empathetic.

- 2. How different is your new environment from India?**

Moving from India to the United Kingdom (UK) has meant adapting to a more protocol-driven system with greater emphasis on documentation and teamwork. The pace and style of patient interaction differ, requiring adjustment, not necessarily better or worse, just different.

- 3. Tell us about your experience at Max Hospital?**

At Max Hospital, I gained invaluable experience managing a high volume of diverse clinical cases, which strengthened my diagnostic and decision-making skills. The fast-paced environment and multidisciplinary collaboration helped me develop resilience, adaptability, and a patient-centred approach to care.

- 4. How was our teaching program at Max? How did you like the organisation of our classes along with clinical exposure?**

The teaching program at Max Hospital was well-structured, combining regular academic sessions with hands-on clinical exposure. I appreciated the balance between theoretical learning and practical case discussions, which helped bridge the gap between classroom knowledge and real-world application.

- 5. What were the most significant and the most helpful features of this program? Any recommendations for improvement?**

The most significant and helpful features were the strong clinical exposure across various specialties and the emphasis on evidence-based practice. Regular bedside teaching, structured assessments, and mentorship from experienced consultants greatly enhanced both confidence and clinical competence.

One recommendation would be to include workshops on audit, quality improvement projects, and research methodology — this could better prepare trainees for leadership roles.

- 6. How helpful was your experience at Max Hospital in securing a placement in the UK and working in the National Health Service (NHS)?**

My experience at Max Hospital was instrumental in preparing me for a role in the NHS. The exposure to a wide range of clinical cases, structured ward rounds, and emphasis on documentation and multidisciplinary teamwork closely aligned with the working style in the UK. It also strengthened my clinical acumen and communication skills, which proved valuable during NHS interviews and in adapting to the system.

- 7. What are your future plans?**

My future plans involve further honing my clinical skills, particularly in the field of Rheumatology. I am joining the Wessex Deanery to pursue Certificate of Completion of Training (CCT) in Rheumatology. I aim to continue contributing to the healthcare system through continuous learning, patient care, and collaborative teamwork, while also exploring opportunities in research and leadership roles in the future.

Bridging Borders:

Dr. Renisha's Medical Journey from Max Hospital to the United Kingdom (UK)



Dr. Renisha Singh

1. So, could you tell us something about yourself? What made you interested in medicine? What is your current designation?

Medicine has always been close to my heart, largely influenced by a personal experience — my grandfather was diagnosed with a rare disease, and I accompanied him for multiple hospital visits and dialysis sessions. That journey sparked my interest in medicine. It was his dream to help others, and over time, that became mine as well. Currently, I work as a Senior House Officer in the Department of Gastroenterology at Hillingdon Hospital, London.

2. How different is your new environment from India?

The environment here is quite different in many ways — both culturally and professionally. I find myself more independent, both in lifestyle and clinical decision-making. However, the essence of medicine remains the same, and that continuity has been grounding for me. One of the most striking differences is how well-structured the escalation protocols are in the National Health Service (NHS). While there's a clear hierarchy, the work environment is approachable and collaborative, which makes learning and contribution much easier.

3. Tell us about your experience at Max Hospital.

Max Hospital has a special place in my journey — it was where I truly grew as a clinician. The exposure I received there helped build my confidence and clinical acumen. I had the privilege of working with inspiring mentors and supportive colleagues, many of whom I remain in touch with. My time at Max not only shaped me as a doctor but also helped me develop strong leadership and communication skills.

4. How was our teaching program at Max? How did you like the organisation of our classes along with clinical exposure?

The teaching program at Max was very well structured. The weekly academic sessions were particularly valuable

— they allowed us to reflect on our clinical experiences, discuss learning points, and explore different management approaches. These sessions fostered a culture of continuous learning and collaboration. I also appreciated the balance between clinical duties and academic learning, which made the overall experience very enriching.

5. What were the most significant and the most helpful features of this program? Any recommendations for improvement?

The most significant aspect of the program was the mentorship and the Max Institute of Medical Education (MIME) team. The support from senior doctors and peers created a nurturing environment. The diversity of clinical cases, simulation sessions, and structured learning were especially helpful. Max being a multi-speciality hospital gave exposure to a broad spectrum of cases. If anything, more frequent simulation-based sessions and inter-departmental teaching could further enhance the program.

