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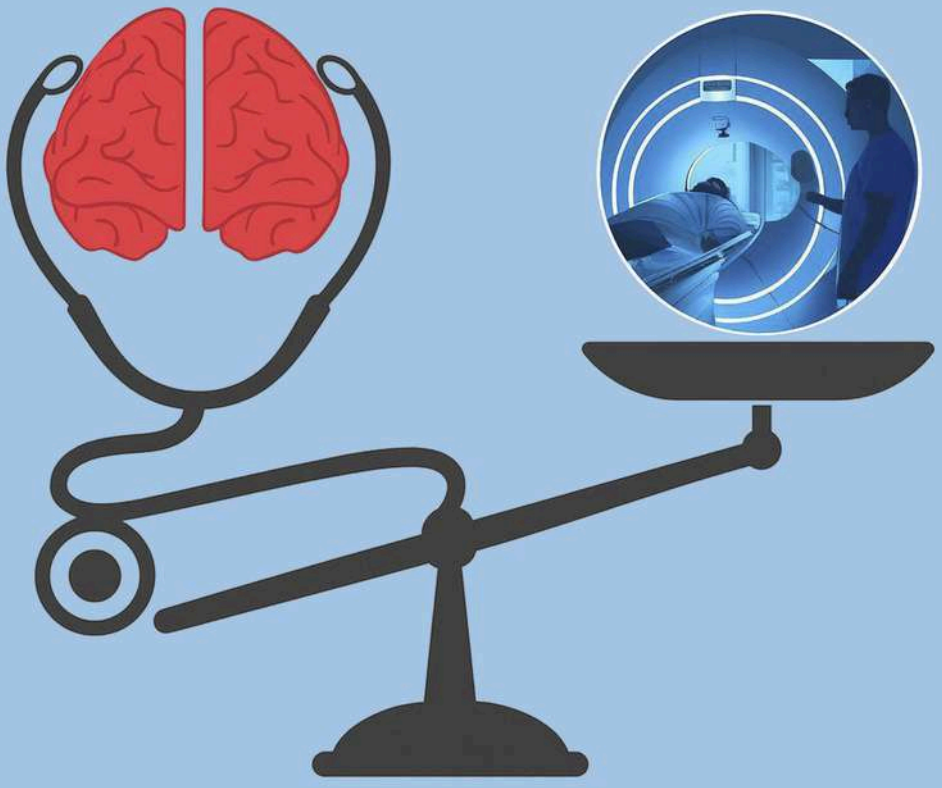

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CASE REPORTS

EDITORIAL

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Diagnostic stewardship: a call for clinical prudence in practice

Manilgama SR[1], Hettiarachchi NM[2], Liyanage ADMD[3], Karunaratna S[4]

Preamble

High-quality patient care depends on accurate and timely diagnosis. Decades back, it relied solely on the clinical skills of the treating physician. However, in the recent past, the stethoscope has often been replaced by scans, and bedside reasoning by biochemical panels. Ordering a test is easy; interpreting it wisely is the art. The increasing availability and reliance on diagnostic technologies have raised questions not only about the appropriateness, timing, and interpretation of such investigations, but also about test accuracy. In this context, the concept of **diagnostic stewardship (DS)** has emerged as a vital framework to optimise the use of diagnostic tools, particularly in resource-limited settings such as Sri Lanka.

Diagnostic stewardship is the thoughtful coordinated strategic guidance to therapeutic decisions and interventions to improve appropriate utilisation of diagnostic tests to ensure patients receive the best possible care. This encompasses **test selection, timing, specimen collection, interpretation,** and **action on results.** This approach not only enhances the accuracy of diagnoses and the effectiveness of treatments, it also optimises the use of healthcare resources—all in service of better outcomes and healthier lives.

This editorial calls for a revival of clinical prudence through the practice of "diagnostic stewardship."

Introduction

The true art of clinical diagnosis relies on thorough history taking and physical examination. While laboratory and imaging tests were initially introduced to support and confirm clinical diagnoses, the rapid evolution of technology and healthcare expectations have shifted the diagnostic paradigm. In many cases, clinical reasoning is now overshadowed by indiscriminate ordering of tests—resulting in **misdiagnosis, overdiagnosis, over-treatment, increased cost, and psychological harm to patients.**(1,2)

A meta-analysis by Zhi M et al. in 2013, highlighted that nearly 20–30% of commonly ordered diagnostic are tests are unnecessary, while under-utilisation of appropriate tests also persists.(2,3) These imbalances exacerbated by defensive medical practices, lack of training, fragmented health records, and poor feedback mechanisms.

In context, the Sri Lankan healthcare system which is publicly funded and free at the point of delivery, is acutely vulnerable to such inefficiencies, due to the cost of redundant or inappropriate diagnostics competing with already scarce resources.

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Diagnostic stewardship in action

DS operates at several levels. At the **pre-analytic** stage, it guides the selection of the right test for the right patient at the right time. During the **analytic** phase, it ensures optimal sample collection, transport, and analysis. The **post-analytic** phase focuses on correct interpretation and clinical action based on results.

DS is considered a parallel force to antimicrobial and infection prevention stewardship programmes, forming a triad often referred to as **AID stewardship**: antimicrobial, infection prevention, and diagnostic stewardship. (4-6) One of the most cited practical frameworks is the **AID stewardship model**, proposed by Dik et al, integrating diagnostic processes with infection control and antimicrobial stewardship to reduce inappropriate test ordering and improve patient outcomes. (4-6) Optimising the use of blood cultures, urine cultures, and inflammatory markers through guidelines are examples of translating DS into practice. (7-9)

In their practical guide by the Society for Healthcare Epidemiology of America, Fabre et al. emphasised the need to develop local guidelines for test ordering, improve communication between laboratory and clinicians, and implement audit-feedback loops. (7) They also called for educational interventions to train clinicians in diagnostic reasoning and test interpretation.

Implications of poor diagnostic stewardship

Consequences of poor DS may be profound:

- **False positives** may lead to unnecessary treatments and iatrogenic harm
- **False negatives** can delay life-saving therapies
- **Redundant testing and broad investigation panels** increase cost, delay care, and overwhelm laboratory services
- **Overuse of imaging** may lead to detection of incidentalomas, cascading further investigations without clinical benefit

In high-burden infectious disease settings, such as dengue and leptospirosis-prone regions in South Asia, limited use of DS for **treating patients, increases unnecessary admissions** and anxiety from inconclusive or misleading results. Overwhelmed healthcare services due to inappropriate ordering of dengue NS1 and IgM panels outside the diagnostic window is a well-known example.

Similarly, the overuse of inflammatory markers like CRP and procalcitonin without context can mislead clinicians.

Diagnostic stewardship in the local healthcare setting

Several systemic factors hinder diagnostic stewardship:

- **Limited clinical audit systems**
- **Inadequate feedback loops between laboratories and treating teams**
- **Limited digitalization and electronic record keeping**
- **Resource constraints in rural settings that prevent timely or repeated testing**

Therefore, investment should not only focus on training clinicians but also on strengthening institutional mechanisms to monitor test utilisation patterns and promote accountability.

Introducing **structured care pathways**, **standardised test panels**, and **decision-support algorithms** at ward level can significantly improve the diagnostic yield while conserving resources.

Future directions and integration with AI

AI-enabled decision tools hold potential avenues to establish roots of diagnostic stewardship in the local healthcare setting.

The AI-enabled decision tools could contribute by:

- Predicting test utility based on patient profile and disease likelihood
- Suggesting alternative tests or suppressing redundant orders
- Flagging inappropriate or underused tests at the point of care

However, AI can only succeed if built upon validated clinical guidelines and accurate data. Stewardship principles must be embedded in the design and evaluation of these technologies.

Conclusion

Diagnostic stewardship is no longer a choice—it is a necessity. It should be embraced in its full capacity, beyond addressing AID stewardship, and incorporated as an integral part of routine clinical practice. As medical technologies advance and healthcare systems grow more complex, clinicians and administrators must collectively commit to the judicious use of diagnostics. In low-resource settings, it is especially crucial to align diagnostic decisions with patient needs, clinical reasoning, and health system capacity.

By integrating diagnostic stewardship into routine medical education, hospital policy, and national clinical protocols, we can improve care quality, reduce harm, and make healthcare more sustainable.

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RESEARCH

Asian J Intern Med. 2025 July; 4(2)

Frequency and associated factors with loss-to-follow-up among people living with HIV followed-up in Parakou, Benin from 2018 to 2022

Alassani A[1], Gouda F[1], Djibril A[1], Djalogue L[3], KonE S[2], Wanvoegbe A[4]

Abstract

Introduction: Human immunodeficiency virus (HIV) infection remains a major public health problem worldwide. One of the main strategies to overcome this infection is proper patient follow-up. This study focused on loss to follow-up among people living with HIV (PLHIV).

Methods: This was a retrospective, descriptive and analytic study. Patients living with HIV of both sexes, over 18 years old, on antiretroviral (ARV) therapy, followed-up from January 1st, 2018 to December 31st, 2022 in Parakou were included in this study. The dependent variable was loss to follow-up. Data analysis was performed using Epi Info version 7.2 software. A p-value less than 5% was considered statically significant.

Results: The study sample consisted of 2,652 PLHIV. The mean age (±SD) was 32.48 ±9.40 years. A female predominance was observed with a sex ratio of 0.53. Among PLHIV of the sample 293 (11.04%) were lost to follow-up. Associated factors with loss to follow-up in multivariate analysis were male gender, age <30 years, monthly income <172.31 USD, being uneducated and a CD4 count ≥350/mm^3.

Conclusions: Approximately one in 10 PLHIV was lost to follow-up. Strengthening pre-treatment education and addressing contributing factors are essential in reducing the frequency of loss to follow-up.

Keywords: PLHIV, lost to follow-up, antiretroviral therapy

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Introduction

The discovery of antiretroviral (ARV) therapy has raised great hope. Antiretroviral therapy has improved the lives of patients with HIV infection, which has gone from being a near-fatal disease to a chronic illness. (1) Antiretroviral therapy is most often a triple therapy combining at least two drugs from different classes. This triple therapy was only available in developed countries. But with the reduction in the cost of ARVs by pharmaceutical companies and the commitment of the highest authorities in African countries, initiatives to improve access to antiretrovirals have emerged in several African countries since 1998. In Benin, antiretrovirals have been used since 2002 and are offered free of charge to PLHIV. Before starting treatment, care teams must inform, educate patients and support them in taking their treatment, taking into account the difficulties related to medication adherence while fighting against any social and professional stigma and/or discrimination. (2,3) Long-term monitoring of patients with HIV is a major challenge faced by healthcare providers. Beyond the medical and technical challenges of this monitoring, maintaining patients in the care pathway is problematic. The lifelong nature of treatment creates several difficulties (weariness, discouragement, lack of time) leading to an increase in the rate of loss to follow-up of cohorts of PLHIV, which can range from 30 to 80% in some developing countries. (4-6) Loss to follow-up is one of the factors that can prevent the achievement of the UNAIDS objectives of screening 95% of PLHIV subjects, 95% of screened subjects put on antiretrovirals and 95% of subjects under treatment with an undetectable viral load. (7) Fear of negative reactions from those around them and the deterioration of social relationships also explain why PLHIV are lost to follow-up. Addressing the critical issue of loss to follow-up of adult patients after the start of treatment requires describing the outcome of these patients and investigating the presumed reasons for non-return to the care site. The consequences of loss of follow-up of PLHIV are multiple and include among other things, HIV resistance to antiretrovirals, opportunistic infections and high mortality. Among the 630,000 HIV deaths in 2022, 70% lived in sub-Saharan Africa. (8-11) Several factors are associated with loss to follow-up among PLHIV, including sociodemographic conditions, comorbidities and treatment. (12,13) Despite the problems associated with frequently encountered loss to follow-up, no studies to our knowledge are currently available in Benin. This study was conducted on loss to follow-up in PLHIV in order to determine the frequency and the associated factors. The results of this study will help in taking decisions to minimise the loss to follow-up in order to improve the care of these patients.

Methods

This was a retrospective, descriptive and analytic study. Data collection was done over a five- month period, from February 1, 2023, to June 30, 2023.

The population consisted of PLHIV of both sexes, followed in the Internal Medicine Department of the Borgou Régional University based Hospital (BRUH) from January 1, 2018, to December 31, 2022 who were 18 years old and above. Patients whose records were illegible or unretrievable were not included in this study.

The dependent variable was loss to follow-up. The criteria for assessing loss to follow-up used were those validated by the World Health Organization. A person living with HIV was considered lost to follow-up when they have missed follow-up appointments for at least three months and no information is available in their file on their outcome. The independent variables included sociodemographic data, lifestyle comorbidities and CD4 count at first screening. Data were collected from patient medical records.

The data collected were recorded, processed, and analyzed using Epi Data 3.1 and Epi info 7.2.0.1 software, respectively. Univariable Cox regression analysis was conducted to identify candidate variables, with variables having a p-value ≤0.25 being entered into the multivariable regression analysis. A forward variable selection method was applied to identify significant predictors. Adjusted hazard ratio (AHR) with corresponding 95% confidence intervals (CIs) and p-values were used to assess the strength and significance of associations. The significance threshold for the results was set at 5% in multivariable analysis.

Results

The study population consisted of 2,652 PLHIV. The mean age(±SD) was 35.82 ± 10.34 years old, with a range of 18 to 84 years. A female predominance was observed, with a sex ratio of 0.53. Uneducated subjects represented 39.67% of the study population. The prevalence of hypertension and diabetes was

Table 1. General characteristics of HIV-positive people monitored in the internal medicine department of CHUD/B from 2018 to 2022 (n=2652)

	n	%
Age		
< 30 years	655	24.69
≥ 30 years	1997	75.31
Gender		
Male	881	33.22
Female	1771	66.73
Marital status		
Married	1418	53.47
Single	1234	46.53
Nationality		
Beninese	2609	98.38
Non-Beninese	43	01.62
Education level		
None	1052	39.67
Primary	1257	47.40
Secondary	285	10.75
Higher education	58	02.18
Comorbidity		
Hypertension	302	11.40
Diabetes mellitus	38	01.45
Monthly income (CFA francs)		
< 100000	2614	98.56
≥ 100000	38	01.44
Lifestyle		
Alcohol consumption	671	25.30
Tobacco use	35	01.31
CD4 count (cells/mm^3)		
< 350	1440	54.30
≥ 350	1212	45.70

11.40% and 1.45%, respectively. The majority of subjects (98.56%) had a monthly income of less than 100,000 CFA francs (160 US dollars). Alcohol and tobacco use were observed in 25.3% and 1.31% of patients, respectively. The CD4 count was <350 cells/µl in 54.3% of subjects (Table 1).

Among PLHIV, 293 were lost to follow up, representing a frequency of 11.04%. Approximately half (n=150, 51.24%) of these subjects were lost to follow-up after two years.

Factors associated with loss to follow-up in multivariate analysis were male gender (p<0.001), age <30 years (p<0.001), monthly income <100,000 CFA francs (p<0.001), uneducated subjects (p=0.010) and a CD4 count ≥350/mm3 (p=0.003) (Table 2).

Discussion

This study addressed loss to follow-up among PLHIV, an important aspect in achieving the UNAIDS objectives. The frequency of loss to follow-up among PLHIV was 11.04%. Ahmed et al.(15) in Ethiopia and Ntabanganyimana et al.(16) in Rwanda had reported frequencies of 13.4% and 15.57% respectively which were closer to our value. Higher frequencies of loss of follow-up had been reported by Bogenya et al.(9) in the Democratic Republic of Congo and Gray et al.(17) in Liberia (47.89% and 41.8% respectively). This difference could be explained by socio-cultural differences and by the threshold of the definition of loss to follow-up which is 6 months whereas in the present study it was 3 months. The factors associated with loss to follow-up were male gender, age less than 30 years, a monthly income of less than 100,000 CFA francs, uneducated PLHIV and a CD4 count ≥350 cells/mm3. The results of the present study are congruent with those reported by several authors. (18,19) Male sex had been reported as an association by Tesha et al.(20) in Tanzania and Wekesa et al.(21) in Kenya. In the studies of Ntabanganyimana et al. (16) in Rwanda and Paundi et al.(22) in Zambia, living far from the center or being unable to afford transportation costs were factors associated with loss to follow-up. Zeleke et al.(23) in Ethiopia reported that PLHIV with a low level of education were more at

Table 2. Factors associated with loss to follow-up among PLHIV monitored in the internal medicine department of CHUD/B from 2018 to 2022

	OR (95%CI)	p-value
Age		
≥ 30 years	1	< 0.001
< 30 years	2.23 (1.22 - 4.07)	
Gender		
Female	1	< 0.001
Male	2.11 (1.31- 4.15)	
Educated patients		
Yes	1	< 0.001
No	4.24 (2.18 -7.02)	
Monthly income (CFA francs)		
< 100000	1	0.010
≥ 100000	0.28 (0.10 - 0.74)	
CD4 count (cells/mm^3)		
< 350	1	0.003
≥ 350	3.49 (1.87 - 8.59)	

risk of being lost to follow-up. In the studies of Gamechu et al.(5) and Ganta et al.(12), a high CD4 count was associated with loss to follow-up. This study was limited to determining the frequency of loss to follow-up and identifying associated factors. It is important for future studies to actively investigate for causes of loss to follow-up. This will allow us to describe their future but above all to identify the main causes of their loss to follow-up.

Limitation

Some data such as nutritional status and viral load at screening were missing. This research could have been extended to all HIV care sites in the north in order to have a more representative sample and reach conclusions that could be generaliszed to the entire population of northern Benin.

Conclusion

Loss of follow-up is frequent among PLHIV monitored in the Internal Medicine department. Younger people, males, those with low monthly income or high CD4 counts are more likely to default follow-up.

Declarations

Author contributions:
All authors designed the study. AA, DA, DL and KS participated in data collection, and data were analysed by AA and WA and AA wrote the main manuscript text . All authors reviewed the manuscript.

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Permission was obtained from hospital officials. Data anonymity and confidentiality were respected. This was a retrospective study using patient records as the data source.

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An audit on the delivery of diabetes care practices at a tertiary care hospital in Sri Lanka

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Abstract

Introduction: Type 2 diabetes mellitus (T2DM) is a major non-communicable disease in Sri Lanka, with rising prevalence and associated high morbidity due to chronic complications. Despite the availability of national and international guidelines, adherence to standard diabetes care practices in busy outpatient settings remains suboptimal. This audit aimed to assess the quality of diabetic care and screening for complications at a medical clinic in a tertiary care medical unit in central province, Sri Lanka.

Methods: A clinical audit was conducted over one month (April–May 2023) among patients aged ≥18 years with T2DM attending a tertiary care medical clinic. Every third eligible patient was recruited. Data were collected using a validated, interviewer-administered questionnaire and clinic records. Audit standards were based on National guidelines for management of diabetes (2021) and the American Diabetes Association (ADA) (2022) recommendations.

Results: Among 140 participants (76 females, 64 males) with a mean age of 62.79 (±10.4) years, monthly blood glucose monitoring (91.43%) and blood pressure recording (100%) met audit standards. However, only 42.86% underwent glycated haemoglobin (HbA1c) testing within six months. Body mass index (BMI) and waist circumference were recorded in just 8.57% and 2.86% of patients, respectively. Annual electrocardiography (ECG) and biannual lipid profiles were done in 40% and 55.71%, respectively. Microalbuminuria screening was notably low (8.57%). Retinopathy screening was completed in 51.43% of patients, while neuropathy screening was not performed in any. Only 25.71% received dietary counselling and 20% were advised on physical activity.

Conclusions: This audit highlights key deficiencies in metabolic monitoring, complication screening, and lifestyle counselling in a tertiary care medical clinic. Structured care pathways and regular audits are essential to improve compliance with established diabetes care standards.

Keywords: type 2 diabetes mellitus, glycaemic control, complication screening, lifestyle counseling

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Introduction

Type 2 diabetes mellitus (T2DM) is a non-communicable disease accounting for approximately 90–95% of all diabetes cases.(1) It results from a combination of peripheral insulin resistance and impaired insulin secretion.(1) This condition is frequently underdiagnosed for several years, as the gradual rise in blood glucose often does not produce the classical symptoms of diabetes in its early stages. (1) While a strong genetic predisposition is often observed, the exact genetic mechanisms underlying T2DM remain unclear.(1)

Similar to obesity and arterial hypertension, T2DM is associated with a range of complications, particularly target organ damage (TOD).(2) Diabetes-related vascular complications may affect either small vessels (microangiopathy) or large vessels (macroangiopathy).(3) Microangiopathies, involving the retinal vessels, kidneys, and vasa nervorum, can lead to retinopathy, nephropathy, and neuropathy respectively.(3) Macroangiopathy, through the promotion of atherosclerosis in the carotid, coronary, and peripheral arteries, increases the risk of stroke, myocardial infarction, and peripheral vascular disease.(3)

The most significant risk factors contributing to these diabetes-related complications are persistent hyperglycaemia, hypertension, and dyslipidaemia.(4) Numerous studies have shown that effective control of blood glucose, blood pressure, and lipid levels can substantially reduce the incidence of such complications.(4) Globally, diabetes and its associated complications are among the leading causes of morbidity and mortality. (4)

Multiple audits have been conducted to evaluate the efficiency of diabetes care including screening for end organ damage. A 2008 audit in Bosnia and Herzegovina, conducted in a primary care setting, highlighted deficiencies in care quality and variability in service delivery among different primary care teams.(5) In 2017, a quality improvement initiative in Qatar assessed the monitoring of diabetes-related complications in home care patients, concluding that structured interventions could successfully enhance monitoring in accordance with international guidelines.(6) Similarly, Melissa et al. (2022) carried out an audit in a Canadian tertiary diabetes care centre to assess screening practices, achievement of therapeutic targets, and patient care outcomes.(7)

Several audits have also been conducted in Sri Lanka. In 2009, a study at a tertiary care hospital in the Southern Province found that 84% of patients met the audit standards for blood glucose control, and 78% met standards for retinopathy screening.(8) Another audit in 2010, conducted at the outpatient department of the university medical unit, National Hospital of Sri Lanka, assessed care standards for patients with T2DM.(9) In 2016, an audit at the same hospital highlighted that while screening for metabolic parameters and diabetes complications was high, there were notable gaps in monitoring HbA1c, lipid profiles, and nephropathy.(10) Additional audits conducted in Sri Lanka further support these findings. (11,12)

Despite the widespread availability of clinical guidelines for diabetes management, consistent adherence to these recommendations remains a significant challenge in the context of overcrowded outpatient clinics in Sri Lanka. Diabetes is highly prevalent among Sri Lankans, with one in five adults affected by either diabetes or prediabetes.(13) Alarmingly, one-third of individuals with diabetes remain undiagnosed and untreated.(13) The rising prevalence of diabetes continues to strain the healthcare system. Poor glycaemic control is strongly associated with the development of complications, which significantly increase both morbidity and mortality. Early detection of end organ damage is therefore critical to preventing disease progression and improving patient outcomes. This underscores the importance of regular and thorough screening for diabetes-related complications.

The rationale of this study is rooted in addressing a critical gap between recommended diabetes care guidelines and actual clinical practice in a tertiary care setting in Sri Lanka. Despite the existence of well-established national and international guidelines for the management of T2DM, real-world implementation is often inconsistent, especially in busy outpatient settings like those in the tertiary care hospitals. Sri Lanka faces a growing burden of T2DM, and poor adherence to care protocols can lead to increased complications, morbidity, and healthcare costs.

The primary objective of this audit was to assess end-organ screening in patients with T2DM attending a tertiary care medical clinic in the central province. In addition to this, the audit aimed to evaluate the screening of metabolic risk factors and parameters, such as BMI, lipid profile, and waist-to hip ratio, in the same patient population. Another important objective was to assess the extent to which patients

received advice on lifestyle modifications, such as dietary counselling and physical activity. Furthermore, the audit sought to initiate and implement structured protocols for end-organ screening for patients with T2DM, aiming to enhance adherence to recommended diabetes care standards.

Methods

This descriptive cross-sectional audit was conducted in patients aged 18 and above, who received treatment for T2DM attending a tertiary care medical unit in the central province over the course of one month (18/04/2023- 18/05/2023). A systematic sampling method was used to select participants from the clinic registry, where every 3rd patient with T2DM, during the study period was recruited to the study. Participants' information sheet was distributed and informed written consent was obtained from the study participants. The questionnaire was filled by investigators of the study who are experienced doctors in the internal medicine field. The medical officers involved in patient care were also engaged in the data collection process. This audit, which represents the first phase of a broader quality improvement initiative, was conducted in adherence to the national guidelines for management of diabetes (2021) (14) and ADA guidelines 2022. (15)

According to the national guideline, blood glucose levels should be assessed each monthly using Fasting Plasma Glucose (FPG) and 2-hour Postprandial Glucose (PPG); if only one test is to be performed, the preferred choice is the 2-hour PPG after the main meal of the day. HbA1c should be measured every three months until good glycaemic control is achieved, and then every six months thereafter. Blood pressure must also be recorded during every monthly clinic visit, with hypertension defined as readings consistently above 130/80 mmHg. Cardiovascular risk should be evaluated with a 12-lead ECG annually and lipid profile testing twice per year. For nephropathy screening, annual urine albumin testing is recommended. If albumin is present, urinary tract infection should be ruled out and testing repeated twice more over a three-month period; confirmation of macroalbuminuria is based on at least two positive results. If macroalbuminuria is excluded, the urine albumin-to-creatinine ratio (ACR) should be checked annually to assess for microalbuminuria. Retinopathy screening through ophthalmoscopy should occur at diagnosis and then annually. Comprehensive foot care includes yearly examination using a monofilament test and Doppler pulse study. Neuropathy screening should also be conducted annually with a monofilament and tuning fork examination. According to ADA 2022 Standards of Care guidelines, weight, BMI and waist circumference should be measured at least annually for all individuals with type 2 diabetes.

A validated interviewer administered structured questionnaire was used to collect data from the subjects. In addition, certain data were obtained from the outpatient clinic records. Demographic information including age and sex were collected from patients. Data regarding glycaemic control, blood pressure monitoring, metabolic screening (weight, height and lipid profile), nephropathy/retinopathy screening, foot examination and lifestyle modification (advice on diet and exercise) were collected. Personal information was not collected to ensure privacy. Ethical approval was obtained from the ethics review committee of NHK. Administrative permission was obtained from the director and relevant unit consultant. Data analysis was done using Microsoft Excel and IBM SPSS version 23. Numerical data was presented with means, and categorical data was presented as percentages. Collected data was compared with audit standards.

Results

A total of 76 females and 64 males with mean age of 62.79 (±10.4) years participated in the study. When the audit results were compared with established standards, several key observations emerged. Monthly blood glucose monitoring was conducted in 91.43% of patients, demonstrating good adherence to recommended practices. However, only 42.86% had their HbA1c tested within the past six months, indicating room for improvement in long-term glycaemic monitoring. All patients (100%) consistently had their blood pressure measured during monthly visits, meeting the standard for hypertension management. While 82.86% of patients had their weight measured annually, only 8.57% had their BMI calculated, and a mere 2.86% had their waist circumference assessed, highlighting a significant gap in comprehensive anthropometric monitoring.

In terms of cardiovascular risk assessment, just 40% of patients underwent an annual ECG, and 55.71% had their lipid profiles checked twice yearly. Screening for nephropathy revealed that 42.12% had an annual urine full report (UFR), but only 8.57% were tested for microalbuminuria. Retinopathy screening

was completed in 51.43% of patients, and among them, 13.88% were diagnosed with diabetic retinopathy. Notably, none of the patients received annual neuropathy screening, and only 30% had a foot care examination. Lifestyle counselling was also limited, with just 25.71% of patients receiving dietary advice and only 20% being advised on physical activity. These findings highlight areas requiring greater focus to improve adherence to comprehensive diabetes care standards.

Discussion

This audit evaluated the extent to which diabetes care provided at a tertiary care medical clinic adhered to national and international standards. The findings demonstrate that while certain components of care, such as blood pressure monitoring, are adequately performed, there are significant gaps in other crucial aspects, including metabolic monitoring, complication screening, and lifestyle counselling.

Blood glucose monitoring in our audit was performed in 91.43% of patients, comparable to the 84% compliance rate found in a 2009 audit in southern Sri Lanka.(8) Similarly, Ranasinghe et al.(9) also reported satisfactory blood glucose monitoring, indicating consistent national adherence to this aspect of care. However, unlike the high HbA1c testing rates reported by Pasqua et al.(7) in Canada, where over 90% of patients had HbA1c checked, our audit showed only 42.86% received this test within the past six months, falling short of both international standards and ADA recommendations for quarterly testing until good control is achieved.(1) This underperformance is consistent with findings from Arambewela et al.(10), who also noted gaps in metabolic monitoring, particularly HbA1c testing, in Sri Lankan outpatient clinics.

Anthropometric measurements were underutilized in our setting, with only 8.57% having BMI calculated and just 2.86% assessed for waist circumference. This mirrors the deficiencies described by Ranasinghe et al.(9), where weight was often recorded but BMI and waist circumference were frequently overlooked. In contrast, global standards as reflected in Canadian and Qatari audits typically emphasize routine assessment of these metrics due to their importance in cardiovascular risk prediction.(6,7) The ADA also recommends annual measurement of weight, BMI, and waist circumference in all individuals with type 2 diabetes (1), underscoring the significance of these omissions.

Cardiovascular risk assessment practices were also suboptimal in our audit. Only 40% of patients underwent annual ECG, and 55.71% had biannual lipid profiles performed. These findings are slightly better than the results in the Qatar audit, which initially reported low baseline compliance but showed improvement following targeted interventions.(6) Within Sri Lanka, Arambewela et al. (10) similarly noted that lipid profile monitoring was inadequate, suggesting a broader systemic issue in implementing full cardiovascular screening protocols.
Regarding nephropathy screening, only 8.57% of patients in our audit were screened for microalbuminuria, a figure consistent with the 2016 Colombo based audit that also found low rates of albuminuria testing.(10) While 42.12% of patients had a general urine full report (UFR), this is insufficient for early detection of microalbuminuria, which is a more specific and sensitive marker of early renal involvement. This pattern suggests that nephropathy detection is often delayed in local settings despite guideline recommendations for annual microalbuminuria testing.(1)

Retinopathy screening was conducted in 51.43% of patients in our audit, with 13.88% of those screened diagnosed with diabetic retinopathy. These figures are significantly lower than the 78.6% screening rate reported in the Canadian study (7) and the 78% rate from the 2009 southern Sri Lankan audit (8), indicating a worrying decline in adherence over time or variability across different institutions. Given the preventable nature of vision loss with early detection, this area needs urgent attention.

One of the most concerning findings of our audit was the complete absence of neuropathy screening. This falls well below national and international standards, and contrasts with the Canadian audit, where neuropathy screening is regularly conducted using standardized methods.(7) Local audits have not specifically quantified neuropathy screening rates, which may point to a broader lack of focus or documentation in this area.

Lifestyle counselling was another area of weakness in our audit. Only 25.71% of patients received dietary advice and just 20% were advised on physical activity. These figures are consistent with findings from Ranasinghe et al.(9), who noted a lack of structured counselling interventions in diabetes care. In contrast, international audits such as that from Qatar demonstrated that structured improvement programs can significantly enhance the delivery of lifestyle advice even in resource-limited or home-based care settings.(6)

Conclusion

This audit highlights critical gaps in the delivery of comprehensive diabetes care at a tertiary hospital outpatient clinic in Sri Lanka. While blood pressure and glucose monitoring are well implemented, other areas, particularly HbA1c monitoring, cardiovascular risk assessment, complication screening, and lifestyle counselling require considerable improvement. The findings align with previous local audits and point to persistent systemic challenges in achieving guideline-based care for diabetes patients.

Limitations

This audit has several limitations that should be acknowledged. First, the study was conducted in a single tertiary care outpatient clinic, which may limit the generalisability of the findings to other healthcare settings across Sri Lanka. The sample size, although adequate for preliminary evaluation, may not fully represent the broader population of patients with type 2 diabetes mellitus in the region.

Second, data collection relied partly on patient recall and self-reporting, particularly for lifestyle counselling and previous screening history. This introduces the potential for recall bias and underreporting of care that may have occurred but was not documented in clinic records.

Third, the audit primarily focused on the documentation of care processes (e.g., whether HbA1c was measured or ECG performed) rather than on the clinical outcomes or quality of those interventions. Therefore, while it assesses adherence to standards, it does not evaluate the effectiveness of care delivered.

Finally, resource limitations in the clinic, including inadequate staffing, equipment availability and overcrowding, may have affected both the provision of services and the ability to document them accurately. These systemic factors must be considered when interpreting the findings and planning future quality improvement interventions.

Recommendations

1. Enhance training for healthcare providers on guideline-based care, especially regarding the importance of HbA1c, BMI, waist circumference, and microalbuminuria testing and neuropathy screening.
2. Develop and implement structured care pathways and checklists to ensure all required assessments are conducted routinely.
3. Improve record-keeping systems to facilitate better follow-up and audit of key diabetes care indicators.
4. Strengthen patient education programs to promote lifestyle modification and empower self-management.
5. Conduct periodic audits and feedback cycles to sustain quality improvement and address areas of deficiency over time.

Declarations

Author contributions:
All authors played an integral role in developing the study's concept and design. Rupasinghe S, Wijesingha WMCR, Rathnayaka DL, Pathirana D and Wijekoon V contributed to data collection. Rupasinghe S wrote the manuscript, conducted data entering and data analysis. Jayasinghe IK supervised the study and revised the manuscript. All authors read and approved the final manuscript.

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REVIEW

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Enhancing resilience in nursing: the role of education, support systems, a multi-level approach to enhancing adaptability and preventing burnout

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Abstract

Resilience is a crucial factor in nursing, empowering nursing professionals to navigate the high-stress, emotionally demanding and fast-paced environments of modern healthcare settings. The ability to adapt to challenges, maintain well-being and sustain professional commitment directly influences patient care and workforce retention. This review explores the role of education, support systems and a multi-level approach to facilitate resilience and prevent burnout among nurses. At the educational level, integrating resilience-focused training within nursing curricula, simulation-based learning, mindfulness practices and mentorship programs strengthen emotional intelligence and coping mechanisms. Additionally, social and interpersonal support systems, including peer networks, mentorship and team-based collaboration, further improve resilience through experience sharing and collective problem-solving. By integrating findings from recent literature, this review accentuates evidence-based interventions for resilience-building. This review further prioritises their impact on the well-being of nurses, patient safety and long-term career sustainability. Future directions emphasise the integration of digital resilience tools, AI-driven coaching and policy recommendations to demonstrate resilience as a fundamental aspect in nursing practice. A coordinated, multi-tiered approach is vital to ensure that nurses receive the necessary support to succeed in their demanding roles while preserving high standards of patient care. Drawing from sources such as PubMed Central, Lippincott Journals, BMC Nursing, ResearchGate, SAGE Journals and Emerald, this review synthesises existing literature to propose a structured framework for resilience-building in nursing.

Keywords: resilience, nursing profession, nursing education

Introduction

Nursing is a demanding profession that requires emotional strength and adaptability. These qualities help nurses navigate high-pressure environments and complex patient needs. Therefore, resilience is essential for professional sustainability.(1) Strengthening resilience helps attenuate burnout, improve well-being and contributes to better patient outcomes. Despite the ongoing commitment to patient care, resilience enables nurses to adapt to the challenging conditions of the healthcare field.(2)

Further, nurses frequently encounter stressors such as high patient workloads, emotionally charged situations and extended working hours, all of which contribute to mental and physical exhaustion. Persistent exposure to these stressors without

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tolerable coping mechanisms can lead to burnout, job dissatisfaction and workforce attrition, ultimately compromising patient care.(3) Therefore, resilience, which means the ability to adapt, recover and thrive despite adversity, is a key factor in sustaining nurses' well-being. Recent studies have shown that resilient nurses demonstrate greater job satisfaction, lower burnout rates, improved patient safety outcomes and enhanced professional engagement. Moreover, within the increasing complexity of modern healthcare, there is a desperate need for structured resilience-building strategies has become more desperate than ever.(4)

Aims and scope of the review

This review encompasses theoretical perspectives, resilience-enhancing strategies, and systemic interventions at the individual, social and organizational levels, with an emphasis on long-term sustainability. The proposed framework includes strengthening resilience in nursing education by incorporating resilience-focused training, simulation-based learning, mindfulness practices and mentorship into nursing curricula. At the individual and social levels, the framework promotes self-care, emotional intelligence, professional development and stress management, along with enhancing peer support networks, team collaboration and mentorship programmes. At the organisational and system level, it is recommended to implement leadership-driven initiatives, institutional policies and mental health resources to create a supportive work environment. Therefore, by integrating insights from recent literature, this review highlights the importance of a structured, multi-level approach to enhancing resilience.

Understanding resilience through theoretical perspectives

Some accepted definitions to describe resilience are as follows: a stable route of healthy functioning after a critical adverse event; a deliberate attempt to move forward in an insightful and integrated positive manner because of lessons learned from a harmful experience; the capacity of a dynamic system to adjust productively to disturbances that threaten the viability, function and development of that system; and an action to utilise resources in order to sustain well-being.(5) Key components of resilience include emotional intelligence, adaptability and problem-solving skills. Social support research highlight that resilience functions as a buffer against workplace stressors and contributes to favourable patient outcomes.(3)

Theoretical perspectives on resilience in nursing provide fundamentals for understanding how nurses adapt to stress and maintain well-being. Theoretical perspectives such as stress adaptation theories, the psychological resilience model and the resilience framework for nursing provide essential insights into how nurses cope with stress. Stress adaptation models such as Lazarus and Folkman's Transactional Model of Stress and Coping interpret how nurses analyse and respond to stressors. Furthermore, it describes the role of cognitive appraisal and coping mechanisms in resilience development.(6) Additionally, Antonovsky's Salutogenic Model (Sense of Coherence) aims to see how people remain healthy even with stress. It prefers that a strong "sense of coherence" equips individuals including nurses to effectively organise resources and deal with challenging working surroundings.(7) Another model called Ungar's Ecological Framework of Resilience explores a broader, system-oriented approach by considering resilience as a dynamic process influenced by both individual features and the availability of external resources.(8)

Current challenges to resilience

Nurses face various critical challenges that block their ability to build and maintain resilience. High patient-to-nurse ratio increases workload, reducing the time available for quality patient care and self care, eventually leading to burnout.(9) Also, emotional weariness and compassion fatigue result from continuous exposure to patient suffering, affecting mental well-being and job satisfaction. Nurses usually deal with emotionally taxing incidents such as patient suffering, palliative care and traumatic events. Long-term exposure to these situations without sufficient coping skills can cause fatigue, emotional exhaustion and reduced job satisfaction.

Other than that, insufficient institutional support leaves nurses without necessary resources to cope and navigate workplace stress. Many healthcare institutions require a structured support system for nurses such as resilience training programmes, mental health resources and peer support networks to overcome stress and manage the workplace effectively and productively.(10). Work-life imbalance further worsens the subject, making it difficult for nurses to retrieve from work-related pressures. Shift

work, long work hours and tight schedules lead to chronic fatigue, disturbed sleeping patterns and limited personal time for stress management.(4) Discussion of these challenges is a must to design multi-level approaches involving policy reforms, resilience-based training programmes and workplace actions for establishing a resilient and sustainable nursing workforce.

Improving resilience in nursing education

Curriculum integration

Integrating resilience practice into nursing education is a crucial step in preparing future nurses and healthcare workers for the challenging nature of their profession. Embedding resilience training into nursing curricula prepares students to handle the emotional, physical and cognitive demands of their future profession.(11) This could involve incorporating coping strategies, stress management techniques and problem-solving skills into the academic content.

Simulation-based training

Using simulations to replicate high-pressure, real-life scenarios allow nursing students and professionals to practice real-life clinical scenarios in a controlled, risk-free environment that enhances problem-solving and emotional adaptability. This hands-on approach helps develop practical skills while allowing students to manage high-pressure situations, reduce anxiety and build emotional resilience which are critical to build resilience.(12)

Mindfulness and emotional intelligence training

Mindfulness and emotional intelligence (EI) training are powerful tools for cultivating self- awareness, empathy and emotional control to manage stress effectively and improve interpersonal relationships with patients and colleagues. Also, this improves and helps nurses navigate high-pressure environments. Mindfulness practices, such as meditation and self-reflection, help individuals become more conscious of their emotions and improve their ability to cope calmly with stressful situations. On the other hand, emotional intelligence training enhances empathy, emotional awareness and interpersonal skills, which are crucial in clinical settings plus peer support delivers guidance from experienced professionals, upgrading knowledge sharing and emotional support. (13) Both approaches foster resilience by helping nurses navigate the emotional complexities of patient care and teamwork.

Mentorship and peer support

Mentorship programmes pair nursing students with experienced professionals who can guide them through demanding situations. Peer support networks also provide a sense of shared experience. Both strategies help students navigate the emotional demands of nursing by providing encouragement and emotional support with guidance, which enhances resilience in real life nursing settings.(14) Basically, it has been shown to positively affect job satisfaction, reduce burnout and enhance overall resilience

Self-care education

Self-care education is the importance of self-care routines and techniques like relaxation, exercise and nutrition. Educating nurses on self-care practices such as stress management, relaxation techniques, maintaining work-life balance, exercise and nutrition is essential. These strategies promote long-term resilience by equipping nurses with the tools needed to manage stress and prevent burnout.(15) Educating students about the importance of self-care establishes a positive approach to mental and physical well-being. Merging these elements into nursing curricula prepares nurses not only to be competent in clinical skills but also to be emotionally resilient, capable of managing stress and focus on their well-being throughout their careers.

Improving resilience at individual level

Professional growth and lifelong learning

Engaging in professional development is crucial to building resilience as a professional nurse. Lifelong learning establishes confidence, enhances job satisfaction ensures that nurses are resilient in dynamic healthcare environments. Continuing education plays a vital role in developing professional resilience.

Time management and stress reduction techniques

Time management is a crucial skill for nurses to reduce stress and prevent burnout. Effective time management and stress reduction techniques consist of mindfulness practices and workload management which empower high quality patient care.(16)

Physical well-being

Maintaining proper nutrition, regular exercise and adequate sleep to improve physical resilience is necessary to ensure that nurses can perform their duties without compromise.(17)

Improving resilience by social and interpersonal support strategies

Peer support network
Basically, these networks are informal or formal groups where nurses can connect with colleagues who share similar experiences and challenges. They offer emotional, professional and psychological support in a collaborative and understanding environment. Benefits such as emotional validation, coping mechanisms and stress reduction can be achieved through this.

Mentorship and coaching programmes
Mentorship and coaching programmes create a platform for professionals to provide guidance and support to junior nurses with valuable insights, encouragement and career development opportunities.(18)

Team-based approaches
Working together fosters a sense of unity where nurses can navigate workplace challenges more productively with minimum stress improving job satisfaction and better patient outcomes.

Improving resilience through organisational and system-level strategies

Leadership support and positive work culture
Effective leadership is not just about managing day-to-day operations but also building an environment where nurses feel valued.(19)

Workload management and staffing policies
Workload management and staffing policies impact on nurse stress and resilience. Unmanageable workloads, understaffing and long shifts can lead to burnout and poor mental health. Adequate nurse-to-patient ratio and flexible schedules could address these issues.

Institutional resilience programmes

Institutional resilience programmes are designed to promote well-being, enhance coping strategies and build resilience across all levels of healthcare organisations.

Mental health and employee assistance services
These are important in supporting nurses' psychological well-being by providing services like counseling, therapy and mental health resources for nurses experiencing stress, anxiety, or burnout.(20)

Career progression and incentives
Providing clear career progression opportunities is an essential strategy for promoting resilience among nurses. Acknowledging their contributions and motivating professional development help nurses feel valued, motivated and committed to their work. Offering competitive compensation, opportunities for advancement and professional development can improve overall well-being, job satisfaction and retention of the nursing workforce.

Assessment of resilience

For the assessment of resilience among healthcare professionals we need validated tools that measure psychological strength, stress management abilities and overall well-being. The commonly used tools are Cannor-Davidson Resilience Scale (CD-RISC), Brief Resilience Scale (BRS), Nurses' Professional Resilience Scale (NPRS) and Resilience Scale for Adults (RSA). Cannor-Davidson Resilience Scale (CD-RISC) is a popular tool that assesses an individual's ability to adjust to stress and overcome misadventure.(21) Brief Resilience Scale (BRS) is another extensive tool which measures the ability to overcome stress in a short period.(22) Another widely used tool named Nurses' Professional Resilience Scale (NPRS) specifically created to assess resilience in nursing professionals by evaluating the workplace obstacles and coping strategies.(23) Resilience Scale for Adults (RSA) used to study resilience based on personal competency, social support and structured environment.(24) By using the mentioned scales, healthcare institutions can follow the impact of resilience-building interventions and modify programmes to discuss specialised areas for improvement.

Future research

Addressing research gaps is necessary to understand how resilience-increasing strategies vary according to different nursing specialties and global healthcare settings. There is a need for longitudinal studies on resilience outcomes to trace the effectiveness of resilience programmes over time. Research should focus on how resilience strategies can adapt to assorted populations involving various cultures and socio-economic backgrounds. To determine effectiveness of digital and AI-based interventions more studies should be done. Research should explore how the integration of resilience training impact on healthcare curricula in medical and nursing education.(25)

Conclusion

Resilience in nursing is a multifactorial concept which includes emotions, workload, education, social support and institutional policies. Healthcare educators, leaders and policymakers should play an active role in prioritising resilience-building initiatives for nurses. Doing so will help safeguard nurses' well-being and ensure professional sustainability. Also, they should try to foster supportive environments, ensuring adequate resources and investing in well-being initiatives. Ultimately, it can create a favourable surrounding for nurses to reduce burnout, increase nurse retention and enhance patient outcomes.