6. How helpful was your experience at Max Hospital in securing a placement in the UK and working in the NHS?

My experience at Max laid a strong foundation for my transition to the NHS. The wide-ranging clinical exposure, robust teaching structure, and emphasis on evidence-based practice were invaluable in my adaptation to UK medical practice. The professionalism, documentation standards, and teamwork I experienced at Max mirrored many aspects of NHS culture, making the transition smoother and more confident.

7. What are your future plans?

I plan to apply for Specialty Training year 4 (ST4) training in Gastroenterology here in the UK. Currently, I'm focused on understanding the NHS system more deeply while continuing to grow both professionally and academically. I am also engaged in audits, research, and teaching activities, all of which I hope will contribute to my development as a future gastroenterologist.

Max Institute of Medical Education Announcements

Max Institute of Medical Education (MIME) is an educational division of Max Healthcare Institute Ltd. MIME was established to meet and enhance the training needs of all medical/non-medical staff working in various healthcare organisations. The institute is committed to enabling medical, nursing, and paramedical professionals to practise their skills with confidence and excellence, maintaining the highest standards in a patient-safe environment.

CREATING THE NEXT GENERATION OF HEALTHCARE LEADERS

10,000+

Students Trained Annually

800

Faculty Members

150

Courses, including Offline and Online

CORE ELEMENTS OF OUR TRAINING



Extensive Practical Training



World-Class Faculty



Customised Training



Online Library - Elsevier Clinical Key



Simulation Lab



Learning Management System (LMS)

DELIVERING UNPARALLELED QUALITY IN MEDICAL EDUCATION

DIPLOMATE OF NATIONAL BOARD (DNB)

Max Healthcare Institute Ltd. is recognized by the National Board of Examinations to provide practical training for students enrolled in DNB broad and super-speciality courses in over 40 disciplines. Currently, we have 618 DNB residents across our network of hospitals.

International Affiliated Programmes



POST GRADUATE PROGRAM IN INTERNAL MEDICINE – IMT

A full-time, three-year postgraduate training in Internal Medicine incorporating the full Membership of the Royal Colleges of Physicians of the United Kingdom (MRCP [UK]). This programme is a partnership between Max Healthcare and the Joint Royal College of Physicians Training Board (JRCPTB-UK).

The IMT program is structured to meet international standards, delivering physician training equivalent to the UK curriculum following the same curriculum and assessments. Our pool of consultants is fully trained by the Royal College of Physicians. Currently, 60 residents are enrolled in IMT training at Max Hospitals in Delhi and Mumbai.

Eligibility: MBBS with valid NMC/ State Medical Council registration

TRAINING LOCATION:

- Max Super Speciality Hospitals, New Delhi
- Nanavati Max Super Speciality Hospital, Mumbai



RCOG-MHC OBSTETRICS & GYNAECOLOGY PROGRAMME (RCOG)

A joint programme by Max Healthcare Institute Limited (MHIL) and the Royal College of Obstetricians and Gynaecologists (RCOG) United Kingdom. This training is equivalent to the Basic (ST1-2) and Intermediate training (ST3-5) in the UK. The programme is underpinned by the RCOG curriculum, Membership of the Royal College of Obstetricians and Gynaecologists (MRCOG) examinations, use of the RCOG e-Portfolio, and an Annual Review of Competence Progression (ARCP) process with UK externality.

Currently, 10 residents are enrolled in the RCOG training programme.

Eligibility: MBBS with valid NMC/ State Medical registration

TRAINING LOCATION:

- Max Super Speciality Hospitals, Delhi



MEM GWU INTERNATIONAL

A 3-year residency programme in Emergency Medicine. The Max Emergency Medicine–George Washington University (MEM–GWU) programme is a skill-building training initiative conducted by the Max Institute of Medical Education in collaboration with the Ronald Reagan Institute of Emergency Medicine (USA), under The George Washington University Medical Center. This programme aims to enrich residents with the knowledge, skills, and compassion required for effective and efficient emergency medical care.

Currently, 90 residents are enrolled in the ongoing programme.

Minimum Eligibility: MBBS with valid NMC/State Medical Council registration

Duration of Course: 3 years

Admission Process: Ongoing for batch 2025-2028

Training Locations:

- Max Super Speciality Hospitals in Delhi, UP, Dehradun, Mohali, Lucknow, Mumbai & Nagpur



Admissions open for
FY: 2025 Session



Admissions open for
FY: 2025 Session



Admissions open for MEM
GWU Session 2025-2028

Fellowship Courses (Non-NBE)

MIME offers diverse fellowship opportunities that enable medical professionals to advance their expertise in specialised fields. These courses last from 6 months to 2 years.