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PRACTICE GUIDELINE Asian J Intern Med. 2025 July; 4(2)

Febrile neutropenia and neutropenic sepsis: a physician's guide to clinical management

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Case vignette

A 30-year-old man with recently diagnosed acute myeloid leukaemia develops a temperature of 39.4°C on the 6th day of induction chemotherapy. He is alert and oriented. BP is 92/58 mmHg and HR 110 bpm. There is no identifiable focus of infection. There is a central venous catheter in place. His white blood cell count is 0.2 × 10^9/L with an absolute neutrophil count (ANC) of 0.05 × 10^9/L, platelet count of 25 × 10^9/L, and haemoglobin of 7.5 g/dL. C-reactive protein (CRP) is 263 mg/dL. The patient is referred to the medical team for further assessment.

Why is this topic important to Internal Medicine Physicians?

Febrile neutropenia and neutropenic sepsis are life-threatening medical emergencies that most commonly occur in patients undergoing treatment for malignancies, particularly haematological and solid organ malignancies, and those who undergo haematopoietic stem cell transplantation (HSCT). Other at-risk populations include those with bone marrow failure syndromes, individuals with autoimmune conditions on immunosuppressive therapy, and solid organ transplant recipients. Disruption of mucosal barriers, indwelling central venous catheters and prolonged hospitalisations further compound the infection risk in these immunocompromised hosts. Febrile neutropenia occurs in over 80% of patients with haematological malignancies and up to 50% of those with solid tumours. Infectious complications, including febrile neutropenia, contribute to up to 50% of the mortality in patients with haematological malignancies or solid tumours, emphasising the critical need for prompt recognition and treatment.(1) Clinical features may be subtle due to impaired inflammatory responses, necessitating skilled evaluation. Internal medicine physicians are critical members of the multidisciplinary team (MDT), especially in early diagnosis and antimicrobial stewardship. Rational use of empiric broad-spectrum antibiotics followed by timely de-escalation is essential to balance immediate infection control with the long-term risk of antimicrobial resistance.(2) This article aims to provide practical insights to internal medicine physicians on the evaluation and management of febrile neutropenia and neutropenic sepsis in oncology patients.

Definitions of key terms

Mild neutropenia is defined as an ANC between 1.0 and 1.5×10^9/L, moderate neutropenia as an ANC between 0.5 and 1.0×10^9/L, and severe neutropenia as an ANC below 0.5×10^9/L.

Febrile neutropenia is defined as a single oral temperature ≥38.3°C or a temperature ≥38.0°C sustained for over 1 hour in a patient with neutropenia.(2)

Neutropenic sepsis refers to the presence of systemic signs of infection and sepsis in a neutropenic patient, often in the absence of classical inflammatory signs due to impaired immune function.(2)

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Causes of fever in neutropenic patients

Fever in neutropenic patients can arise from both infectious and non-infectious causes. While infectious aetiologies are the most common, clinicians should consider a broad differential in the clinical evaluation.

Infectious causes:

Bacterial infections are the most common and pose a significant threat, especially those caused by gram-negative organisms. Translocation of gut flora into the bloodstream due to chemotherapy-induced mucosal injury is a key mechanism.

- **Common organisms** include:
  - *Escherichia coli*
  - *Klebsiella* spp.
  - *Pseudomonas aeruginosa*

- **Multidrug-resistant (MDR) organisms** are an increasing concern:
  - Extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*
  - Methicillin-resistant *Staphylococcus aureus* (MRSA)
  - Vancomycin-resistant *Enterococci* (VRE)
  - Other MDR pathogens

Fungal infections become more prominent in cases of prolonged neutropenia.

- Common pathogens:
  - *Candida* species
  - *Aspergillus*
  - *Pneumocystis jirovecii* (PCP)

Viral infections are important considerations, particularly in immunocompromised individuals:

  - Cytomegalovirus (CMV)
  - Epstein–Barr virus (EBV)
  - Herpes simplex virus (HSV)
  - Influenza viruses
  - SARS-CoV-2 (COVID-19)

Considering the local epidemiology, gram-negative organisms such as *Escherichia coli* and *Pseudomonas aeruginosa* have been shown to predominate in bloodstream infections among neutropenic patients in Sri Lanka(4), and antimicrobial resistance is a growing concern.(5) A microbiological diagnosis is only achieved in 20–30% of febrile neutropenia episodes.(7)

Non-infectious causes:

These should not be overlooked.(6)

- **Drug-induced fever:**
  Commonly triggered by:
  - β-lactam antibiotics
  - Chemotherapeutic agents
  - Granulocyte colony-stimulating factors (G-CSF)

- **Malignancy-related fever:**
  - Occurs in conditions such as leukaemia, lymphoma and tumour necrosis.

- **Transfusion reactions**

- **Immune-mediated causes:**
  - Graft-versus-host disease (GVHD)
  - Engraftment syndrome

Evaluation of the febrile neutropenic patient(2)

- Perform a **focused clinical examination** to identify signs of infection.

- Document the presence of **indwelling catheters, drains**, and mucosal ulceration.

- Baseline investigations should include:
  - Full blood count and differential
  - Renal and hepatic function tests
  - Coagulation profile
  - Inflammatory markers (e.g., CRP)

- Microbiological studies:
  - Two sets of **blood cultures** (including from indwelling lines)
  - **Site-specific cultures** (e.g., urine, sputum, stool, skin lesions)

- Radiology:
  - **Chest X-ray** in all patients
  - High-resolution CT and bronchoalveolar lavage if fever persists beyond 72 hours

- Previous microbiology should be reviewed to assess colonisation or resistant organisms.

Place of serum lactate levels and procalcitonin in oncology patients with sepsis

In oncology patients, elevated lactate levels can arise from both infectious and non-infectious mechanisms, making it challenging to interpret lactate as a biomarker for sepsis. Non-infectious contributors include cancer cells favouring glycolysis over oxidative phosphorylation, resulting in increased lactate production. Furthermore, hepatic dysfunction secondary to liver metastases or chemotherapy-related hepatotoxicity may reduce lactate clearance. Although high lactate levels are linked to poorer outcomes in sepsis, their diagnostic specificity is diminished in patients with cancer. Consequently, monitoring lactate, particularly serial measurements and clearance over time, may offer greater prognostic value and assist in distinguishing sepsis from other causes of elevated lactate in this population.(8)

Similarly, studies support the use of procalcitonin as a complementary tool in the management of febrile neutropenia. It provides both diagnostic and prognostic information, with a stronger negative predictive value in excluding severe bacterial infections. However, its utility is maximised when integrated with clinical judgment and existing risk stratification models.(9,10)

Risk stratification tools in febrile neutropenia

Several validated clinical scoring systems aid in the risk stratification of patients with febrile neutropenia. The Multinational Association for Supportive Care in Cancer (MASCC) Risk Index Score (Table 1) is a validated clinical tool designed to identify low-risk febrile neutropenia patients who may be appropriate for outpatient management with close follow-up.(2) CISNE Score (Clinical Index of Stable Febrile Neutropenia) (Table 2) is a validated risk-stratification tool specifically for clinically stable adult patients with solid tumours who present with febrile neutropenia.(6)

Clinicians can consider patients to be **high-risk** if they have:

- **Profound neutropenia** (ANC <500 cells/μL) expected to last **>7 days**
- Presence of **haematological malignancy**
- Undergoing **HSCT**
- Significant **comorbidities** (e.g., hypotension, dehydration, COPD, liver/renal disease)
- Poor **ECOG** performance status (Eastern Cooperative Oncology Group performance status)
- Clinical **instability** or hypotension at presentation

Table 1. MASCC Risk Index Score

Clinical Characteristic	Score
Burden of illness: No or mild symptoms	5
No hypotension (SBP ≥90 mmHg)	5
No COPD	4
Solid tumor or no previous fungal infection	4
No dehydration	3
Outpatient at the onset of fever	3
Age <60 years	2
Total Score ≥21 = Low Risk	

Table 2. CISNE Score components

Clinical Parameter	Points
ECOG Performance Status ≥2	2
COPD	1
Cardiovascular disease	1
Mucositis grade ≥2	1
Monocytes <200/μL	1
Stress-induced hyperglycaemia	1
Score 0 = Low Risk; 1–2 = Intermediate; ≥3 = High Risk	

Principles of treatment

Empirical antimicrobial therapy in febrile neutropenia (2,3,6)

Empirical antimicrobial therapy should be initiated promptly in all patients with febrile neutropenia after obtaining appropriate cultures.

- **Low-risk patients:**

- Outpatient oral regimens may be used. Options include:
  - Ciprofloxacin monotherapy
  - Quinolone + amoxicillin-clavulanate

- **High-risk patients:**

- Require inpatient management with IV broad-spectrum β-lactam antibiotics with antipseudomonal activity. Recommended agents:
  - Piperacillin-tazobactam
  - Ceftazidime
  - Cefepime
  - Imipenem
  - Meropenem

- **Critically ill or haemodynamically unstable patients:**

- Empirical antibiotic therapy may include:
  - IV meropenem or imipenem (broad-spectrum Gram-negative and anaerobic coverage)
  - IV amikacin (enhanced activity against resistant Gram-negative organisms)
  - IV vancomycin or teicoplanin (Gram-positive coverage including MRSA)

- **Penicillin allergy:**

  - Mild hypersensitivity:
    - Cefepime or piperacillin-tazobactam may be used cautiously
  - Moderate to severe reactions:
    - Ciprofloxacin + vancomycin
    - Aztreonam + vancomycin
  - If resistant Gram-negative organisms are suspected:
    - Meropenem or aminoglycosides may be added
  - For low-risk patients when beta-lactams are contraindicated:
    - Oral ciprofloxacin + clindamycin is an alternative

Management of persistent fever without identification of a source (2,6)

- Fever persisting >48 hours:
  - Broaden therapy to ensure coverage for resistant Gram-negative and Gram-positive organisms.

- Fever persisting >4–7 days despite adequate antibacterial therapy:

  - Consider empirical antifungal therapy, especially in:
    - High-risk haematologic malignancies
    - HSCT recipients
  - Recommended agents:
    - Echinocandins (e.g., caspofungin)
    - Liposomal amphotericin B
    - Voriconazole
  - Choice depends on:
    - Local epidemiology
    - Prior antifungal exposure

- **Place of antiviral treatment:**

  - Indicated in selected high-risk patients, particularly:
    - Those undergoing HSCT
    - Acute leukaemia induction chemotherapy

  - Agents:
    - Acyclovir for HSV and VZV reactivation prevention

  - Not routinely recommended in low-risk patients, unless clinically indicated

- Multidisciplinary approach:

  - Management decisions should involve consultation with:
    - Clinical microbiology/mycology
    - Particularly important for MDR organism coverage when indicated

- **Supportive Management**

  - Fluid resuscitation and haemodynamic support:
    - Should be initiated promptly and guided by clinical/haemodynamic parameters
  - Protective isolation:
    - May be warranted in profound or prolonged neutropenia to reduce infection risk

- Nutritional support:
  - Preferably enteral
  - With strict food hygiene practices
- Adequate hydration:
  - Essential due to:
    - Fever
    - Potential nephrotoxic effects of antimicrobials

De-escalation and discontinuation of antimicrobials (2,3)

- Antibiotic therapy can be discontinued when:
  - ANC ≥0.5 × 10^9/L
  - Patient is:
    - Asymptomatic
    - Afebrile for ≥48 hours
    - Blood cultures remain negative
- If ANC remains ≤ 0.5 × 10^9/L but patient is:
  - Afebrile for 5–7 days
  - Without signs of infection or complications:
    - Antibiotics may be safely stopped in low-risk patients
- In high-risk groups (e.g., acute leukaemia, intensive chemotherapy):
  - Continue antibacterials for up to 10 days or until neutrophil recovery

Figure 1 summarises the key points in assessment and management.

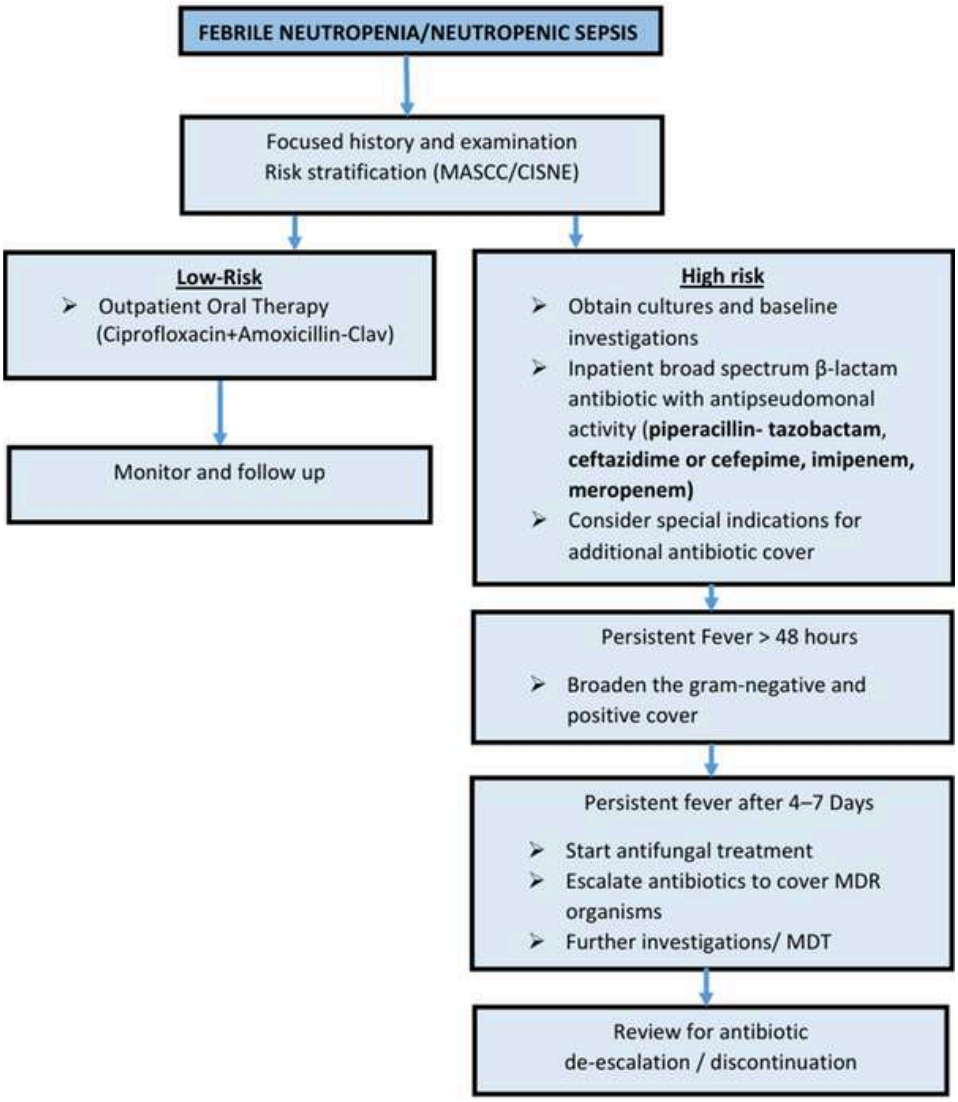

Figure 1. Overview of management of febrile neutropenia/neutropenic sepsis

Place of antimicrobial prophylaxis

Antimicrobial prophylaxis is recommended for high-risk patients with prolonged neutropenia (>7 days), particularly those with acute myeloid leukaemia (AML), myelodysplastic syndromes (MDS), haematopoietic stem cell transplantation (HSCT), or profound neutropenia (absolute neutrophil count <100 cells/mm^3). These patients are at increased risk of severe bacterial and fungal infections. In contrast, routine prophylaxis is not recommended for patients with solid tumours undergoing standard chemotherapy or those with short-duration neutropenia (<7 days), where the risk of invasive infection is lower.(2,3)

Role of GM-CSF

Granulocyte-macrophage colony-stimulating factor (GM-CSF) is not routinely recommended for the treatment of febrile neutropenia, as it does not significantly reduce overall mortality. However, it has been shown to shorten the duration of hospitalisation and accelerate neutrophil recovery, and may offer benefit in select high-risk patients, such as those with prolonged or profound neutropenia.(3,11)

Back to the case vignette .....

This patient with acute myeloid leukaemia on induction chemotherapy, presenting with high fever, hypotension and profound neutropenia (ANC 0.05 × 10^9/L), meets criteria for high-risk febrile neutropenia and requires immediate hospital admission. Initial management should include IV meropenem or imipenem for broad-spectrum Gram-negative and anaerobic coverage, IV amikacin to enhance activity against resistant Gram-negative organisms and IV vancomycin or teicoplanin to cover Gram-positive organisms, including MRSA, particularly given the presence of a central venous catheter. These antibiotics should be initiated promptly after obtaining blood cultures from both central and peripheral sites. Supportive care includes intravenous fluids for haemodynamic stabilisation and transfusions for thrombocytopenia and anaemia. Management should be coordinated by a multidisciplinary team.

Conclusion

Febrile neutropenia is a medical emergency requiring immediate empirical antimicrobial therapy. Patients with haematological malignancies and allogeneic HSCT are particularly at high risk, warranting aggressive and timely intervention. Risk stratification using validated tools enables rational use of antimicrobial treatment. While early antifungal initiation is crucial in high-risk patients, routine use of GM-CSF is not recommended, and its application should be limited to selected high-risk patients based on clinical judgment. Management decisions should involve a multidisciplinary team (MDT), and as internal medicine physicians, we have a pivotal role in the initial assessment of these patients as well as the rational use of antimicrobials in management.

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(1) A 48-year-old woman presents to the dermatology clinic with a slowly enlarging lesion on the lateral aspect of her left upper arm, first noticed approximately eight months ago. She reports intermittent itching and mild discomfort but denies systemic symptoms such as fever or weight loss. The lesion has gradually increased in size and recently developed a central crust with occasional oozing. (Image A)

What is the diagnosis?

(A) Basal cell carcinoma
(B) Cutaneous Anthrax
(C) Cutaneous Leishmaniasis
(D) Lupus Vulgaris
(E) Squamous Cell Carcinoma

Image A

(2) A 45-year-old man presents with a skin rash for 6 months. These mildly itchy lesions are seen in most of the body parts including elbows and knees. (Image B)

What is the most likely diagnosis?

(A) Lichen Planus
(B) Nummular Eczema
(C) Prurigo Nodularis
(D) Psoriasis
(E) Tinea incognito

Image B

(3) A 55-year-old man presents with a chronic, intensely pruritic widespread skin rash, predominantly affecting the limbs. (Image C)

What is the most likely diagnosis?

(A) Cutaneous T-Cell Lymphoma
(B) Hypertrophic lichen planus
(C) Lichen simplex chronicus
(D) Post-inflammatory hyperpigmentation
(E) Psoriasis

Image C

(4) A 32-year-old, previously healthy woman presents with a 3-day history of abrupt-onset fever and arthralgia. She also reports painful swelling of both ankles, predominantly the right leg. Her laboratory investigations show; white cell count of 4600x10^6/L, platelet of 134X10^6/L, and CRP of 32 mg/L. (Image D)

What is the most likely diagnosis?

(A) Cellulitis
(B) Chikungunya infection
(C) Gonococcal arthritis
(D) Panniculitis
(E) Reactive arthritis

Image D

(5) A previously healthy 38-year-old man presented with an acute febrile illness accompanied by headache and a generalised skin rash. At the time of admission, he was hypotensive and required fluid resuscitation. A picture of his left foot on the third day of hospitalisation is shown here. (Image E)

What is the most likely underlying diagnosis?

(A) Anti-phospholipid syndrome
(B) Meningococcal septicaemia
(C) Rickettsial infections
(D) *Staphylococcus* septicaemia
(E) Thromboangiitis Obliterans

Image E

N.B.: The above photographs were published with consent from the respective patients.
**Refer the PICTURE QUIZ-KEY; pages 112-114 for answers and explanations.*

Osteitis Condensans Ilii (OCI): a benign but under-recognised cause of chronic low back pain

Butt NI[1], Waris B[1], Ghoauri MSA[2]

Osteitis Condensans Ilii (OCI) is a non-inflammatory condition and systemic symptoms such as morning stiffness, weight loss or fever are usually not reported.(1) A 42-year-old woman presented to us with persistent lower back pain without back stiffness or systemic features. The pain was predominantly on the left buttock, having no specific aggravating or relieving factors, but having mild tenderness on palpation. She was multiparous, having 6 children, the youngest being 5 years old. Her inflammatory markers including ESR and CRP were within normal limits. Plain radiography revealed characteristic triangular sclerotic areas on the iliac side of the left sacroiliac joint as shown in Figure 1. There was no x-ray evidence of sacroiliitis, joint space narrowing or erosions. Based on these clinical and radiographic findings, the diagnosis of OCI was established.

Considering OCI as a differential diagnosis of chronic low back pain is crucial, especially in women of child-bearing age, postpartum and middle-aged women. A benign, self-limiting condition, OCI is often under-recognised as it mimics more serious pathologies on imaging such as sacroiliitis, ankylosing spondylitis, metastatic lesions and other sclerotic bone disorders including Paget's disease.(1,2). Therefore, distinguishing OCI from inflammatory sacroiliitis is important because misdiagnosis may result in inappropriate extensive workup and immunosuppressive therapy. Features including sclerosis confined to iliac side of the sacroiliac joint, lack of erosions or joint space narrowing, normal inflammatory markers such as ESR and CRP, and absence of systemic features help to differentiate OCI.(2,3) Although MRI is useful in ambiguous cases, OCI diagnosis can be clinched with a good clinical history and plain radiographs. Management of OCI is conservative, usually relying on patient education, pain relief with NSAIDs and physical therapy.(1,3) OCI typically has an excellent prognosis with the majority of patients experiencing resolution of symptoms over time with adequate treatment. In conclusion, increasing awareness about OCI will aid in preventing misdiagnosis and overtreatment.

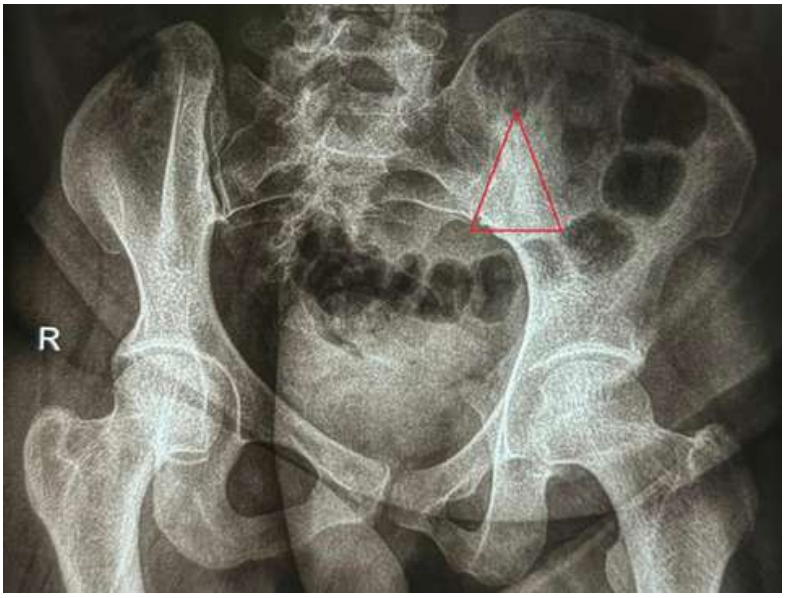

Figure 1. X-ray of the pelvis and sacroiliac joints (AP view)

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Detailed informed consent was obtained from the patient with assurance of maintaining confidentiality.

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Pleuroparenchymal fibroelastosis: An unusual cause of upper lobe fibrosis and platythorax

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A 45-year-old woman with no history of smoking, occupational or environmental exposure, or prior respiratory illness presented with long-standing exertional dyspnoea and copious sputum production. At rest, she had a respiratory rate of 25/min and oxygen saturation of 95%. Physical examination revealed bilateral apical flattening, a deep suprasternal notch (Figure 1A), and crepitations over the upper thorax. There was no lymphadenopathy, and the trachea was central.

Erythrocyte sedimentation rate was normal, and bronchoalveolar lavage was negative for *Mycobacteria*. Pulmonary function tests revealed a restrictive pattern. High-resolution CT (HRCT) of the chest showed apical pleural capping, volume loss, reticular changes, honeycombing, and traction bronchiectasis in the upper lobes. Axial images demonstrated a deep suprasternal notch with posterior retraction of the trachea (platythorax), supporting a diagnosis of pleuroparenchymal fibroelastosis (PPFE) (Figure 1B & 1C). Over the subsequent year, her symptoms progressed, and she became oxygen-dependent.

PPFE is a rare and under-recognised form of idiopathic interstitial pneumonia, characterised by fibrosis of the visceral pleura and subpleural fibroelastosis, predominantly affecting the upper lobes.(1,2) While often idiopathic, secondary causes such as prior chemotherapy, autoimmune disorders, and asbestos exposure have been reported.(1,2) PPFE may coexist with other interstitial lung diseases, notably usual interstitial pneumonitis involving the lower lobes.(2)

Clinically, PPFE is slowly progressive, leading to restrictive lung physiology and, eventually, irreversible respiratory failure. Morphological features such as platythorax and upper lobe fibrosis are characteristic. Although imaging strongly supports the diagnosis, histopathological confirmation remains the gold standard.(2) This case highlights the importance of recognising PPFE in patients with unexplained upper lobe fibrosis and atypical radiological findings, even in the absence of classical risk factors.

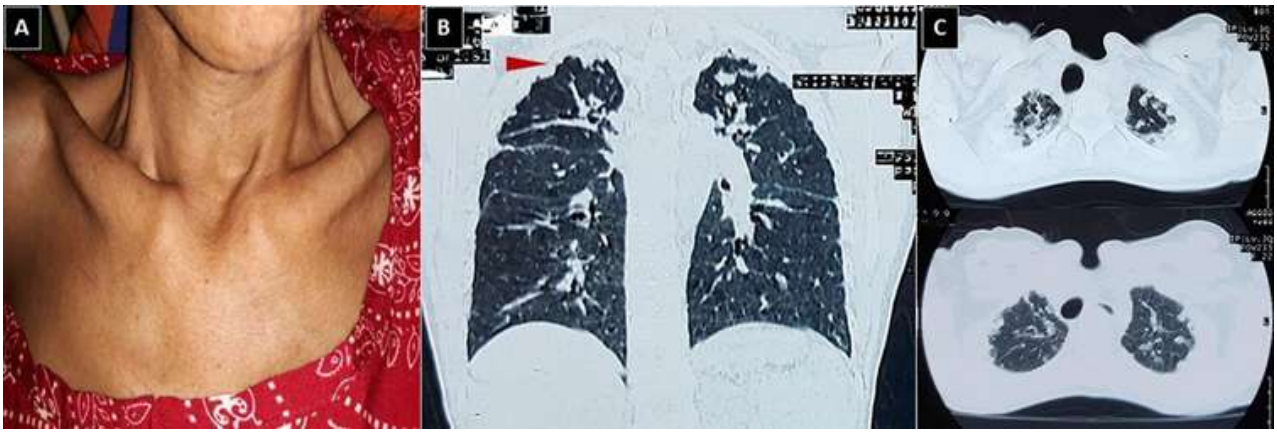

Figure 1. Panel A: prominent suprasternal notch, retracted trachea and apical flattening. **Panel B:** HRCT chest images, coronal showing apical pleural thickening (arrowhead), apical volume loss, reticular abnormalities and traction bronchiectasis. **Panel C:** axial images showing reduced anteroposterior diameter of lung apices, deep suprasternal notch, and posterior retraction of trachea up to the vertebrae.

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Decoding the hair-on-end appearance: a radiographic insight into chronic anaemias

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The "hair-on-end" appearance on skull X-rays is a radiographic pattern marked by thin, elongated vertical striations within the diploic space, indicative of marrow hyperplasia. This finding is strongly associated with haemoglobinopathies such as beta thalassemia and sickle cell disease, where chronic anaemia drives excessive erythropoiesis. In beta thalassemia, ineffective erythropoiesis expands the diploic space and thins the outer table, producing this distinct radiographic sign.(1,2) Similarly, sickle cell disease, characterised by chronic haemolysis, leads to compensatory marrow hyperplasia and a comparable X-ray pattern.(3)

This radiographic feature has significant clinical implications, often serving as an early indicator of severe anaemia requiring prompt intervention. Beta thalassemia management involves regular transfusions and iron chelation to prevent iron overload, whereas sickle cell disease necessitates a multifaceted approach, including prophylactic antibiotics, vaccinations, and patient education to reduce complications.(1,3)

When this pattern is identified, a structured diagnostic approach is essential. Laboratory investigations, including complete blood count, haemoglobin electrophoresis, and peripheral blood smear, help confirm underlying haemoglobinopathies. Additional imaging of other skeletal sites can assess the extent of marrow hyperplasia and related complications.(1,3)

Although most commonly linked to beta thalassemia and sickle cell disease, other conditions such as congenital dyserythropoietic anaemia and severe iron deficiency anaemia can present with similar findings. Distinguishing between these requires comprehensive clinical and laboratory evaluation. (2,3)

Recognising the hair-on-end sign facilitates timely diagnosis and targeted management, ultimately improving patient outcomes. Effective care requires collaboration among haematologists, radiologists, and primary physicians to ensure comprehensive treatment strategies.

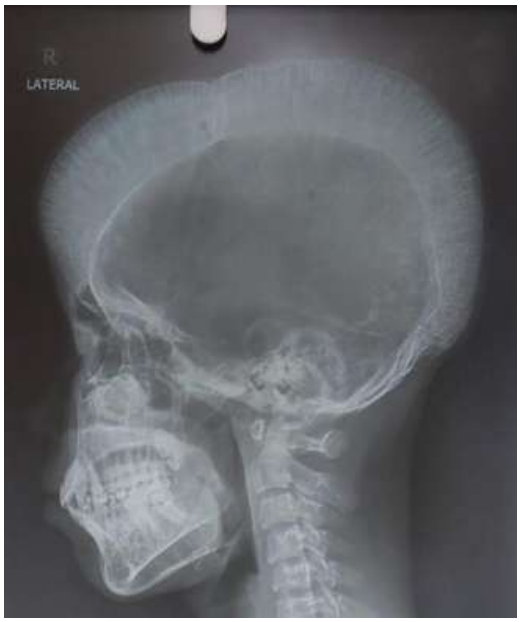

Figure 1. X-Ray skull (lateral view) of a 25-year-old male patient, known case of transfusion dependent thalassaemia, who presented to the Emergency Room with heart failure

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Informed written consent was obtained from the patient before preparation and submission of this report.

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CASE REPORT

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Meningococcal meningitis complicated by septic shock, myocarditis and purpura fulminans

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Abstract

Meningococcal disease is a rapidly progressive, life-threatening infection caused by *Neisseria meningitidis*. Typical presentations include meningitis, septicaemia, or a combination of the two. Rarely, it can be complicated by purpura fulminans and myocarditis, contributing to increased morbidity and mortality. We report a case of a previously healthy 16-year-old boy presenting with a 3-day history of fever, headache and altered consciousness. He was hypotensive, febrile and tachycardic on admission, with a purpuric skin rash suggestive of purpura fulminans and neck stiffness. Investigations revealed leukocytosis, thrombocytopenia, elevated inflammatory markers, and cerebrospinal fluid analysis consistent with bacterial meningitis. PCR confirmed *Neisseria meningitidis*. Elevated troponin I and echocardiography indicated myocarditis. He was treated in the ICU with fluids, inotropes and intravenous ceftriaxone. The patient made a full recovery, with normalisation of cardiac function and inflammatory markers. This case underscores the severe and aggressive nature of meningococcal disease, emphasising the importance of early recognition and timely multidisciplinary intervention in preventing poor outcomes in healthy individuals.

Keywords: *Neisseria meningitidis*, meningococcal meningitis, purpura fulminans, myocarditis

Introduction

Neisseria meningitidis, a Gram-negative diplococcus, frequently colonises the nasopharynx but can invade the bloodstream, leading to invasive disease. Typical presentations include meningitis, septicaemia, or a combination of the two. Despite widespread vaccination strategies, meningococcal infections remain a global health threat, particularly in children and young adults.(1,2) The classical clinical presentation of meningococcal disease includes fever, neck stiffness and altered mental status. However, the disease can progress rapidly and complications such as purpura fulminans and myocarditis, although uncommon, can significantly worsen prognosis.(3)

Purpura fulminans is an uncommon but severe thrombotic disorder marked by rapidly progressing haemorrhagic skin lesions, widespread microvascular clot formation and disseminated intravascular coagulation (DIC). It often arises in the setting of severe sepsis and carries a high risk of complications such as tissue necrosis, limb amputation and death, if not promptly treated.(4) Myocarditis, another rare but serious complication, results from direct microbial or immune-mediated myocardial injury, often leading to impaired cardiac function and contributing to haemodynamic instability.(5,6)

Both complications are uncommon but clinically significant and often underrecognised in the early phase of meningococcal illness. Their presence may

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obscure the typical clinical picture and delay appropriate management. Therefore, timely recognition and multidisciplinary care are critical to improving outcomes.

Herein, we report a case of fulminant meningococcal meningitis complicated by septic shock, purpura fulminans and myocarditis, in a previously healthy boy.

Case presentation

A 16-year-old boy with no significant past medical history presented with a 3-day history of high-grade fever, headache and progressive drowsiness. There was no history of seizures, photophobia, or travel. He had received routine childhood immunisations.

On admission, he was febrile (39.6°C), hypotensive (BP 80/40 mmHg), tachycardic (HR 138 bpm), and tachypnoeic (RR 34/min). He was drowsy (GCS 12/15) and had neck stiffness. A purpuric skin rash was noted on his chest, upper limbs and thighs, raising suspicion of purpura fulminans.

Given the clinical picture of fever, hypotension, rash and altered consciousness, several differential diagnoses were initially considered. These included dengue haemorrhagic fever, especially in the local epidemiological context; rickettsial infections such as tick typhus, which can present with fever and a rash; and other forms of acute bacterial meningitis, caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*. However, the rapid progression, purpuric rash and haemodynamic instability favours the suspicion of invasive meningococcal disease.

Laboratory investigations revealed a white blood cell count of 25×10^9/L with 90% neutrophils, thrombocytopenia with a platelet count of 89×10^9/L, and a markedly elevated C-reactive protein (CRP) level of 326 mg/L. Peripheral blood smear findings were consistent with severe sepsis associated with thrombocytopenia. Renal function tests were within normal limits, and dengue NS1 antigen testing was negative.

The patient was promptly transferred to the intensive care unit (ICU) for further management. Treatment included aggressive intravenous fluid resuscitation and inotropic support to stabilise haemodynamics.

Empirical treatment was initiated promptly. The

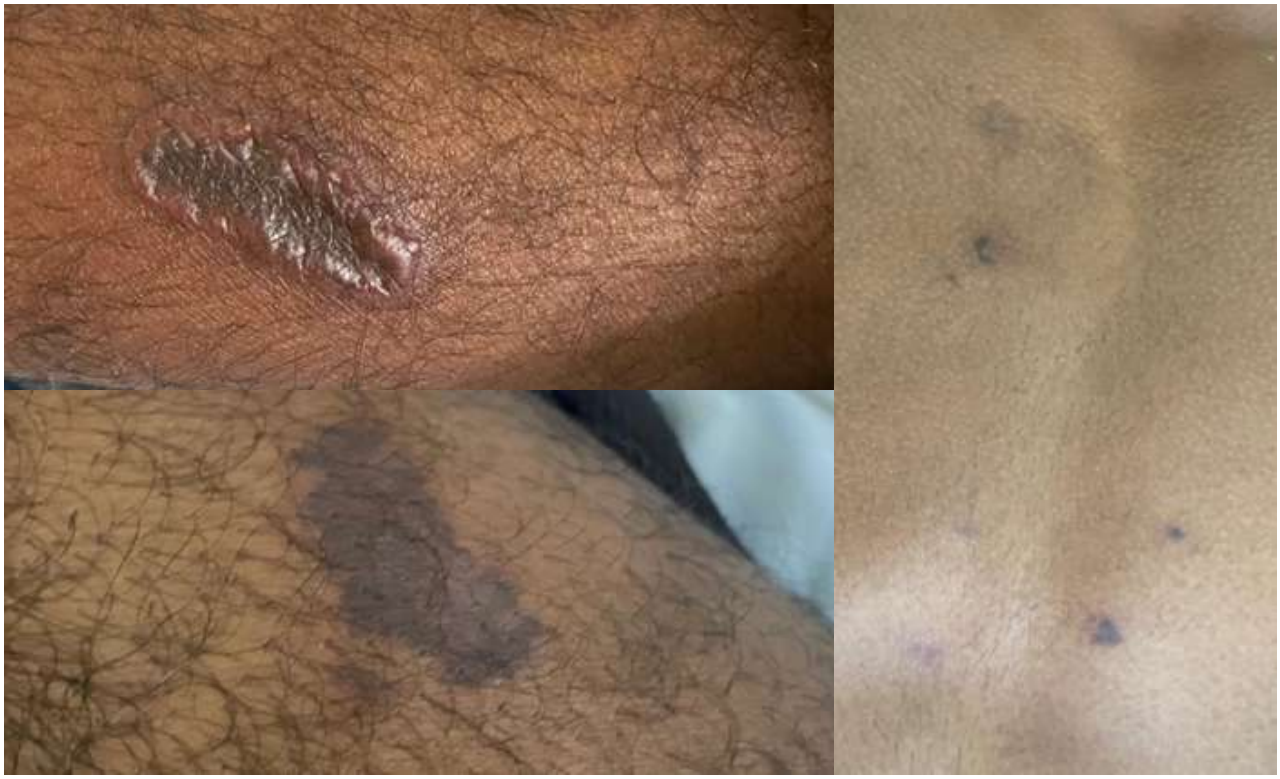

Figure 1. Purpuric, non-blanching skin rash over the lower limbs and chest at presentation

patient received intravenous ceftriaxone at a dose of 2 g twice daily (100 mg/kg/day divided every 12 hours). Dexamethasone 6 mg every 6 hours for four days was also administered alongside the first antibiotic dose, to reduce the risk of neurologic complications associated with bacterial meningitis.

Blood cultures were obtained prior to the initiation of antibiotics. However, no organisms were isolated. Cerebrospinal fluid (CSF) analysis revealed a protein concentration of 56 mg/dL, glucose of 76 mg/dL (with a corresponding serum glucose of 120 mg/dL) and a total cell count of 350/µL, predominantly neutrophils. Red blood cells were noted at 510/µL. CSF Gram stain and culture were negative; however, PCR testing confirmed the presence of *Neisseria meningitidis* DNA. Serogrouping was not performed due to local laboratory limitations.

Due to persistent hypotension and tachycardia, a cardiac workup was initiated. Troponin I was >30,000 ng/L. Echocardiography showed global hypokinesia with an LVEF of 50%, confirming myocarditis.

Following confirmation of *Neisseria meningitidis* infection by PCR, public health authorities were notified in accordance with notifiable disease protocol. A contact tracing process was initiated by the local public health officials. All identified close contacts including health care workers were offered chemoprophylaxis with ciprofloxacin 500 mg single dose and no secondary cases were reported during the surveillance period.

The patient was discharged in stable condition on hospital day 14, with resolution of purpuric skin lesions and normalisation of inflammatory markers and vital signs. Outpatient follow-up assessments were arranged at two weeks and again at six weeks to monitor for long-term complications.

At both follow-up visits, he showed no signs of residual cognitive impairment, focal deficits, or hearing loss. Repeat echocardiography at four weeks post-discharge demonstrated normal left ventricular function with an ejection fraction of 60%, confirming resolution of myocarditis. The previously noted purpuric lesions had completely healed without ulceration or necrosis. No surgical or dermatological intervention was required.

Discussion

Meningococcal infection continues to be a medical emergency due to its rapid progression and life-threatening complications. Common signs at presentation include fever, neck stiffness and impaired consciousness. Myocarditis and purpura fulminans are rare but severe complications of invasive meningococcal disease associated with significant morbidity and mortality.(2)

In tropical regions, differential diagnoses often include dengue haemorrhagic fever, rickettsial infections such as tick typhus and severe leptospirosis.(7) All of these can present with fever, rash, altered consciousness and haemodynamic instability. The development of shock alongside a purpuric, non-blanching rash raised clinical suspicion for invasive meningococcal disease, resulting in prompt antibiotic therapy and intensive care management.

Meningococcaemia carries a mortality rate ranging from 9% to as high as 40%, depending on the severity and presence of complications. Myocarditis, though uncommon, has been reported in both children and adults with meningococcal infection and is associated with increased mortality.(8) Purpura fulminans is a much rarer but devastating complication, occurring in approximately 10–20% of meningococcaemia cases. It carries a mortality rate of up to 50%, especially when diagnosis or treatment is delayed. Among survivors, long-term sequelae such as limb amputations and dermatologic scarring are common.(9)

The pathophysiology of meningococcal sepsis involves complex interactions between bacterial endotoxins, pro-inflammatory cytokines and coagulation pathways.(3) Pathan et al. described how this interaction contributes to complications such as purpura fulminans and multi-organ dysfunction.(3)

Purpura fulminans, results from DIC and widespread microvascular thrombosis. It manifests as haemorrhagic skin lesions that may rapidly progress to necrosis. Prompt recognition and management, including haemodynamic support and correction of coagulopathy, are critical. Chalmers et al., have underscored the importance of immediate supportive care alongside targeted antimicrobial therapy.(4)

Myocarditis complicating meningococcal infection is infrequent but contributes to shock and end-organ hypoperfusion. It results from the combined effects of bacterial endotoxins, inflammatory cytokines, and direct myocardial invasion. Elevated cardiac biomarkers and echocardiographic findings aid in diagnosis.(5,6) Dhainaut et al. emphasised the detrimental impact of endotoxin-induced

inflammatory cascades on myocardial function in septic states.(6)

Taldir et al. described a case of a 47-year-old man with meningococcal septicaemia with fever and gastrointestinal symptoms. Despite early improvement with antibiotics, he developed acute heart failure with elevated troponin and ST changes, which resolved within 24 hours. Blood cultures identified Neisseria meningitidis serogroup C. This case illustrates transient myocarditis as a rare complication of meningococcaemia.(10)

In our case, elevated troponin I and echocardiographic evidence of reduced ejection fraction confirmed the diagnosis, highlighting the importance of routine cardiac evaluation in severe meningococcal disease, even in the absence of overt cardiac symptoms.

Negative CSF cultures are frequently encountered, particularly if antibiotics are administered before lumbar puncture or if fastidious organisms are involved. In such cases, molecular diagnostics like PCR are invaluable.(14) The utility of PCR in enhancing diagnostic yield has been demonstrated in the work of Brouwer et al., particularly in culture-negative meningitis cases.(13) Similarly, Borrow et al. highlighted its importance for meningococcal serogroup identification. PCR has the added advantage of enabling serogroup identification, which is essential for public health management, outbreak control and tailoring national vaccination policies. Unfortunately, in this case, serogrouping could not be performed due to logistical constraints.(14)

Management of fulminant infection requires early, aggressive resuscitation, inotropic support for shock, and correction of haematologic abnormalities. ICU admission is recommended for close haemodynamic, respiratory and neurological monitoring. Timely initiation of appropriate antibiotics remains the cornerstone of management. Ceftriaxone or cefotaxime are first-line agents, given their excellent bactericidal activity against Neisseria meningitidis.(2) The patient received intravenous dexamethasone early in his management. The evidence supporting corticosteroid use in bacterial meningitis is strongest for Haemophilus influenzae type B, where it may reduce the risk of hearing loss and neurologic sequelae.(11) However, its role in meningococcal meningitis remains controversial, particularly in the presence of septic shock, where corticosteroids may alter haemodynamics and immune response unpredictably.(12) Current guidelines suggest a tailored approach, considering each case individually, particularly in severe presentations.

Conclusion

This case highlights the potentially devastating course of meningococcal meningitis and its rare complications, purpura fulminans and myocarditis. The coexistence of these two conditions, as seen here, is exceptionally rare and signifies a fulminant disease process requiring prompt, multidisciplinary intensive care. The patient's favourable outcome underscores the importance of early clinical suspicion, the utility of molecular diagnostics like PCR in culture-negative cases, and the value of comprehensive ICU support. Heightened awareness of these uncommon but critical manifestations is essential for timely diagnosis and life-saving intervention.

Declarations

Author contributions:
History taking, examination, necessary investigations arrangement, management under supervision, daily monitoring of the patient, and writing of the manuscript were done by Perera HMUAS. All authors contributed to writing the manuscript, read and approved the final manuscript.

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CASE REPORT

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Rituximab induced sympathetic crashing acute pulmonary oedema in a patient with interstitial lung disease: a rare and life-threatening complication

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Abstract

Rituximab is a monoclonal antibody widely used to treat autoimmune diseases and haematologic malignancies. Although generally well tolerated, it can cause severe infusion-related reactions, including pulmonary complications. Sympathetic crashing acute pulmonary oedema (SCAPE) is a rare but potentially life-threatening manifestation of autonomic deregulation, characterised by sudden hypertensive crisis, pulmonary congestion and respiratory distress. We report a case of a 77- year-old Sri Lankan man with Interstitial lung disease (ILD), radiologically consistent with a usual interstitial pneumonia (UIP) pattern, likely associated with rheumatoid arthritis. He did not respond adequately to mycophenolate mofetil (MMF) and was switched to Rituximab. Four hours after infusion, he developed acute respiratory distress, hypertension and pulmonary oedema. Immediate management with intravenous glyceryl trinitrate (GTN), furosemide infusion and continuous positive airway pressure (CPAP) ventilation led to rapid symptom resolution, preventing invasive ventilation. Rituximab-induced pulmonary oedema is a rare but critical complication, likely mediated by excessive sympathetic activation, cytokine release and haemodynamic shifts. Patients with preexisting ILD may be at higher risk due to reduced pulmonary reserve. This case underscores the need for clinical vigilance during rituximab infusion in a patient with ILD and highlights the importance of early recognition and intervention.