- Abdominal & Transplant Imaging
- Aesthetic Medicine & Surgery
- Bariatric Anaesthesia
- Breast Imaging
- Critical Care Medicine
- CT & MRI
- Emergency Department
- Dialysis
- Orthopaedic Oncology & Reconstruction Foot & Ankle
- Gastroenterology
- General Nephrology
- Gynaecological Onco-Surgery
- GI Endoscopy
- Head & Neck Surgery
- Hip & Knee
- Pulmonology
- Radiology
- IVF
- Robotic & Renal Transplant
- Neuro Imaging
- Non-invasive Cardiology
- Pain Management
- Rheumatology
- Robotics
- Spine Surgery
- Surgical Oncology
- Transplant Hepatology
- Ultrasound-Guided Regional Anesthesia (UGRA)
- Uro-Oncology & Robotic Surgery
- Women's Imaging
- ...and many more.

Open fellowships:

- Cross-Sectional Imaging
- Cardiac Anaesthesia
- Ultrasound Guided Regional Anaesthesia
- Neuro Imaging
- Neuro Anaesthesia
- Endo-Urology & Renal Transplant

Master of Sciences (MSc) Course

MIME is offering two-year full-time Master courses at Max Healthcare Institute Ltd. These programmes are a post-graduate-level degree that allows students to acquire knowledge and skills. In addition, the course will prepare them to work with specific populations and communities to improve health through education, awareness, policy, and real-time exposure.

Provide career advancement and 100% placement opportunities through these Programmes:

Minimum Eligibility - Bachelor's Degree/Graduation in Science

Duration: 2 years

- **Master of Public Health** certified by Academy of Scientific and Innovative Research (AcSIR).
- **Master of Healthcare Quality Management** certified by Academy of Scientific and Innovative Research (AcSIR).
- **MSc in Clinical Research** certified by Regional Centre for Biotechnology (RCB).
- **PhD in Public Health** (affiliated to AcSIR)

Admissions open: For session 2025-2027

Post-Graduate (PG) Diploma Course

MIME is offering one-year full-time PG Diploma courses at Max Healthcare Institute Ltd.

Minimum Eligibility - Bachelor's Degree/Graduation in Science

Duration: 1 year

- **PG Diploma of Public Health** certified by Academy of Scientific and Innovative Research (AcSIR).
- **PG Diploma in Clinical Research** certified by Regional Centre for Biotechnology (RCB).
- **PG Diploma in Healthcare Quality Management** certified by Academy of Scientific and Innovative Research (AcSIR).

Admissions open: For session 2025-2026

Observerships

MIME offers Medical Observership Programmes in various clinical departments to provide Indian and International students with customised training programmes to develop the skills and knowledge. The observership applications are evaluated by the head of the department based on determined criteria that ensures students receive best-in-class training.

Internships

Internships are provided to expose the students to the industry and give hands-on expertise to enhance their skills and knowledge.

Duration: 1-6 months

Allied:

- Physiotherapy
- Dietetics
- Laboratory
- Operation Theatre
- Psychology
- Blood Bank
- Dialysis

Support Services:

- Biomedical Engineering
- Service Excellence
- Human Resource
- Finance
- Medical Records Department
- IT
- Fire and Safety
- Healthcare Supply Chain Management

Upcoming Internship Locations

- Max Super Speciality Hospital, Saket
- Max Super Speciality Hospital, Dwarka
- Max Super Speciality Hospital, Vaishali & PPG

Upcoming Courses Announcement

Life saver training programmes & bespoke/workshop

Max Healthcare Institute is an International Training Centre certified by the American Heart Association and offers short courses in emergency/resuscitation.



**Basic Life Support
Provider Course (BLS)** -
Provider and Instructor



**Advanced Cardiac Life
Support Provider Course
(ACLS)** - Provider and
Instructor



**Paediatric Advanced Life
Support Course (PALS)** -
Provider and Instructor

Upcoming BLS & ACLS training: June 2025

Max Super Speciality Hospital, Saket

- 3rd June – BLS Provider
- 4th/5th June – ACLS Provider (Traditional)
- 23rd June – BLS Provider
- 23rd/24th June – ACLS Provider
- 25th June – BLS Instructor
- 26th June – ACLS Instructor

Max Super Speciality Hospital, Nagpur

- 4th June – BLS Provider
- 11th June – BLS Provider
- 12th/13th June – ACLS Provider (Traditional)
- 18th June – BLS Provider
- 23rd June – BLS Provider
- 24th-25th June – ACLS Provider (Traditional)

Max Super Speciality Hospital, Shalimar Bagh

- 5th June – BLS Provider
- 6th/7th June – ACLS Provider (Traditional)

Nanavati Max Super Speciality Hospital, Mumbai

- 13th June – BLS Provider
- 14th/ 15th June – ACLS Provider (Traditional)

Bespoke / workshop

- Advanced Trauma Life Support® (ATLS®) Course under the aegis of ATLS India certified by American College of Surgeons-Committee on Trauma

Upcoming Courses:

19th, 20th & 21st June 2025

24th, 25th & 26th July 2025

- Precision use of Modern Insulin Pumps Workshop organised by MIME in collaboration with DDF & Endocrinology department, Saket on 11th May 2025
- Liver Forum MIME in collaboration with Radiology Department on 19th July 2025
- Interventional Neurology Workshop on 16th May 2025

Foreign Medical Graduate (FMG) Clinical Skills Course

These courses enhance clinical skills and familiarize FMGs with India's healthcare system. One of the primary challenges FMGs face in clearing the Foreign Medical Graduate Exam (FMGE) is the lack of adequate clinical training. Our experience shows that structured hands-on training significantly improves success rates. The upcoming NEXT exam further underscores the need for clinical skill-building. We propose a programme with the aim to bridge this gap and provide students with an opportunity to advance their career in field of medicine.

Eligibility: Foreign Medical Graduates

Duration:

- **Basic course:** 15 days
- **Advanced course:** 20 days

MIME Online Courses

MIME brings online training courses for healthcare professionals including doctors, nurses and paramedics. These online courses have been curated by our stellar faculty keeping in mind the need of the learners and the healthcare industry:

Mode: Self-paced online learning (Hybrid).

Successful candidates will be awarded a certificate by MIME.

Online Fellowship Courses

- Diabetes Management
- Infectious Disease
- Emergency Medicine
- ENT
- Critical Care
- Obstetrics & Gynaecology (OBS & GYN)
- Bariatric Anaesthesia
- Management of Liver Disorder

Online Certificate Courses

- Aesthetic Medicine and Surgery
- Healthcare Quality Management
- Public Health
- Clinical Research
- Bariatric Nutrition
- Acute Liver Failure (ALF)
- Geriatrics Care
- Difficult Airway Management

For more information, contact us:

Max Institute of Medical Education (MIME)

Max Healthcare Institute Ltd, Press Enclave Road, Saket, New Delhi- 110017

Call: +91 8826 600 461, 9999 853 797

E-mail: education@maxhealthcare.com/ jay.prakashpandey@maxhealthcare.com

Website: www.maxhealthcare.in



Scan for more details

About Max Healthcare

Max Healthcare Institute Limited (Max Healthcare) is one of the largest integrated healthcare providers in the country. We own, operate and provide medical services to facilities in Delhi NCR, Mumbai, Punjab, Uttar Pradesh and Uttarakhand. Max Lab supplements our commitment towards patient care by providing accurate testing and diagnostics. We are also revolutionising the care-continuum through Max@Home, ensuring treatment options are available to our patients in the comfort of their homes. Our continued emphasis on patient-centric care accompanied by our patients' trust has strengthened our position to become one of India's top private healthcare providers.

FACILITIES - **22**

BED CAPACITY - **5,000+**

CLINICIANS - **5,000+**

EMPLOYEES - **35,000+**

4 JCI accredited hospitals

3 AACI accredited hospitals

17 NABH accredited hospitals

12 NABL accredited labs

645+ clinical research projects

2,550+ high index journal research publications till date

1,20,000+ students enrolled in various courses

OUR FACILITIES

SOUTH DELHI

Max Super Speciality Hospital (East Block), Saket

(A Unit of Devki Devi Foundation)
2, Press Enclave Road, Saket,
New Delhi - 110 017
Phone: +91-11-2651 5050

Max Super Speciality Hospital (West Block), Saket

1, Press Enclave Road, Saket,
New Delhi - 110 017
Phone: +91-11-6611 5050

Max Smart Super Speciality Hospital, Saket

(A Unit of Gujarmal Modi Hospital and Research Centre for Medical Sciences)
Mandir Marg, Press Enclave Road, Saket,
New Delhi- 110017
Phone: +91-11-7121 2121