Keywords: rituximab, SCAPE, severe crashing acute pulmonary oedema, interstitial lung disease

Introduction

Rituximab, a chimeric monoclonal antibody targeting CD20, is widely used in the treatment of haematologic malignancies and autoimmune diseases such as rheumatoid arthritis and systemic vasculitis.(1) While generally well tolerated, infusion-related adverse effects are known and can range from mild symptoms to severe complications, including cytokine release syndrome and cardiovascular instability and pulmonary events.(2)

Sympathetic crashing acute pulmonary oedema (SCAPE) is a rare but life-threatening form of acute pulmonary oedema caused by excess sympathetic stimulation.(3) It presents with a rapid rise in blood pressure, severe respiratory distress and pulmonary congestion. Although most commonly associated with hypertensive emergencies and acute heart failure (3), SCAPE has also been described as a rare infusion related reaction in patients receiving

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monoclonal auto antibody therapy.(4)

Interstitial lung disease (ILD) is a recognised risk factor for adverse pulmonary events. Patients with underlying pulmonary fibrosis, particularly usual interstitial pneumonia (UIP) pattern, have reduced pulmonary compliance and are more susceptible to acute fluid shifts and haemodynamic stress. This may increase their risk of developing severe pulmonary complications following immunosuppressive or biologic therapy.(5)

We report a case of a 77-year-old Sri Lankan man with UIP-pattern ILD, likely secondary to rheumatoid arthritis, who developed acute pulmonary oedema consistent with SCAPE shortly after receiving rituximab infusion. This case emphasises the importance of early recognition and intervention for infusion related pulmonary complications especially in patients with underlying ILD.

Case presentation

A 77- year-old Sri Lankan man with a known diagnosis of interstitial lung disease (ILD) presented for continuation of treatment. High resolution computed tomography (HRCT) of the chest revealed radiological features consistent with a usual interstitial pneumonia (UIP) pattern (Figure 1). He had a positive rheumatoid factor, raising the possibility of rheumatoid arthritis- associated ILD. The patient had previously been treated with mycophenolate mofetil (MMF) but showed inadequate clinical response.

Due to poor disease control and suspected autoimmune aetiology, a decision was made to initiate rituximab therapy. He had no other significant comorbidities.

On admission, his body mass index (BMI) was 21 kg/m^2. His vital signs were stable with a blood pressure of 130/80 mmHg, heart rate of 90 beats per minute, respiratory rate of 22 breaths per minute and oxygen saturation of 95% on room air. Chest auscultation revealed fine bibasal end-inspiratory crepitations in both lungs. The remainder of the physical examination was unremarkable.

Following routine pre-infusion assessments, the patient received 500 mg of rituximab in 500 ml of normal saline, administered intravenously over four hours (from 11 AM to 3 PM). He remained stable during and immediately after the infusion. However, at 7.30 PM on the same day, he developed acute shortness of breath. On examination, his respiratory rate had increased to 32 breaths per minute, heart rate was 150 beats per minute and blood pressure had risen to 213/130 mmHg. His oxygen saturation dropped to 72% despite administration of 6 L/min of supplementary oxygen. Chest auscultation revealed worsening of bi basal end-inspiratory crepitations.

A bedside lung ultrasound showed diffuse B-lines, consistent with pulmonary interstitial oedema. An electrocardiogram (ECG) demonstrated sinus tachycardia (Figure 2). The clinical presentation was consistent with acute pulmonary oedema. Given the sudden hypertensive crisis and respiratory failure following rituximab infusion, a diagnosis of sympathetic crashing acute pulmonary oedema (SCAPE) was made.

The patient was immediately transferred to the high dependency unit (HDU). He was initiated on an intravenous infusion of glyceryl trinitrate (GTN) at a rate of 5 µgm/min with an intravenous infusion of furosemide 10 ml/hour. Noninvasive ventilation using continuous positive airway pressure (CPAP) at 10

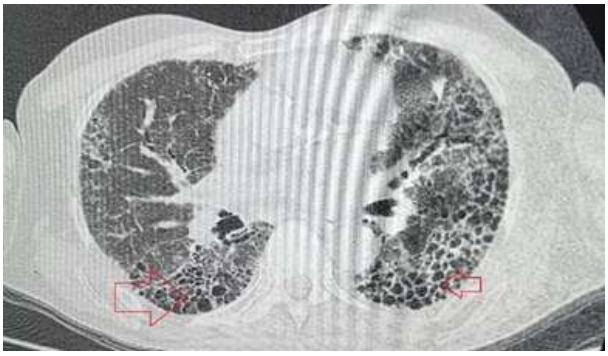

Figure 1. High resolution computed tomography showing UIP pattern (red arrows) of interstitial lung disease.

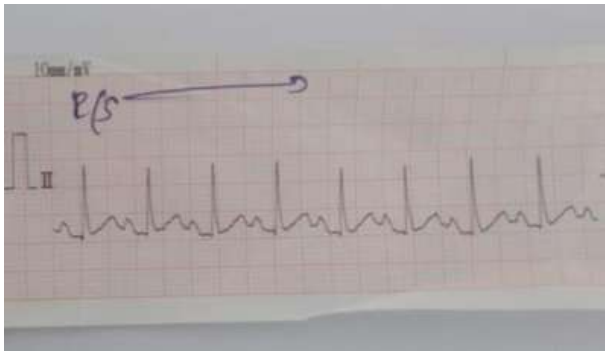

Figure 2. Lead 2 of electrocardiogram showing sinus tachycardia

cmH20 was initiated. A transthoracic 2D echocardiogram performed after stabilisation showed normal left ventricular function without evidence of pulmonary hypertension or structural heart disease. Over the next 48 hours, his symptoms improved steadily. GTN and furosemide were gradually tapered and stopped. The patient was discharged in a stable condition and was followed up at the clinic for ILD management.

Discussion

Sympathetic crashing acute pulmonary oedema (SCAPE) is a rare, life-threatening manifestation of acute pulmonary oedema caused by sudden and excessive sympathetic nervous system activation.it is typically associated with hypertensive emergencies or acute heart failure, presenting with abrupt onset of respiratory distress, severe hypertension, and pulmonary congestion.(3) While SCAPE has been recognised in cardiac conditions, its occurrence as an infusion related complication, particularly with monoclonal antibodies like rituximab is extremely rare and poorly understood.

Rituximab can trigger infusion reactions ranging from mild to severe, often mediated by cytokine release or autoimmune dysregulation. Excess catecholamine release may lead to abrupt vasoconstriction and acute increases in cardiac afterload which can precipitate pulmonary oedema even in absence of underlying cardiac dysfunction.(1) In our patient, this surge in sympathetic tone likely induced a transient hypertensive crisis and capillary hydrostatic pressure imbalance, resulting in flash pulmonary oedema. Notably, a 2D echocardiogram performed after stabilisation showed normal ventricular function and no signs of pulmonary hypertension or structural heart disease, supporting a non-cardiogenic mechanism.

Patients with intestinal lung disease (ILD), particularly those with a UIP-pattern, may be more vulnerable to such complications. Reduced pulmonary compliance and impaired lymphatic clearance in fibrotic lungs can amplify the effects of acute haemodynamic stress, predisposing patients to rapid fluid accumulation in the alveolar spaces.(5). Although a direct association between ILD and increased risk of SCAPE has not been definitely established, this case raises important questions regarding the pulmonary vulnerability of ILD patients receiving biologic therapies.

Several alternative differential diagnoses were considered. An IgE-mediated hypertensive reaction was deemed unlikely given the absence of rash, fever or eosinophilia. Volume overload was also excluded based on normal echocardiographic finding and lack of significant fluid administration. Cytokine release syndrome may have contributed, but the predominant hypertensive response and the dramatic improvement with vasodilators were more characteristic of SCAPE.

Management of SCAPE requires urgent haemodynamic stabilisation.(3) In this case, a combination of intravenous glyceryl trinitrate (GTN) and furosemide effectively reduced preload and afterload, while CPAP ventilation improved oxygenation and prevented intubation. Prompt initiation of these interventions likely prevented further deterioration and reduced the need for invasive mechanical ventilation.

This case highlights the importance of recognising rituximab-associated pulmonary complications, particularly in patients with preexisting ILD. Clinicians should maintain a high index of suspicion for SCAPE-like reactions in the first few hours following infusion, especially when patients develop acute dyspnoea and hypertension. Further studies are warranted to clarify the underlying mechanism, determine predisposing risk factors, and develop preventive strategies.

Conclusion

This case underscores the potential for rituximab to trigger acute pulmonary oedema consistent with Sympathetic crashing acute pulmonary oedema (SCAPE), even in the absence of underlying cardiac dysfunction. In patients with preexisting ILD, particularly those with a UIP-pattern – reduced pulmonary reserve may heighten susceptibility to autoimmune or cytokine driven pulmonary complication.

Early recognition of this life threatening but reversible condition is essential. Close monitoring during and after infusion, especially in high risk patients, can facilitate timely diagnosis. Prompt intervention with vasodilation, diuretics and noninvasive ventilation may prevent respiratory failure and reduce the need for invasive support.

As the use of biologic therapies continues to expand, greater awareness of rare but serious infusion related complications is crucial. Further research is needed to better define the risk factors, underlying

mechanisms, and prevention strategies for SCAPE in vulnerable patient populations.

Declarations

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CASE REPORT

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Unsuspected deep venous thrombosis and pulmonary embolism in melioidosis

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Abstract

Melioidosis is caused by the gram-negative, intracellular bacterium *Burkholderia pseudomallei* which can be life-threatening. This organism is found in soil and surface water in tropical and subtropical regions including Southeast Asia and northern Australia. While it usually presents as pneumonia or septicaemia in immunocompromised individuals, its manifestation as deep venous thrombosis (DVT) and pulmonary embolism (PE) remains underrecognised. We report a case of a 43-year-old man with poorly controlled diabetes mellitus who presented with fever, cough and progressive dyspnoea. Blood cultures confirmed *Burkholderia pseudomallei*. Further imaging revealed pulmonary embolism and extensive iliac vein thrombosis, which had not been clinically suspected. This case draws attention to an uncommon, yet serious complication of melioidosis, and it highlights the importance of maintaining a high index of suspicion for thrombotic events in patients with melioidosis, particularly those with underlying diabetes. Early recognition and prompt treatment of both infection and thrombosis are vital to improve patient outcomes.

Keywords: *Burkholderia pseudomallei*, melioidosis, pulmonary embolism, deep venous thrombosis

Introduction

Melioidosis is a serious infectious disease caused by *Burkholderia pseudomallei*, a gram-negative, saprophytic bacterium commonly found in Southeast Asia and northern Australia. Transmission can occur through direct inoculation, inhalation or ingestion. Diabetes mellitus is the most significant predisposing factor, primarily due to its association with immune dysfunction. Other risk factors include male sex, chronic alcohol use and immunosuppression.(1)

The environmental distribution of B. *pseudomallei* is influenced by multiple factors. Physical factors such as rainfall, humidity and temperature play a critical role, while chemical factors including soil composition, vegetation and fertiliser use may alter bacterial survival. Additionally, human activities like excavation can disturb contaminated soil, increasing exposure risk.(2)

Melioidosis presents with a broad clinical spectrum, ranging from acute bacteraemic pneumonia to disseminated visceral abscesses and localised infections, involving the lungs, liver, spleen and central nervous system. Pneumonia and bacteraemia are the most common manifestations. However, thrombotic complications, though under-recognised, are increasingly reported.

The literature review revealed only a limited number of reports describing venous thromboembolic events associated with melioidosis, highlighting the rarity and under-recognition of this clinical manifestation.

Although sporadic cases of DVT and PE in melioidosis

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have been described in literature, their association with disease pathogenesis remains poorly understood. However, as thrombotic manifestations are increasingly recognised, healthcare providers, particularly in endemic regions, should maintain clinical suspicion when encountering sepsis with no clear source for thromboembolism.

Case presentation

A 43-year-old man with poorly controlled diabetes mellitus presented with a two-week history of fever, productive cough and progressive dyspnoea. He had no prior history of tuberculosis, chronic lung disease or thromboembolic events. However, he had worked as a caregiver in Israel nine months prior to presentation. There was no history of prolonged immobility or a familial predisposition to thrombophilia.

On examination, the patient was acutely ill, tachypnoeic and febrile (39.5°C). His respiratory rate was 28 breaths per minute, with an oxygen saturation of 88% on room air. Auscultation revealed bilateral coarse crepitations, most prominent in the right lower lung zone. Cardiovascular examination was unremarkable, with no clinical signs of deep vein thrombosis.

Laboratory investigations revealed a white blood cell count of 16,000/mm^3 (neutrophilic predominance), haemoglobin of 10.5 g/dL and a platelet count of 210,000/mm^3. HbA1c was 11.2%, indicating poorly controlled diabetes. Inflammatory markers were elevated with C-reactive protein (CRP) at 98 mg/L and procalcitonin at 3.5 ng/mL. Liver and renal function tests were normal.

Chest imaging revealed bilateral lower zone consolidations, with greater involvement on the right side, suggestive of infective pneumonia (Figure 1).

Initial blood cultures grew *Burkholderia* species, which was later confirmed as *Burkholderia pseudomallei*, establishing the diagnosis of melioidosis. Serological testing for melioidosis antibodies was positive, further supporting the diagnosis. Given the severity of the infection and the high risk of complications, the patient was promptly initiated on intravenous meropenem.

A contrast-enhanced computed tomography (CECT) of the chest, abdomen and pelvis was conducted to evaluate for potential deep-seated abscesses. Surprisingly, the scan revealed acute pulmonary thromboembolism (PTE) involving the left pulmonary artery, along with extensive venous thrombosis affecting the left common iliac, external iliac and internal iliac veins. Notably, there was no evidence of hepatic, splenic or other visceral abscesses (Figure 2).

A 2D echocardiogram was done to evaluate for right-sided endocarditis as a potential source of embolism. It was unremarkable, and given the presence of DVT, embolism was attributed to venous thromboembolism.

Given the extensive thrombosis in an otherwise low-risk patient, a thrombophilia screen was conducted. Thrombophilia screening was partially limited due to test availability and the influence of ongoing anticoagulation therapy. Protein C, Protein S, Antithrombin III and Factor V Leiden mutation analysis were not performed. However, antiphospholipid antibody testing was completed,

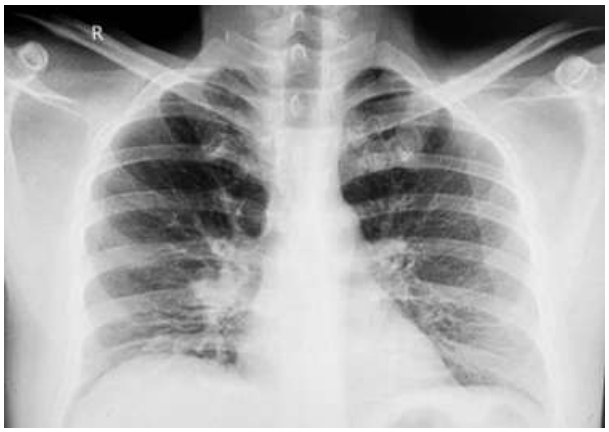

Figure 1. Chest X-ray on admission: bilateral lower zone consolidations, more marked on the right side, suggestive of infective pneumonia

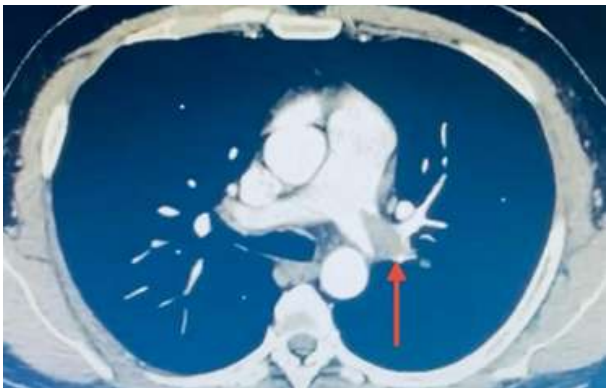

Figure 2. Contrast-enhanced computed tomography (CT) image of the chest shows a filling defect in the left main pulmonary artery (indicated by the red arrow), consistent with pulmonary embolism

including anticardiolipin antibodies, β2-glycoprotein I antibodies and dilute Russell viper venom test (DRVVT), all of which were negative.

The patient was initiated on therapeutic anticoagulation with enoxaparin and later changed to warfarin. He received four weeks of intravenous meropenem, followed by oral trimethoprim-sulfamethoxazole (co-trimoxazole) for eradication therapy, planned for three to six months. His fever subsided and respiratory symptoms improved.

Upon discharge, diabetes management was optimised and instructions on warfarin titration were given. Regular follow-up visits were arranged. CRP became normalised by the sixth week. No new embolic events occurred. Blood cultures remained sterile throughout follow-up. Doppler ultrasonography was planned after two months, for assessment of recanalisation of iliac veins.

Discussion

Melioidosis is increasingly recognised for its vascular complications. In this case, DVT and PE were unsuspected until imaging was performed, despite the absence of limb swelling or localised signs. The pathogenesis of thrombosis in melioidosis involves inflammatory-mediated endothelial damage, platelet activation and disruption of anticoagulant pathways.(4)

Sepsis is a well-established trigger for coagulopathy and in melioidosis. The inflammatory response plays a pivotal role in disrupting the balance between coagulation and anticoagulation. B. *pseudomallei* infection leads to endothelial dysfunction via direct bacterial invasion, release of pro-inflammatory cytokines and activation of toll-like receptors, which amplify the systemic inflammatory response. This cascade results in endothelial injury, platelet activation, and the upregulation of prothrombotic mediators, including plasminogen activator inhibitor-1, leading to impaired fibrinolysis and a hypercoagulable state.(3)

Severe melioidosis induces profound coagulation system activation, evidenced by increased levels of soluble tissue factor, prothrombin fragment F and thrombin-antithrombin complexes. Concurrently, fibrinolytic activation manifests as elevated tissue-type plasminogen activator, plasmin-alpha2-antiplasmin complexes and D-dimer levels. The predominance of the prothrombotic pathway is associated with worse disease severity and higher mortality rates. Furthermore, depletion of key endothelial modulators such as protein C, protein S, and antithrombin has been documented in melioidosis patients, further predisposing them to thrombosis.(4)

Additionally, neutrophil extracellular traps (NETs) have been implicated in thrombogenesis during bacterial sepsis, contributing to microvascular thrombi and disseminated intravascular coagulation. The combination of endothelial injury, hypercoagulability and suppressed anticoagulant mechanisms results in extensive thrombotic complications.(5)

Diabetes mellitus, particularly when uncontrolled, further exacerbates the thrombotic risk in patients with melioidosis. Hyperglycaemia leads to endothelial dysfunction and increased platelet aggregation, enhancing the prothrombotic environment. Additionally, the prolonged hospital stay required for managing severe melioidosis increases the risk of venous thromboembolism, particularly when patients are immobilised and have multiple comorbidities.

Niyasom et al. described a case of dural sinus thrombosis linked to melioidosis in a 42-year-old man with septicaemic melioidosis. The patient experienced neurological complications, further supporting the idea that B. *pseudomallei* can lead to widespread vascular involvement beyond its well-known pulmonary and soft tissue infections.(6)

Saïdani et al. reported a case of disseminated melioidosis in a patient presenting with pulmonary and hepatic abscesses, who subsequently developed splenic vein thrombosis. This case emphasised the potential involvement of the abdominal vasculature in melioidosis.(7)

Wu et al. described a case of a 54-year-old diabetic man who presented with fever, cough, chest tightness and swelling in his left lower limb. Imaging revealed deep vein thrombosis in the left common femoral vein along with multiple pulmonary emboli and B. *pseudomallei* was identified in blood cultures. This case highlights the severe coagulopathic complications of melioidosis and reinforces diabetes as a major risk factor for poor outcomes.(8)

Sivaselvi et al. documented a case of systemic melioidosis presenting with pulmonary septic emboli, necrotising pneumonia and septic arthritis. This case further suggests that B. *pseudomallei* has the

potential to cause widespread vascular complications and multi-organ involvement.(9)

These cases underscore the need for early consideration of venous thromboembolism (VTE) in melioidosis. Early intervention with appropriate antibiotics and anticoagulation therapy is crucial. The interplay between infection, inflammation and coagulation warrants further research to develop targeted therapeutic strategies aimed at mitigating the risk of thrombosis and improving patient outcomes.Melioidosis is increasingly recognised for its vascular complications. In this case, DVT and PE were unsuspected until imaging was performed, despite the absence of limb swelling or localised signs. The pathogenesis of thrombosis in melioidosis involves inflammatory-mediated endothelial damage, platelet activation and disruption of anticoagulant pathways.(4)

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Conclusion

This case highlights an unusual and serious manifestation of melioidosis presenting as unsuspected DVT and PE. Prompt diagnosis and treatment with antibiotics and anticoagulation led to a favourable outcome. Clinicians managing septic diabetic patients in endemic regions should consider VTE as a potential complication. Further studies are warranted to better understand the mechanisms linking melioidosis and thrombosis.

Declarations

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History taking, examination, necessary investigations arrangement, management under supervision, daily monitoring of the patient, and writing of the manuscript were done by Perera HMUAS. All authors contributed to writing the manuscript, read and approved the final manuscript.

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CASE REPORT

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Hypereosinophilic syndrome associated with idiopathic eosinophilic vasculitis

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Abstract

Hypereosinophilic syndrome (HES) is a complex heterogenous syndrome associated with hypereosinophilia and end organ involvement. A 46-year-old woman presented with swelling of the upper and lower limbs, neck and face, with shortness of breath. On examination there was evidence of dermal oedema with an urticarial rash. Investigations revealed high absolute eosinophil count, evidence of cutaneous vasculitis and increased bone marrow eosinophilic precursors. There was no other end-organ involvement. There was a recurrence of symptoms despite an initial course of glucocorticoids. However, she later responded to long-term imatinib. This case highlights the importance of considering HES with idiopathic cutaneous vasculitis even in the absence of significant systemic involvement.

Keywords: hypereosinophilic syndrome, eosinophilic dermal vasculitis, primary eosinophilia, clonal eosinophilia lymphocytic variant HES

Introduction

Hypereosinophilia syndrome (HES) is a complex heterogenous syndrome associated with persistent elevation of eosinophils (hypereosinophilia) and end organ involvement regardless of aetiology.(1) Criteria required for diagnosis of HES include; peripheral blood eosinophilia with eosinophil counts >1500/μL for at least 6 months; no evidence of parasitic, allergic or other known causes of eosinophilia; symptoms and signs of multiple organ involvement.(2) Eosinophils secrete many mediators which exhibit potent proinflammatory, prothrombotic and pro-fibrotic properties. These mediators lead to organ infiltration resulting in end-organ dysfunction. HES encompasses a range of subtypes, including primary (clonal myeloid or lymphoid), overlap, familial/genetic and idiopathic forms.(2) Several cases of HES-associated idiopathic eosinophilic vasculitis have been described which are distinctly different from eosinophilic granulomatosis with polyangiitis (EGPA) in their clinical manifestations and management.(3,4) Our patient is rather unusual because of the overlap of clinical features she demonstrated between both myeloid and lymphoid clonal forms of eosinophilia and minimal response to glucocorticoids. We describe a case of HES associated with idiopathic eosinophilic vasculitis with dermal infiltration and minimal involvement of other organ systems.

Case presentation

A 46-year-old woman presented with swelling and pain of upper and lower limbs. The swelling initially commenced in the distal parts of the upper limbs and then progressed to involve the distal parts of the lower limbs. There was arthralgia involving the large joints, myalgia, constitutional symptoms of low-grade fever with loss of appetite, generalised body

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weakness and malaise. She subsequently developed an itchy erythematous rash over the forearm of the upper limb with no evidence of angioedema. Figure 1 demonstrates the lower limb rash and swelling of the upper limb. There was worsening of shortness of breath with a non-productive cough and dysphagia with pain and discomfort on swallowing. There were no genitourinary or connective tissue related symptoms. She had a past history of dyslipidaemia, hypertension, hypothyroidism and asthma during pregnancy. She had encountered a flea bite during her recent visit to Cyprus. On examination there was dermal oedema of upper and lower limbs with an erythematous palpable rash over the forearm. Cardiovascular, respiratory, abdomen and neurology examinations were unremarkable. Her investigations are shown in Table 1. She was initially given deworming treatment and diethylcarbamazine for three weeks, but showed suboptimal response to treatment. Initially diagnoses such as parasitic infestations and allergies were considered due to her recent travel history and the prior history of atopic tendencies. Clonal eosinophilias, either myeloid or lymphocytic variants, eosinophilic granulomatosis with polyangiitis (EGPA), idiopathic eosinophilic vasculitis and eosinophilic fasciitis were considered as probable differential diagnoses due to the high eosinophil counts and prominent cutaneous involvement. Bone marrow biopsy revealed evidence of granulocytic eosinophil precursors with a hypercellular marrow with no evidence of genetic abnormalities or rearrangements suggestive of common clonal eosinophilias. However, as we were unable to screen for all known genetic rearrangements, HES due to other unscreened genetic rearrangements were still considered a possibility. Skin biopsy revealed evidence of cutaneous infiltration with eosinophils and evidence of vasculitis. However, there was no evidence of muscle or fascial involvement. Her pANCA and cANCA were negative and there was no evidence of other organ involvement suggestive of EGPA. Thus HES with idiopathic eosinophilic vasculitis was considered the most likely aetiology. Lymphocytic variant HES was considered due to predominant cutaneous involvement. Hence, she was treated with a trial of intravenous glucocorticoid pulses, with bone protection measures, for which she initially responded with resolution of cutaneous rashes and gradual return of eosinophil counts to normal over two weeks. She was discharged on oral glucocorticoids, hydroxyurea and allopurinol.

One month later despite good haematological response there was persistence of the constitutional symptoms and mild recurrence of cutaneous

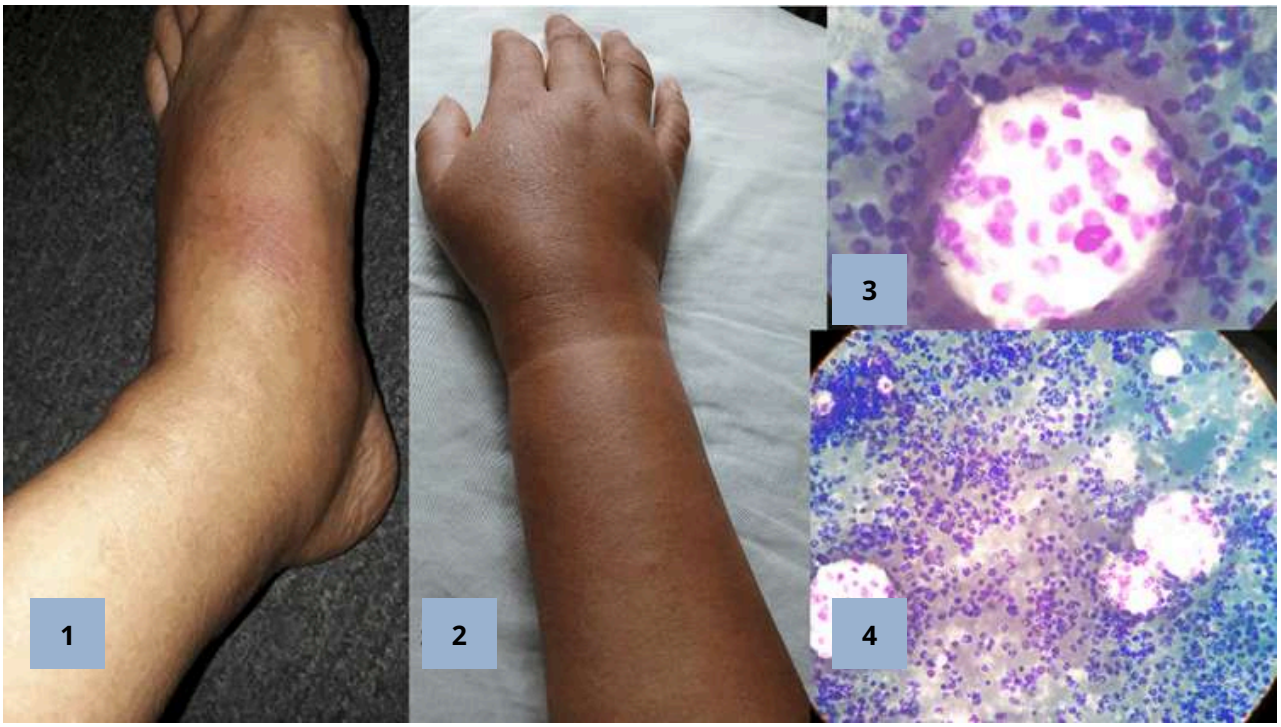

Figure 1. Evidence of cutaneous oedema and reddish rashes (1 and 2), an abundance of eosinophils in the bone marrow biopsy (3 and 4) in high and low power fields respectively

oedema. Three months later she developed worsening shortness of breath, swelling of the neck, face and upper limbs and urticarial plaques lasting less than 24 hours, without angioedema. There were no features of Raynaud's phenomenon, photosensitivity and joint pains. There was no evidence of exertional desaturation on the six minute walking test. Her investigations during the second admission showed eosinophils of 1.9 x 10^3/ µL with cutaneous involvement but no other end organ involvement. She was again commenced on a course of oral glucocorticoids but had a poor response. Hence, she was started on imatinib along with oral glucocorticoids and her eosinophil counts gradually returned to the normal range. She is still under follow-up three monthly and her eosinophil count is monitored. One year after the diagnosis she remains symptom free with normal eosinophil counts and is currently on oral imatinib. She has a good functional level and has returned to her profession as a caregiver.

Table 1. Summary of haematological, biochemical and imaging findings

Investigation	Result	Reference range
White blood cells (10^3/µL)	79.77 (1st admission) → 103.92 -> 89.80 → 41.28 → 11.28 12.23 (2nd admission) → 10.4 → 8.5 → 6	4.5 - 11
Neutrophils (10^3/µL)	5.18	2-7
Lymphocytes (10^3/µL)	5.92	1-4
Eosinophils (10^3/µL)	102 (1st admission) → 68.03 → 92.05→ 79.36 → 20.13 → 1.28 (on discharge following 1st admission)	0.04-0.35
Monocytes (10^3/µL)	0.51	0.2-0.4
Basophils (10^3/µL)	0.13	0–0.3
Blood picture	Severe eosinophilia with mild left shift. No abnormal cells or blasts.	
Sodium (mmol/L)	139	135-145
Creatinine (mg/dL)	0.89	0.5-1.1
Potassium (mmol/L)	3.9	2-5
Aspartate transaminases (U/L)	36	8-33
Alanine transaminases (U/L)	32	7-56
Total bilirubin (mg/dL)	0.4	1-12
Direct bilirubin (mg/dL)	0.1	<0.3
C reactive protein (mg/dL)	16.3	<6
ESR (mm per 1st hour)	60	<20
Albumin (g/dL)	3.0	3.5-5.5
Total calcium (mg/dL)	8.1	8.5-10.5
Corrected calcium (mg/dL)	8.9	8.5–10.2

Table 1. Summary of haematological, biochemical and imaging findings (continued...)

Investigation	Result	Reference range
Urine full report Chest X-ray High resolution CT (HRCT) 2D Echocardiogram Ultrasound scan Nerve Conduction study	Normal	
Toxoplasma Ab (IgM/IgG) Filarial antibody test	Negative	
Muscle biopsy	There is no evidence of endomysial or perimysial inflammation. Eosinophilic vasculitis and a significant perivascular eosinophilic infiltrate with degranulation is evident. Adjacent fibroadipose tissue also contains perivascular eosinophils. Conclusion: eosinophilic vasculitis and perivascular eosinophilic collections	
Skin biopsy	Skin biopsy with multiple thrombi within the dermal small blood vessels, red cell extravasation and moderate perivascular eosinophilic infiltrate in the dermis. Epidermis is histologically unremarkable.	
Bone marrow biopsy	Moderately hypercellular bone marrow with granulocytic hyperplasia predominantly with eosinophil precursors, mildly suppressed erythropoiesis and active megakaryopoiesis. No evidence of marrow infiltration of any kind. No granuloma formation/necrosis in the biopsies.	
ANA	Nuclear pattern 1:1280 Cytoplasmic pattern 1:80 Mitotic pattern 1:80	
C3	125 mg/dL	90-180 mg/dL
C4	25 mg/dL	20-50 mg/dL
LDH	555 IU/L	140-280 IU/L
Total IgE	4840 IU/mL	0-60 IU/mL
Vitamin B12	601 pg/mL	200-900 pg/mL
MPN panel (Myeloproliferative neoplasm panel) FIP1L1-PDGFRA translocation BCR-ABL cANCA pANCA	Not detected	
Upper gastrointestinal endoscopy CECT – Chest abdomen pelvis	Normal	

Discussion

HES complicated with idiopathic eosinophilic vasculitis is a rare disease which is challenging to diagnose. Our patient had eosinophilic dermal infiltration with evidence of vasculitis, an eosinophil count of around 60-110 x 10^3/μL, with significant cutaneous symptoms and constitutional symptoms without end-organ involvement.

Primary HES is caused by neoplastic disorders such as clonal myeloid and lymphoid disorders. These clonal forms are associated with genetic rearrangements such as FIP1L1-PDGFRA. We performed a limited set of tests for the genetic rearrangements typical of HES. We were unable to carry out PDGFRB or FGFR1 with PCM1-JAK2, ETV6-JAK2 or BCR-JAK2. Thus we were unable to definitively diagnose or rule out HES. Many other mutations and epigenetic imbalances are postulated to drive myeloid HES. Others include idiopathic HES and overlap forms like EGPA. Reactive HES is the expansion of eosinophils driven by cytokines such as IL-5. This could be the result of adverse drug reactions, parasitic infections, connective tissue diseases, lymphomas and certain solid malignancies. There are rare familial forms of HES. They are detected at the time of birth and have been attributed to a chromosome defect. Idiopathic forms are known to have a genetic aetiology.(5) Atopy, drug reactions with eosinophilia and systemic symptoms, eosinophilic gastrointestinal disorders and allergic bronchopulmonary aspergillosis are common causes of hypereosinophilia.(1) They are considered to be overlap-eosinophilic syndromes due to the associated organ involvement and eosinophilia.(5)

Eosinophilic granulomatosis with polyangiitis, idiopathic eosinophilic vasculitis and recurrent cutaneous eosinophilic vasculitis are several examples of eosinophilia associated vasculitis.(3,6) It is often difficult to discern between the above types in the early stages when the disease is in evolution as ANCAs are positive only in about 30% of patients. There are no reliable biomarkers to differentiate between HES from EGPA. Although certain indices have been derived using logistic regression to delineate between the two such as HES–suggesting laboratory index (HSLI), due to the smaller cohort sizes in these studies there is no universal applicability of these indices.(7,8)

Considering elevated IgE, presence of extensive cutaneous, soft tissue involvement and relative sparing of other organ systems this patient demonstrates certain clinical features of lymphoid HES compared to myeloid HES which is more likely to have chromosomal abnormalities, cytopenias, elevated vitamin B12 levels and organomegaly. However, these were not present in this patient. Certain variants of lymphoid HES like Gleich syndrome present with angioedema along with other cutaneous involvement which was also not observed in our patient.(2) Presence of a significantly positive ANA is rather unusual in HES but has rarely been described.(3) Eosinophilia has been described in certain forms of connective tissue disease and vasculitis. However there were no clinical features of connective tissue disease in our patient.

Despite extensive cutaneous and hematological involvement there was no pulmonary, cardiovascular, gastrointestinal and neurologic involvement. They need to be monitored with disease related activity scores and end-organ involvement.(4)

It is imperative that underlying malignancies are conclusively excluded in patients presenting with features of hypereosinophilia. They need to be subsequently monitored for additional end organ involvement which may progress with time. CECT chest, abdomen and pelvis and HRCT did not reveal any evidence of malignancy or interstitial lung involvement. Initial lack of response to glucocorticoids and later, response to imatinib increases the likelihood of myeloid HES disorders whereas the cutaneous symptoms raise the likelihood of lymphoid HES. However, they do not usually respond effectively to imatinib. To date, our patient has been on imatinib for close to a year with good control of both her cutaneous symptoms and normalisation of the eosinophil counts. Patients with severe symptoms who are refractory to glucocorticoids are often treated with anti IL-4 and IL-5 biologic therapy with considerable success.(9, 10) However, there are considerable gaps in the understanding of pathobiology, confusions around diagnosis and management of these patients.(11)

Conclusion

This case describes HES presenting with isolated eosinophilic vasculitis and prominent cutaneous symptoms. Diagnostic work-up, including histology and exclusion of secondary causes are essential to confirm the diagnosis.

Declarations

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All authors contributed to the conceptualization of the case report and contributed to the acquisition of data writing the manuscript. All authors read and approved the final manuscript.

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CASE REPORT

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Fahr’s Disease presenting with isolated dysarthria

Keerthisinghe BDCH[1*], Premaratna BAHR[2]

Abstract

Fahr's disease is a rare neurodegenerative disorder marked by abnormal calcium deposits in the basal ganglia, cerebellar dentate nuclei and white matter tracts, resulting in progressive brain atrophy. The disease typically presents in the fourth or fifth decade of life. It manifests with a variety of symptoms, including motor dysfunction, muscle tone abnormalities, involuntary hand movements, impaired eye movements, speech difficulties, cognitive decline, ataxia, seizure and neuropsychiatric symptoms, ranging from memory and concentration deficits to psychosis. Imaging studies reveal extensive, symmetric calcification in the basal ganglia and subcortical white matter. Diagnosis of primary Fahr’s disease, also referred to as primary familial brain calcification, involves excluding secondary causes, such as metabolic or endocrine disorders. The condition may have a genetic origin, typically inherited in an autosomal dominant or recessive manner. We present a case of a 48-year-old previously healthy man with speech difficulty found to have idiopathic cerebral calcifications leading to a diagnosis of Fahr’s disease.

Keywords: Fahr’s disease, idiopathic cerebral calcification, dysarthria

Introduction

Fahr's disease, also referred to as familial idiopathic basal ganglia calcification, bilateral striopallidodentate calcinosis, primary familial brain calcification (PFBC) or calcinosis nucleorum, is a rare neurodegenerative condition with a prevalence of less than 1 in 1,000,000 individuals. It primarily affects young to middle-aged adults.(1) The disease is characterised by abnormal calcifications, typically found in the basal ganglia, though they may also be present in other areas such as the thalamus, hippocampus, cerebral cortex, cerebellar subcortical white matter and dentate nucleus.(2-4) Fahr's disease is inherited in an autosomal dominant pattern, although both familial and non-familial cases have been documented. The term "Fahr's disease" refers to idiopathic basal ganglia calcification, while "Fahr's syndrome" is used to describe cases of secondary basal ganglia calcification.(5) We present a case of a 48-year-old previously healthy man who presented with progressive dysarthria and found to have idiopathic cerebral calcifications suggestive of Fahr’s disease.

Case presentation

A 48-year-old previously healthy man, a businessman educated up to advanced level, presented with a two-month history of progressively worsening slurring of speech. He denied any associated limb weakness, dizziness or vertigo, and did not report any gait disturbances or unsteadiness while walking. There was no history of seizures, dysphagia, or similar neurological symptoms. The patient also denied any

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family history of comparable presentations.

On examination, the patient was afebrile with a Glasgow Coma Scale (GCS) score of 15/15. His vital signs were within normal limits, with a blood pressure of 110/70 mmHg and a heart rate of 76 beats per minute. Respiratory examination revealed clear bilateral lung fields. Abdominal examination showed a soft, non-tender abdomen without organomegaly.

Neurological examination demonstrated intact cranial nerves, normal motor strength in all limbs and a normal gait. There were no involuntary movements such as tremors or chorea, and no features suggestive of a movement disorder. Except for dysarthria, there were no other signs indicative of cerebellar involvement. He scored 30/30 in the Mini-Mental State Examination (MMSE).

Non-contrast CT of the brain showed dense calcifications involving the dentate nuclei, basal ganglia, occipital lobe and cerebellar region (Figure 1). Serum calcium, serum phosphate and serum magnesium levels were within the normal range. Intact PTH level was normal. The diagnosis of Fahr's disease was made. The patient was informed about the condition, and speech therapy along with symptomatic management was initiated.

Discussion

Fahr's disease is a rare neurodegenerative disorder which was first described in 1930 by German neurologist Karl Theodor Fahr.(1) It is most commonly inherited in an autosomal dominant pattern, but it can also be passed down as an autosomal recessive trait or occur sporadically without a family history.(2-4)

Abnormal calcium buildup in Fahr's disease is thought to result from either disrupted calcium metabolism in the brain or metastatic deposition caused by changes in the local blood-brain barrier. The process involves defective iron transport and the generation of free radicals, which lead to tissue damage. This damage triggers the formation of calcification around a central core made up of mucopolysaccharides and related substances. Initially, calcium deposits form within the vessel walls and the surrounding perivascular space, gradually spreading to involve the entire neuron. As the calcification progresses, it compresses nearby blood vessels, reducing blood flow and perpetuating a harmful cycle of decreased circulation, tissue injury, and further mineral deposition.(6)

The deposits in Fahr's disease are primarily made up of mineral compounds such as calcium phosphate and calcium carbonate. In addition, substances like mucopolysaccharides, and various metals, such as iron, copper, magnesium, zinc, aluminium, silver and cobalt can also be present in these calcifications.(7-9) Koller et al. has done a review of 4,219 CT scans and found that the majority of calcifications in Fahr's disease occur bilaterally and symmetrically, with only a small number of cases presenting with unilateral calcifications.(10)

The diagnostic criteria for Fahr's disease are as follows: progressive neurological dysfunction, which

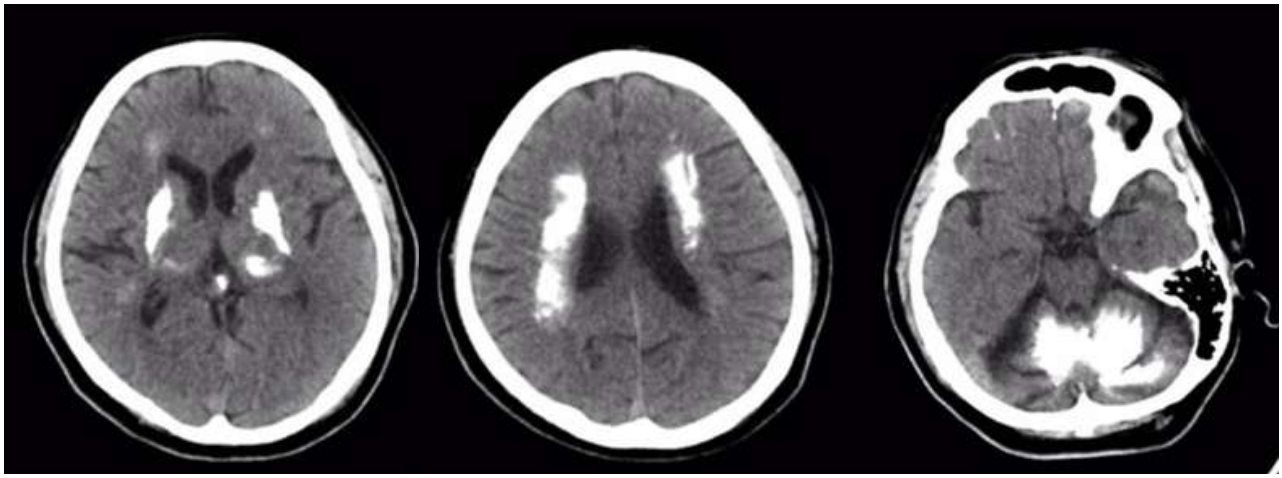

Figure 1. Non-contrast CT of the brain showing dense calcifications involving the dentate nuclei, basal ganglia, occipital lobe and cerebellar region

Table 1. Summary of investigations

Investigation	Result
White blood cell count (10^9/L)	6.4
Haemoglobin (g/dL)	11.6
Platelet count (10^9/L)	243
Erythrocyte sedimentation rate (mm/1st hour)	15
C-reactive protein (mg/L)	<0.5
Procalcitonin (mcg/L)	0.05
Calcium (mmol/L)	2.3
Phosphate (mmol/L)	1.3
Magnesium (mmol/L)	0.7
Sodium (mmol/L)	138
Potassium (mmol/L)	3.6
Intact Parathormone (PTH) (ng/L)	27
Toxoplasma antobody CMV antibody Mantoux test HIV 1 and 2 antibodies	Negative

can begin at any age; radiographic evidence showing bilateral calcification in the basal ganglia, as well as other regions of the brain; no biochemical abnormalities indicating endocrinopathies, mitochondrial disorders or other systemic conditions; exclusion of infections, toxins, or trauma as causes; a family history suggesting autosomal dominant inheritance.(4,10)

Fahr's disease presents with a wide range of neurological, movement and neuropsychiatric symptoms. Neurologically, it can cause tetany, seizures and epileptic disorders, along with gait disturbances, spasticity, speech impairments, dementia, myoclonus, and in severe cases loss of consciousness and coma. Additionally, individuals may experience paroxysmal choreoathetosis, dystonic choreoathetosis and papilloedema which is indicative of intracranial hypertension. Pleocytosis in the cerebrospinal fluid (CSF) may also be observed. Movement disorders include clumsiness, fatigability, unsteady gait, involuntary movements, and muscle cramps. On the neuropsychiatric front, affected individuals may suffer from psychosis, depression, apoplexia (sudden loss of consciousness or stroke-like episodes), cognitive decline and an inability to make decisions. These symptoms collectively reflect the progressive and complex nature of Fahr's disease. (12)

It is important to recognise the distinctive feature of presentation, isolated progressive dysarthria as in our case. Unlike some reported cases in the literature our patient did not present with movement disorders or other neuropsychiatric symptoms. This difference underscores the clinical variability often seen in Fahr's disease, highlighting that patients may exhibit a broad range of symptoms, with each case

potentially differing substantially in its presentation.