Max Multi Speciality Centre, Panchsheel Park

N - 110, Panchsheel Park,
New Delhi - 110 017
Phone: +91-11-4609 7200

Max Institute of Cancer Care, Lajpat Nagar

(A Unit of Devki Devi Foundation)
26 A, 2nd Floor, Ring Road,
Lajpat Nagar,
New Delhi - 110 024
Phone: +91-11-4720 3000

Max MedCentre, Lajpat Nagar

26 A, 1st Floor, Ring Road, Lajpat Nagar,
New Delhi - 110 024,
Phone: +91-11-4720 3030

CENTRAL DELHI

BLK-Max Super Speciality Hospital

Pusa Road, Rajendra Place,
New Delhi - 110 005
Phone: +91-11-3040 3040

EAST DELHI

Max Super Speciality Hospital, Patparganj

(A Unit of Balaji Medical and Diagnostic Research Centre)
108 A, Indraprastha Extension, Patparganj,
New Delhi - 110 092
Phone: +91-11-4303 3333

NORTH WEST DELHI

Max Super Speciality Hospital, Shalimar Bagh

FC - 50, C & D Block, Shalimar Bagh,
New Delhi - 110 088
Phone: +91-11-6642 2222, 7194 1000

SOUTH WEST DELHI

Max Super Speciality Hospital, Dwarka

(A Unit of Muthoot Hospitals Pvt Ltd)
Plot No. 1, Sector 10, Dwarka,
New Delhi - 110 075
Phone: +91-11-3511 3511

NCR

Max Super Speciality Hospital, Vaishali

(A Unit of Crosslay Remedies Ltd.)
W-3, Sector - 1, Vaishali,
Ghaziabad - 201 012, (U.P.)
Phone: +91-120-4173 000, 4188 000

Max Hospital, Gurugram

(A Unit of ALPS Hospital Ltd.)
Opposite HUDA City Centre Metro Station,
B - Block,
Sushant Lok - I, Gurgaon - 122 001
Phone: +91-124-6623 000

Max Super Speciality Hospital, Noida

Wish Town, Sector-128, Noida - 201 303
Phone: +91-120-4122 222

Max Multi Speciality Centre, Noida

(A Unit of Crosslay Remedies Ltd.)
A-364, Sector - 19, Noida - 201 301
Phone: +91-120-662 9999

MAHARASHTRA

Nanavati Max Super Speciality Hospital, Mumbai

S.V. Road, Vile Parle (West),
Mumbai - 400 056
Phone: +91-22-6836 0000

Max Super Speciality Hospital, Nagpur

(A Unit of Alexis Multispeciality Hospital Pvt. Ltd.)
Survey No. 232, House No. 1313,
Mankapur Square, Koradi Road,
Nagpur - 440030, Maharashtra
Phone: +91-712-7120 000

PUNJAB

Max Super Speciality Hospital, Mohali

(A Unit of Hometrail Buildtech Pvt. Ltd.)
Near Civil Hospital, Phase - 6, Mohali,
Punjab - 160 055
Phone: +91-172-521 2000

Max MedCenter, Mohali

Plot No - A-19, Industrial Area Phase VI,
S.A.S Nagar, Mohali - 160 055
Phone: +91-172 521 2000

Max Super Speciality Hospital, Bathinda

(A Unit of Hometrail Buildtech Pvt. Ltd.)
NH - 64, Near District Civil Hospital, Mansa
Road, Bathinda,
Punjab - 151 001
Phone: +91-164-521 2000

UTTARAKHAND

Max Super Speciality Hospital, Dehradun

Near Indian Oil Petrol Pump, Malsi,
Mussoorie Diversion Road,
Dehradun - 248 001
Phone: +91-135-7193 000

UTTAR PRADESH

Max Super Speciality Hospital, Lucknow

(A Unit of Starlit Medical Centre Private Limited)
Viraj Khand, Gomti Nagar,
Lucknow - 226 010, U.P.
Tel.: +91-522-6780 001, 6780 002



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CIN: L72200MH2001PLC322854

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or visit www.maxhealthcare.in

Submit your articles for the June 2025 edition by 31st April 2025.
Email us at mmjeditorialboard@maxhealthcare.com