The severity and location of lesions in Fahr's disease are thought to impact the clinical symptoms, with more widespread calcifications often leading to more severe dementia and extrapyramidal signs. According to Lopes-Villega's study, which examined patients with Fahr's syndrome, 11.1% developed parkinsonism associated with calcifications in the pallidum, thalamus and cerebellar dentate nucleus. About 22.2% patients experienced transient ischaemic attacks linked to calcification in the pallidum and putamen, while 5.6% had dysarthria and orthostatic hypotension due to calcifications in the caudate and putamen.(13)

Iqbal et al. had reported a case involving a 77-year-old patient who presented with confusion, altered mental status, dystonia, tremors and hallucinations. Imaging had revealed significant calcification in the dentate nuclei, basal ganglia, as well as subcortical calcifications in the frontal and occipital lobes. These findings are strongly indicative of late-onset Fahr's syndrome.(14)

Aghemo et al. described a case involving a 38-year-old man with a history of schizophrenia who presented with generalised weakness, rigid movement, cognitive impairments in attention, memory and orientation, as well as a spastic ataxic gait. Metabolic and infectious pathology had been excluded. A non-contrast CT scan of the head had revealed widespread calcification in the cerebral hemispheres, strongly suggesting a diagnosis of Fahr's disease.(15)

There are some cases in the literature, where patients were asymptomatic and cerebral calcifications were found incidentally. Sara Ez-zaky et al. reported a case of Fahr's disease in a 50-year-old woman with no significant medical history, who presented after a head injury with an initial loss of consciousness. A CT scan of the brain was conducted to evaluate potential lesions, revealing bilateral intracerebral calcifications with no signs of post-traumatic damage. The clinical examination was normal, and subsequent laboratory tests, including calcium and parathyroid hormone (PTH) levels, as well as infectious disease screening, showed no abnormalities.(16)

Currently, there is no cure for the calcifications associated with Fahr's disease, and treatment focuses primarily on managing the symptoms of movement and psychiatric disorders. Medications commonly used for Parkinsonian symptoms, such as levodopa, have generally shown limited effectiveness. (17) It is important to avoid first-generation antipsychotics, as they can worsen pyramidal symptoms and increase the risk of neuroleptic malignant syndrome. Instead, atypical or second-generation antipsychotics are typically considered. Given that Fahr's disease is a progressive neurodegenerative condition, the only way to track its progression is through periodic CT scans over the patient's lifetime.

Conclusion

This case highlights the crucial role of brain imaging in reaching the correct diagnosis, even when clinical signs are minimal. The key message of the case is to highlight the need for clinicians to consider the possibility of Fahr's disease, when confronted with unexplained neuropsychiatric symptoms and characteristic CT findings, as early recognition of the condition can significantly impact patient management. With ongoing research, there is hope that clinicians may one day be able to target the underlying mechanisms of the disease, rather than simply managing the symptoms.

Declarations

Author contributions:
BDCH Keerthisinghe wrote the initial case report and did the literature review. BAHR Premaratna edited the manuscript and contributed to the literature review. Both authors agreed on the final version of the manuscript submitted.

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The authors declare that there are no conflicts of interest.

Consent to participate/publish:
Written informed consent for publication of this case report was provided by the family of the patient.

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CASE REPORT

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Dermatomyositis as an initial presentation of underlying breast malignancy: a paraneoplastic manifestation

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Abstract

Though dermatomyositis is a well-known paraneoplastic syndrome, its particular relationship with breast cancer is yet to be thoroughly defined and there are no established guidelines for the treatment. The occurrence of dermatomyositis seems to be associated with more advanced stages of breast cancer, particularly with invasive ductal carcinoma. Our case elaborates a primary presentation of breast cancer as dermatomyositis, its musculoskeletal manifestation and management. Treating the cancer alone does not sufficiently address the symptoms of dermatomyositis, which can greatly impact quality of life. Thus, employing a multidisciplinary strategy with strong collaboration of rheumatologists is crucial for the diagnosis and treatment.

Keywords: dermatomyositis, breast cancer, paraneoplastic syndrome

Introduction

Dermatomyositis (DM) is an autoimmune inflammatory myopathy that presents with proximal muscle weakness, skin rashes and various systemic symptoms. The skin manifestations include; erythematous papules on the knuckles (Gottron's papule; flat reddish-rash over extensor surfaces of the fingers, elbows and knees (Gottron's sign); erythematous papules on the palmar aspect of the fingers (inverse-Gottron's papule); swelling and redness around the eyes (heliotrope sign), thigh (holster-sign); and a widespread photosensitive violaceous rash (shawl-sign, V-sign) which can closely resemble acute cutaneous lupus. The rash associated with DM can vary greatly, making the diagnosis difficult, particularly in individuals without muscle weakness or raised creatine-kinase levels.(1,6) Diagnostic procedures include electromyography and muscle MRI followed by tissue confirmation with muscle biopsy. The link between dermatomyositis and malignancy is widely recognised, with 15%–30% of individuals with DM having a concurrent malignancy, observed in lung, ovarian, breast, pancreatic, gastric, colorectal cancers and non-Hodgkin lymphoma.(2,7,8) Here, we discuss a case to guide the diagnosis and management of DM associated to breast cancer.

Case presentation

A 41-year-old previously healthy woman presented with proximal muscle weakness and skin rash with recent onset dysphagia. The progressive proximal muscle weakness which started one month back and was later associated with a photosensitive, hyper and hypopigmented, non-itchy rash over the neck, face, upper back, chest, and arms (Figure 1). Within two weeks, the rash covered 70% of her body surface

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area. She was experiencing difficulty in swallowing, predominantly for solids, and cough for three days. She was earlier treated with a short course of oral and topical corticosteroids by a dermatologist for a presumed atopic dermatitis with minimal improvement.

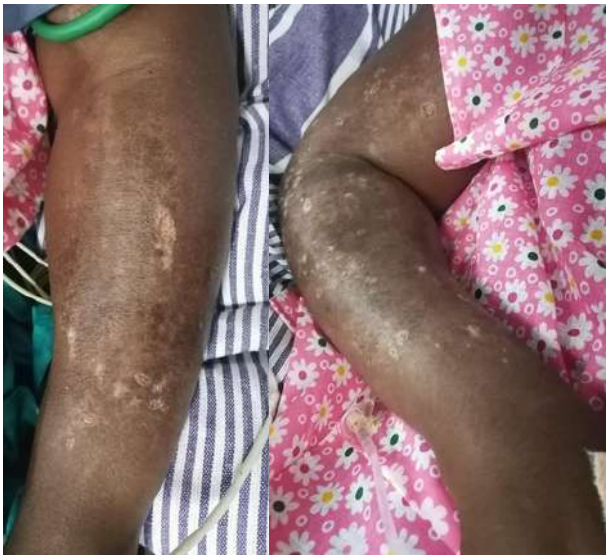

Figure 1. Photosensitive, hyper and hypopigmented, non-itchy rash over arms

On examination, her body temperature was 38.2°C, blood pressure was 150/100 mmHg and heart rate was 130 beats per minute. She was oedematous, tachypnoeic with an oxygen saturation of 96% on 5 L/minute oxygen via facemask. Lung auscultation revealed coarse crepitations over bilateral bases. Examinations of the precordium and abdomen were unremarkable except for diffuse hyper-hypopigmented rashes all over her body. No heliotropic rash, Gottron papules or signs, periungual erythema or abnormal nail-fold capillaries were observed. Her proximal muscle strength was decreased in a symmetrical pattern around her shoulders including neck flexors (3/5) and in pelvic girdles and thighs (2/5) , but was preserved in distal muscle groups (5/5). Her muscle tone was reduced. However, sensory, deep tendon reflexes and cranial nerve examinations were normal. On breast examination, she had a firm, mobile 1.5 cm mass in the left outer-quadrant of the breast, with palpable axillary lymphadenopathy.

A left breast ultrasonography showed BIRADS-V lesion at 3 o'clock position measuring 1.4x1.2 cm, together with malignant looking left axillary lymph nodes up to level-II. Computed tomography scan of brain, chest, abdomen, pelvis and bone scan demonstrated no other primary malignancies or distant metastatic lesions. HRCT-Chest showed mixed ground-glass appearance/consolidation in bilateral lower lobes. FNAC of the left axillary lymph-node revealed cells from an adenocarcinoma deposit likely from the diagnosed ipsilateral breast carcinoma. A left breast mass tru-cut biopsy showed invasive breast carcinoma with ductal carcinoma in-situ. Immunohistochemistry was positive for oestrogen receptor (8/8) while, HER2 (human epidermal growth-factor receptor) was equivocal (2+) and progesterone receptor was negative (0/8). Later, her FISH for HER2 was also found to be negative. As her axillary lymph node was found to be positive following a malignant smear with no distant metastasis, tumor staging of T2N1M0 was made.

The investigations revealed very high inflammatory markers with neutrophil leukocytosis, normocytic anaemia and thrombocytopenia. Her renal functions, thyroid profile and amylase were normal and anti Jo-1 antibody levels, urine for myoglobin, venereal and chronic granulomatous disease screenings were unremarkable. AST was 176 U/L (15-37), ALT-71U/L (16-63), LDH-997 U/L (120-246), aldolase-22 U/L (<7.6) and creatine-kinase was peaked at 2615 U/L (<170), corresponding to the development of muscle weakness. ANA titre was high (1:640, nuclear and cytoplasmic pattern) though it was a paraneoplastic DM. Muscle biopsy showed features of an inflammatory myopathy. Electromygraphy was not done due to severe soft tissue oedema. Blood picture showed anaemia of chronic disease with reactive neutrophilic leukocytosis and moderate thrombocytopenia.

IV Methylprednisolone 1 g daily was given for 4 days and then oral prednisolone 60 mg daily was started. Three weeks later it was switched to dexamethasone 4.5 mg every other day and tailed off to 3.5 mg every other day as there was a suspicion of steroid induced myopathy. IV immunoglobulin was administered at 2 g/kg/d for 2days. An urgent left side mastectomy with level I and II axillary clearance was done and post-operative care given in the intensive care unit. As the tumour size was 24x20x15 mm (Nottingham grade-2), 13/16 lymph nodes showed tumour metastasis and all resection margins were more than 2 mm away from the tumour, the histopathological tumour grade was pT2N3a invasive ductal carcinoma. Persistent respiratory muscle weakness led to difficulty in weaning-off from the ventilator and she underwent tracheostomy. As her sputum cultured Coliform,

Table 1. Summary of haematological, biochemical and imaging findings (continued...)

Basic blood tests	Reference range	15/10/2024	09/12/ 2024
White cell count (10^9/L)	4-10	15	10.4
Neutrophil (%)	50-70	91	74
Lymphocyte (%)	20-40	4.7	21
Haemoglobin (g/dL)	11-15	10.7	12.5
Mean corpuscular volume (fL)	80-100	88.1	85.3
Mean haemoglobin concentration (pg)	27-34	28.2	29.6
Platelets (10^9/L)	150-450	79	478
Erythrocyte sedimentation rate (mm/1st hour)	<20	90	20
C-reactive protein (mg/L)	0-3	235	10.2

Acinetobacter and *Pseudomonas*, diagnosis of hospital-acquired pneumonia was made and treated with IV piperacillin tazobactam 4.5 g thrice daily for three weeks, IV. Colistin 2 mu twice daily for two weeks and later escalated to culture guided antibiotics, amikacin and imipenem. Thrombotic prophylaxis, vitamin D and folic acid supplements were given. Subcutaneous goseralin 3.6 mg monthly was started with oral tamoxifen 20 mg daily as the oestrogen receptor was positive. Intramuscular testosterone 100 mg once in every two weeks (total of 6 doses) were given to improve muscle power. Feeding was established through a PEG-tube and physiotherapy was started. Dermatology, oncology, endocrinology, onco-surgery and rheumatology inputs were obtained throughout. She gradually improved clinically and biochemically. Her skin rashes were healing slowly while leaving post inflammatory marks. In three months, she gained good muscle power and was able to be taken off the tracheostomy and PEG-tube.

Discussion

Dermatomyositis as an initial presentation in breast cancer is an uncommon finding, and there are no established guidelines for managing these patients. The median duration from presentation with dermatomyositis to a diagnosis of breast cancer is one month (range: 29-36 months) like in our case. Majority of patients have a cancer diagnosis prior to being diagnosed with dermatomyositis whereas only 24% show myositis symptoms initially.(4,9) The occurrence of DM is linked to advanced tumours, with 72% of the women showing stage III-IV disease. (3,4,10) No patterns in hormone receptor status have been noted in breast cancer patients with DM. Myositis-specific antibodies are not consistently positive, but they can aid in diagnosis and subtyping of dermatomyositis. ACR 2022 recommendations for malignancy screening in patients with idiopathic inflammatory-myopathy can be used for further evaluation, but in low-middle income countries, where the cancer screening facilities are not readily available, monthly self-examination of the breast should be advised, followed with clinical breast examination whenever suspicious.

The goal of therapy is to reduce muscle inflammation, regain muscle strength, tackle extra-muscular issues and eliminate dermatological symptoms. The skin manifestation of DM can be difficult to handle and can lead to discomfort due to severe itching. Sunscreen can be beneficial since the skin symptoms are frequently sensitive to light. The mainstay of treatment is high-dose oral glucocorticoids, usually initiated at a daily dosage of 1 mg/kg and may need additional intravenous glucocorticoids.(5) The literature reviews showed that 75% of patients were able to gradually reduce their steroid usage later. In critical situations, IVIG is administered at 2 g/kg daily for two days. Methotrexate and azathioprine are widely used to reduce steroid reliance. As the tumour of our patient was in an early stage, surgery and hormonal therapy were adequate to control the disease rather than chemo-radiotherapy. Hydroxychloroquine and topical agents are employed to manage active skin involvement.(5) Skin

manifestations serve as an effective indicator for the recurrence. The relapse, recurrence or aggravation of rash indicate the activity of the underlying malignancy.

Conclusion

Patients exhibiting proximal muscle weakness, skin rashes and symptoms suggestive of dermatomyositis should raise high level of clinical vigilance for a paraneoplastic syndrome due to underlying malignancy, and undergo careful clinical assessment to render prompt treatment and minimise irreversible damage. A multidisciplinary strategy should be adopted because, addressing the underlying malignancy by itself is inadequate and treating dermatomyositis and other systemic involvements should be considered as well. Mainstay of treatment includes high-dose glucocorticoids, steroids-sparing agents, prompt start of IVIG therapy, treatment of underlying malignancy and supportive-care.

Declarations

Author contributions:
All authors contributed to the conceptualization and design of the study, contributed to the acquisition of data, conducted the data analysis, contributed to data interpretation and writing of the manuscript. All authors read and approved the final manuscript.

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CASE REPORT

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A fatal case of disseminated intravascular coagulation and multiple systemic complications following multiple wasp stings

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Abstract

Disseminated intravascular coagulation (DIC) is a rare but severe complication of wasp envenoming, caused by systemic toxic effects. We report a case of a 50-year-old Sri Lankan man who sustained over 35 wasp stings, presenting with localised pain and swelling, along with systemic complications including DIC, rhabdomyolysis, mild acute kidney injury and liver dysfunction, notably without anaphylactic shock or bleeding manifestations. The management involved systemic corticosteroids, antihistamines, aggressive hydration and supportive care. The patient fully recovered. Clinical and laboratory parameters normalised by day 14. This case underscores the importance of early recognition, timely supportive care, and close monitoring to mitigate severe systemic complications from wasp stings to achieve favourable outcomes.

Keywords: acute kidney injury, disseminated intravascular coagulation, rhabdomyolysis, wasp stings

Introduction

Disseminated intravascular coagulation (DIC) is characterised by extensive intravascular fibrin deposition, resulting from excessive activation of blood proteases that disrupt the body's natural anticoagulant mechanisms. It is commonly associated with bacterial sepsis, malignancies like acute promyelocytic leukaemia, obstetric complications and envenoming from insects and snakes.(1)

Wasps, bees and ants are members of the order *Hymenoptera*, and approximately 56% to 94% of individuals experience a sting from one of these insects at least once in their lifetime.(2) A wasp sting is often encountered in remote areas of developing nations. The stinging apparatus in the order *Hymenoptera* is a modified ovipositor (egg-laying organ) present exclusively in females. Wasps will sting if provoked or a threat to their nest is perceived. In such situations, numerous wasps may attack the perceived threat, potentially leading to mass envenoming.(3)

The responses to *Hymenoptera* stings are categorised as: systemic anaphylactic responses, systemic toxic manifestations, normal local reactions, extensive local reactions and atypical or uncommon reactions. (2) Wasp stings can lead to fatal outcomes through anaphylaxis and multiorgan involvement, encompassing complications such as acute kidney injury, rhabdomyolysis, hepatic and cardiac dysfunction, as well as coagulopathy.(4)

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Disseminated intravascular coagulation (DIC) is not commonly observed among the toxic and allergic reactions caused by *Hymenoptera* stings.(5)

Case presentation

A 50-year-old agricultural worker from the Eastern Part of Sri Lanka, who had no significant medical history, was stung by over 35 wasps when he was cleaning his garden. The stings were predominantly on his scalp, back, arms and chest (Figure 1). He immediately experienced severe pain, swelling and redness at the sting sites but denied symptoms such as chest pain, difficulty breathing, or other allergic reactions. He had no prior history of wasp stings. He was conscious, oriented and haemodynamically stable when he arrived at the local hospital. However, he began experiencing severe bodyaches. He received intravenous hydrocortisone 200 mg, chlorpheniramine 10 mg, subcutaneous morphine 5 mg and hydration with normal saline. After initial management at the local hospital, he was transferred to a tertiary care facility the following day.

Upon admission, the patient reported severe bodyaches while his vital parameters remained stable. Multiple circular punctate lesions were observed at the sting sites.

The wasp species responsible for the envenoming was identified as *Polistes apachus* (Texas paper wasp), a large, golden-brown social wasp with distinct yellow markings on the abdomen and thorax (Figure 2). Identification was based on characteristic morphological features, including yellow striping on the thorax, a flat clypeus and the presence of sublateral yellow patches on the second tergite.(6)

His laboratory results were suggestive of disseminated intravascular coagulation (DIC), rhabdomyolysis, liver dysfunction and acute kidney injury, with elevated blood urea and serum creatinine levels. Liver enzymes were markedly elevated despite the patient not showing any clinical signs of liver failure. His haematological profile was also abnormal, showing anaemia and thrombocytopenia. Coagulation parameters were prolonged, and there was a significant rise in lactate dehydrogenase levels. A peripheral blood smear revealed the presence of schistocytes and evidence of haemolysis (Figure 3). Unfortunately, due to the limitations of the setting, we were unable to assess FDP levels. Given these findings, DIC induced by wasp stings was considered a likely diagnosis, with elevated creatine phosphokinase levels of 13488 U/L attributed to rhabdomyolysis.

Additional investigations revealed a serum sodium value of 137 mmol/L, a potassium value of 5.8

Figure 2. The offending wasp: *Polistes apachus*

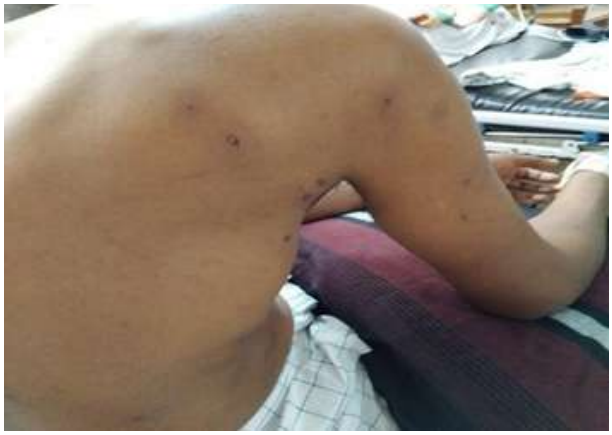

Figure 1. Multiple wasp stings on the right side of chest and arm

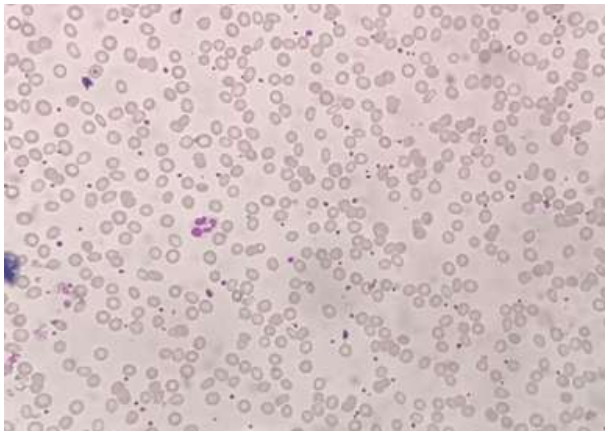

Figure 3. Blood picture showing polychromatic cells, spherocytes and micro spherocytes

mmol/L, and a corrected serum calcium level of 2.0 mmol/L. However, urine for myoglobinuria was negative in the urine analysis, and the tests for hepatitis B, hepatitis C, hepatitis A, and HIV markers were negative. As the region is endemic for leptospirosis, it was also excluded as a possibility. Ultrasonography of the hepatobiliary system revealed the absence of any focal lesions or obstructions. He did not develop any bleeding manifestations, and his urine output was adequate.

He received intravenous fluid therapy with 3 litres of normal saline daily, maintaining adequate urine output throughout his hospital stay. From the third day after the event, his liver function, coagulation profile, creatine kinase levels and renal function demonstrated an improving trend. Platelet counts began to recover after day five. He was discharged on day five with advice to maintain adequate hydration. Throughout his hospitalisation, he remained haemodynamically stable. A reassessment on day 14 confirmed that the blood parameters had returned to normal, as detailed in the table (Table 1).

Discussion

Stings from *Hymenoptera* insects represent a significant occupational hazard in various regions worldwide(7), as demonstrated in this patient's case. The clinical manifestations of Hymenopterans envenoming are primarily categorised into IgE-mediated immediate hypersensitivity reactions and direct toxin-induced effects. Local reactions, commonly resulting from IgE-mediated responses, present immediately post-sting, and they typically settle within a few days without requiring targeted treatment. In contrast, systemic reactions, predominantly driven by the toxin's direct effects, can progress to severe and potentially life-threatening

Table 1. Summary of investigations

Laboratory tests	Normal ranges	Day 1	Day 2	Day 3	Day 4	Day 14
Haemoglobin (g/dL)	11.0-15.0	15.7	14.9	12.6	11.8	15.2
White blood cell count ($\times 10^3$/uL)	4.0-11.0	6.3	5.7	5.7	5.6	6.7
Platelets ($\times 10^3$/uL)	150-450	185	72	13	39	200
Creatinine (µmol/L)	62-115		97	134	84	67
Blood urea (mmol/L)	1.8-6.3		4.4	7.1	3.1	2.8
Total bilirubin (µmol/L)	3.4-17.1		121	80	55	10
Direct bilirubin (µmol/L)	0 -3.4		20	14	8	5.9
Lactate dehydrogenase (U/L)	81-234		2470	2075	1111	200
Alanine aminotransferase (U/L)	12.0-78.0		1527	872	614	50
Aspartate aminotransferase (U/L)	15-37		10823	4198	598	25
Prothrombin time (s)	13		26	26.1	21.9	14.2
Activated partial thromboplastin time (s)	27-42		120	59	31	30
International normalised ratio			2	2.01	1.71	1.04
Reticulocyte count (%)	0.3-3.0		3	2.7	2.5	1
Creatinine kinase (U/L)	39-308		13488	9000	7000	300
Peripheral blood smear for schistocytes			Present			

conditions.(8) Wasp venom contains various vasoactive amines, such as histamine and kinins, along with phospholipases, hyaluronidase, acid phosphatases and distinctive toxic peptides, including apamine, melittin and the anti-inflammatory mast cell-degranulating peptide.(9) Our case did not exhibit an immediate hypersensitivity reaction but instead developed life-threatening systemic complications.

Phospholipase A2 (PLA2), a component of wasp venom, contributes significantly to coagulation dysfunction. This enzyme accelerates the breakdown of two-acyl bonds in lipids, including phospholipids found in cell membranes, Golgi apparatus and mitochondria, thus leading to cellular dysfunction. Melittin, through its interaction with PLA2, is known to induce intravascular haemolysis. Antithrombin plays a key role in the pathophysiology of coagulation abnormalities associated with the anaphylactic reaction provoked by a wasp sting. This reaction leads to the liberation of bradykinin and kallikrein into the bloodstream, further promoting coagulation dysfunction. Additionally, neutrophils secrete tissue thromboplastin, while mast cells activate the extrinsic coagulation pathway.(10) In our patient, both the INR and the aPTT were markedly prolonged, indicating consumptive depletion of multiple clotting factors, supporting DIC. Schistocytes were present, but primary microangiopathic haemolytic anaemia (MAHA) syndromes (e.g., thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome) usually have normal or only minimally prolonged coagulation times.(11) Thus the MAHA here is secondary to DIC.

The development of acute kidney injury (AKI) can be attributed to mechanisms such as pigment-induced acute interstitial nephritis (AIN), acute tubular necrosis (ATN), and, less commonly, acute cortical necrosis.(12) Melittin and phospholipase present in wasp venom contribute to rhabdomyolysis and haemolysis.(13) The AKI in our patient was likely attributed to pigment-induced acute tubular necrosis, rhabdomyolysis and haemolysis.

In rare cases, extensive envenoming can directly cause cellular injury through toxins, leading to conditions such as rhabdomyolysis, intravascular haemolysis, disseminated intravascular coagulation, cardiovascular dysfunction, liver damage, acute kidney failure and varying degrees of neurological deficits.(14-17) However, our patient exhibited neither cardiovascular nor neurological manifestations. Despite the considerable venom exposure from multiple stings, the typical signs of severe anaphylaxis, especially anaphylactic shock, were not observed in this case.

The primary approach to managing massive Hymenopterans envenoming remains supportive care, as no specific antivenom is currently available. Although early administration of corticosteroids and antihistamines is recommended for anaphylaxis, these interventions were ineffective in preventing toxin-induced multisystem injury in our patient and in previously reported cases.(18,19)

Conclusion

This case demonstrates that multiple wasp stings can result in disseminated intravascular coagulation (DIC) and systemic complications, even without anaphylactic shock. Timely supportive care, including hydration and monitoring, enabled full recovery without blood product transfusions. Early recognition and prompt intervention are vital in managing severe envenomation, especially in resource-limited settings.

Declarations

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The authors declare that they have no conflicts of interest.

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CASE REPORT

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Idiopathic pleuroparenchymal fibroelastosis in a patient with pectus excavatum: an overlooked association

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Abstract

Pleuroparenchymal fibroelastosis (PPFE) is a rare, progressive interstitial lung disease characterised by prominent upper lobe fibrosis and elastotic changes. Its aetiology remains unclear, with most cases classified as idiopathic. While pectus excavatum has been noted in some PPFE cases, its potential role in disease pathogenesis has not been explored. We report a 76-year-old Sri Lankan man diagnosed with idiopathic PPFE who also had pectus excavatum. He had no features of connective tissue disease, no history of prior infections or environmental exposure that could explain his condition. A literature review identified seven global cases of PPFE with pectus excavatum, none of which discussed a possible association. Six of these cases, including ours, were idiopathic. We propose that pectus excavatum can lead to chronic restrictive mechanics and upper lobe atelectasis and may play a role in PPFE pathogenesis rather than being an incidental finding. This case is the third reported case of PPFE in Sri Lanka and one of few worldwide, highlighting its potential association with pectus excavatum. Given that PPFE remains underdiagnosed, particularly in tuberculosis endemic regions, recognising such atypical risk factors may aid in earlier detection and management. Further studies are needed to determine whether pectus excavatum contributes to PPFE development or coexists as a structural abnormality.

Keywords: pleuroparenchymal fibroelastosis, pectus excavatum, upper lobe fibrosis, interstitial lung disease

Introduction

Pleuroparenchymal fibroelastosis (PPFE) is a rare, progressive form of interstitial lung disease (ILD), histologically characterised by predominant fibrosis of the upper lobe with marked elastotic changes involving both the pleura and subsequent lung parenchyma.(1) Although formally recognised as a distinct clinicopathological entity in 2004, similar cases have previously been described under the term idiopathic pulmonary upper lobe fibrosis.

PPFE can be idiopathic or associated with a wide range of secondary causes, including autoimmune diseases, prior infections, bone marrow or lung transplantation, occupational dust inhalation and familial/genetic predisposition.(1) The underlying pathophysiology involves aberrant wound healing with excess elastic fiber deposition, but its precise mechanisms remain unclear.

In regions with a high burden of tuberculosis (TB), such as Sri Lanka(2), PPFE may be under recognised or misdiagnosed as a post-infectious upper lobe fibrosis or chronic sequelae of TB. To date, only two cases of PPFE have been reported in Sri Lanka, highlighting the limited awareness and diagnostic challenges associated with this condition.(3,4)

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We present the third documented case of PPFE in Sri Lanka, occurring in a 76-year-old man with coexisting pectus excavatum, a congenital chest wall deformity. This report aims to contribute to the growing understanding of PPFE, emphasise the potential association between pectus excavatum and upper lobe fibrosis and highlight the importance of recognising PPFE in underreported settings like Sri Lanka.

Case presentation

A 76-year-old Sri Lankan man presented with a three-day history of progressive shortness of breath and a productive cough. He denied fever, constitutional symptoms, haemoptysis or chest pain. There was no history of pulmonary or extra pulmonary tuberculosis, no hospital admissions or known chronic lung disease.

His occupational history revealed that he was a retired farmer with no significant exposure to asbestos, silica dust or industrial fumes. He had not undergone chemotherapy, radiotherapy, or organ transplantation. There was no family history of interstitial lung disease or autoimmune conditions.

He denied symptoms suggestive of connective tissue diseases, such as skin thickening, joint pain, oral ulcers, Reynaud phenomenon or gastrointestinal symptoms. There were no features to suggest scleroderma, rheumatoid arthritis or inflammatory bowel disease.

On examination, the patient appeared emaciated with a body mass index (BMI) of 12 kgm^{-2}, and had a visible pectus excavatum deformity (Figure 1). His respiratory rate was 22 breaths per minute, and auscultation revealed bilateral rhonchi and fine crepitations in both lung fields. Cardiovascular examination showed a pulse rate of 96 bpm and a blood pressure of 100/60 mmHg, with normal heart sounds. No skin changes, synovitis, digital clubbing, or vasculitic signs were noted. Abdominal and neurological examinations were unremarkable.

Laboratory investigations revealed mild normocytic anaemia with haemoglobin of 9.9 mg/dL. Inflammatory markers were within normal levels with a C-reactive protein level of 1.08 mg/dL and ESR 40 mm/1st hour. Autoimmune Screening showed a negative ANA and normal rheumatoid factor (RF). However, anti -Scl-70 was not tested due to limited resources representing a limitation in fully ruling out connective tissue disease.

A chest X-ray showed hyper infiltrated lungs and mild right upper zone haziness (Figure 2). Three sputum samples were negative for acid-fast bacilli, and sputum GeneXpert® testing was also negative. A Mantoux test showed no induration and a 2D echocardiogram revealed normal biventricular function with an ejection fraction of 55% without evidence of pulmonary hypertension.

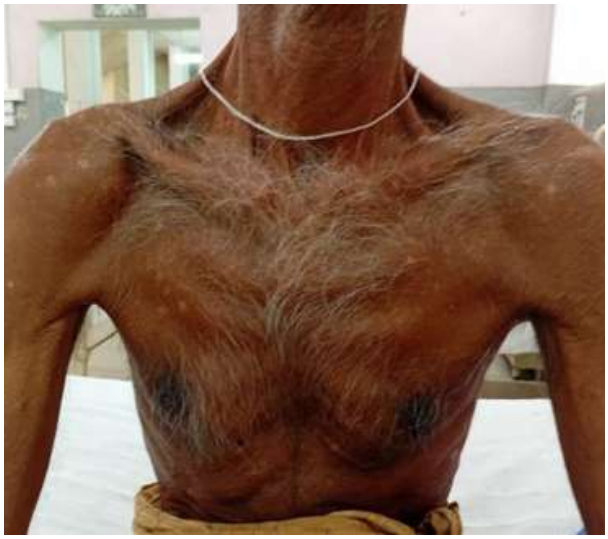

Figure 1. Patient with pectus excavatum

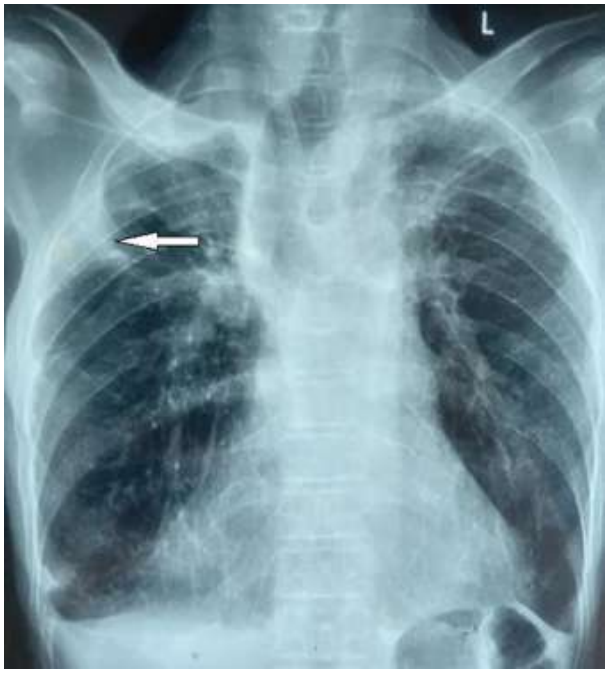

Figure 2. CXR with opacity in right lung

High resolution CT (HRCT) chest was performed due to persistent upper lobe abnormalities. It revealed significant pectus excavatum with a Haller index of five and irregular sub plural fibrotic streaks, upper lobe bronchiectasis, apical pleural thickening and patchy fibrosis in other lung areas, consistent with pleuro-parenchymal fibroelastosis (Figure 3).

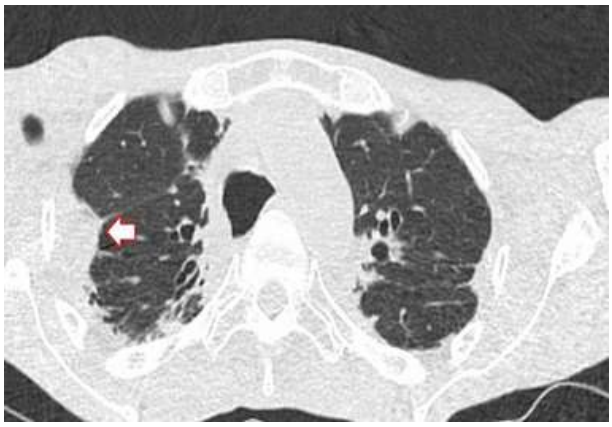

Figure 3. Irregular streaky shadows in the right upper lobe

Lung function testing was attempted but could not be completed due to the patient's limited cooperation. A six-minute walk test did not show desaturation.

Given the radiological findings, lack of evidence for tuberculosis or connective tissue disease, and relevant exposures, a diagnosis of idiopathic pleuro-parenchymal fibroelastosis was made.

Discussion

The coexistence of PPFE and pectus excavatum made our case unique, which gave us a unique opportunity to explore a potential but previously unexamined association between these two conditions. Our literature review identified seven previously reported cases of PPFE where pectus excavatum was noted as an examination finding (Table 1).

The seven reported cases of PPFE with pectus excavatum, non-explicitly explored a potential relationship between the two conditions, suggesting that pectus excavatum has been regarded more as an incidental finding rather than a contributing factor. Interestingly, five of seven cases and our patient were male, indicating a possible male predominance in PPFE cases with pectus excavatum. Additionally, our case and six of those cases, were classified as idiopathic PPFE with no identifiable secondary cause, such as autoimmune disease, chronic infections, or environmental exposures. The repeated documentation of idiopathic PPFE in a patient with pectus excavatum raises the question of whether chest wall abnormalities could play a role in PPFE pathogenesis rather than being coincidental findings.

Only two cases of PPFE have been reported in Sri

Table 1. Previously reported cases of PPFE where pectus excavatum was noted as an examination finding (Abbreviations; HRCT- High-Resolution Computed Tomography)

	Case ID	Age	Sex	PPFE Diagnosis	Pectus excavatum noted	Other associations	Attributed cause for PPFE
1	Yokoyama S et al. (5)	9	female	Clinical+ HRCT	yes	Neuroblastoma	Chemotherapy
2	Ali MS et al. (6)	26	female	Clinical +HRCT+ biopsy	yes	Not mentioned	idiopathic
3	Rasciti E et al. (7)	46	male	Clinical+ HRCT	yes	Not mentioned	idiopathic
4	Türktaş HS et al. (8)	37	male	Clinical +HRCT+ biopsy	yes	Pigeon exposure +	idiopathic
5	Nunes H et al. (9)	59	male	Clinical +HRCT+ biopsy	yes	Not mentioned	idiopathic
6	Faccioli E et al. (10)	51	male	Clinical+ HRCT	yes	Not mentioned	idiopathic
7	Valdivia D et al. (11)	38	male	Clinical+ HRCT	yes	Not mentioned	idiopathic

Lanka.(2, 3) However, neither case described the presence or absence of pectus excavatum as part of the physical examination, nor was a discussion made regarding chest wall anatomy. Therefore, this case not only represents the third reported instance of PPFE in Sri Lanka but also the first to raise the possibility of a link between PPFE and pectus excavatum.

Given that PPFE is a predominant upper lobe disease, the chronic restrictive mechanics, reduced lung expansion, and upper lobe atelectasis associated with pectus excavatum may contribute to fibro elastic changes over time. Structural abnormalities in the thoracic cavity lead to chronic hyperventilation and mechanical stress, potentially triggering fibrotic remodeling in predisposed individuals.(1) Since most reported cases of PPFE with pectus excavatum have been classified as idiopathic, unrecognised mechanical or developmental factors may contribute to disease progression. However, the above findings raise an important clinical question; whether pectus excavatum could be a risk factor for PPFE rather than a coincidental finding?

Since no previous reports have examined this possible link, our case contributes novel insight into an underexplored association. Identifying pectus excavatum in patients with unexplained restrictive lung disease could aid in the early recognition of PPFE, allowing for timely diagnosis and intervention. Further research is needed to determine whether chest wall deformities influence disease development or coexist with PPFE without a causal relationship. Understanding this potential link could lead to better screening strategies, earlier clinical suspicion and improved patient outcomes.

Conclusion

This case, the third reported instance of PPFE in Sri Lanka, highlights a potential but previously unexamined link between PPFE and pectus excavatum. While pectus excavatum has been noted in several PPFE cases globally, its role in disease development remains unclear. Given the idiopathic nature of most reported cases, including ours, it is worth considering whether chest wall abnormalities contribute to PPFE pathogenesis rather than being coincidental findings. Recognising this possible association may raise clinical suspicion and enable earlier diagnosis, particularly in a region where PPFE is often under-recognised.

Declarations

Consent for publication:
The patient has given verbal and written consent to publish his history and images as a case report.

Funding:
None

Conflicts of interest:
The authors report no conflicts of interest.

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CASE REPORT

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Enterococcus faecalis endocarditis presenting as meningitis

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Abstract

Infective endocarditis is a disease with variable presentations and multi-systemic manifestations. It is associated with life-threatening neurological complications including stroke, meningitis, seizures and cerebral and spinal abscesses which arise due to systemic septic embolisation from the infected heart valves. Neurological complications may be the initial presentation of infective endocarditis. We report a case of a patient who presented with fever, confusion and a cardiac murmur following recent orthopaedic surgery of the hand. Although meningitis was the initial working diagnosis, positive blood cultures, echocardiogram and neuroimaging aided the final diagnosis of *Enterococcus faecalis* positive infective endocarditis complicated with meningitis and a haemorrhagic cerebral infarct. He was successfully treated with intravenous antibiotics.

Keywords: infective endocarditis, meningitis, *Enterococcus faecalis*

Introduction

Infective endocarditis is a disease with a myriad of systemic manifestations. It can present as acute or subacute illness resulting in numerous complications and sequelae. Risk factors for infective endocarditis include rheumatic valvular heart disease, congenital heart disease, prosthetic heart valves, instrumentation (central venous catheters, pacemakers, dental procedures, etc.), cardiac and non-cardiac surgery and intravenous drug abuse. Common organisms causing native valve infective endocarditis are *Streptococcus viridans*, *Streptococcus bovis*, *Enterococcus* spp., and *Staphylococcus aureus* while HACEK organisms (*Haemophilus, Actinobacillus, Cardiobacterium, Eikenella* and *Kingella*) are less frequently implicated.(1) Infective endocarditis is associated with many neurological complications including stroke, meningitis, seizures and cerebral and spinal abscesses due to systemic septic embolisation from the infected heart valves.(2) Neurological complications may be the initial presentation of infective endocarditis. We report a case of *Enterococcus faecalis* positive endocarditis presenting as meningitis.

Case presentation

A 55-year-old previously healthy man presented with subacute onset fever, headache and confusion following a K-wire fixation of the right-hand 4th finger a week before. He had a mild generalised headache, but denied photophobia, phonophobia or neck pain. He did not have vomiting, symptoms of systemic infection, limb weakness, fitting episodes or cardiac symptoms. He was febrile, confused and disorientated (GCS 14/15; E4, M6, V4). He had neck

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stiffness but Kernig's sign was negative. Pupils were bilaterally 3 mm and reactive to light. There was no papilloedema. He had right sided sensory inattention and cortical blindness but the rest of the neurological examination was unremarkable. Haemodynamic parameters were stable. A pansystolic murmur radiating to the axilla was heard in the apex.

His full blood count revealed neutrophil leukocytosis, and he had elevated inflammatory markers. His laboratory investigations are summarised below (Table 1). There was mild hyponatraemia which was subsequently corrected with oral salt. The possibility of syndrome of inappropriate ADH secretion (SIADH) was entertained, but it was not considered as the cause for confusion. Osmolality studies were not available to further evaluate hyponatraemia. Blood culture was positive for *Enterococcus faecalis*. Non-contrast CT scan of the brain showed heterogeneously hypodense areas involving multiple vascular territories (Figure 1) while contrast enhanced CT scan revealed a hypodense mass lesion involving left posterior parietal, temporal and occipital regions with multiple haemorrhagic foci and perilesional oedema (Figure 2).

The K-wire was removed and he underwent an MRI scan of the brain, which showed posterior cerebral artery territory infarction with haemorrhagic transformation. There was no evidence of a neoplasm. Cerebrospinal fluid (CSF) analysis which was performed 5 days after commencing antibiotics showed evidence of partially treated bacterial meningitis while the CSF culture yielded no bacterial

Table 1. Summary of haematological and biochemical investigations

Investigation	Result	Normal range
White blood cell count (x10^3/uL)	12.4	4.0-10.0
Neutrophils (x10^3/uL)	9.1	2.0-7.0
Lymphocytes (x10^3/uL)	4.1	0.8-4.0
Haemoglobin (g/dL)	13.2	11.0-16.0
Platelets (x10^3/uL)	254	140-400
C-reactive protein (mg/dL)	109	<6
Erythrocyte sedimentation rate (mm/1st hour)	45	<20
AST (U/L)	31	0-40
ALT (U/L)	16	0-40
Serum sodium (mmol/L)	130	136-145
Serum potassium (mmol/L)	4.2	3.5-5.1
Serum albumin (g/L)	39	35-45
Serum creatinine (umol/L)	75.3	49-115
Cerebrospinal fluid analysis		
White blood cells	7 (90% lymphocytes)	<5
Red blood cells	20	
Protein (mg/dL)	65	<40
Sugar (mg/dL)	85	50-80
Plasma glucose (mg/dL)	130	

growth. Transthoracic echocardiogram revealed an ejection fraction of 60% with mild mitral regurgitation and multiple irregular masses attached to the anterior mitral valve leaflet, which was highly suggestive of mitral valve infective endocarditis. Colonoscopy was negative for bowel pathology.

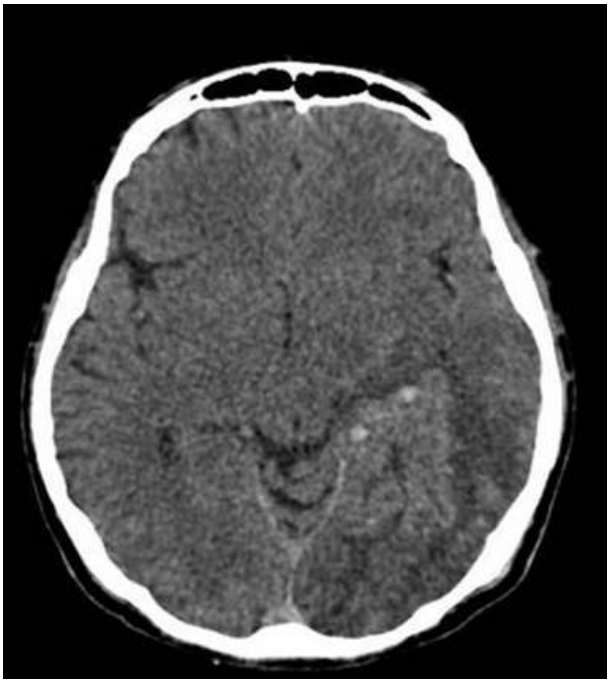

Figure 1. Plain CT scan of brain showing heterogeneously hypodense mass lesion in multiple vascular territories with multiple haemorrhagic foci

A diagnosis of mitral valve infective endocarditis with septic cerebral emboli was made. He was treated with IV vancomycin empirically and once the blood culture report was available, the antibiotic was changed to IV ampicillin. It was continued for 42 days following which his inflammatory markers and blood cultures were negative, and the vegetation size was reduced. He made a marked recovery, but had residual visual impairment.

Discussion

The commonest presentation of subacute infective endocarditis is with a prolonged febrile illness in a patient with risk factors. Detection of a new onset regurgitant cardiac murmur in a febrile patient should raise the suspicion of infective endocarditis. Life-threatening neurological complications such as stroke, intracerebral haemorrhages, mycotic aneurysms, meningitis, toxic encephalopathy, seizures and cerebral and spinal abscesses may complicate the clinical course of infective endocarditis, and carry a poor prognosis with high mortality.(2) Cerebrovascular complications may be symptomatic or silent, occurring in up to 35% and 80% of patients with infective endocarditis respectively.(3) Less commonly, it can have atypical presentations as in the case of our patient. The initial working diagnosis of our patient was meningitis as he presented with fever and confusion. The identification of a cardiac murmur in the background

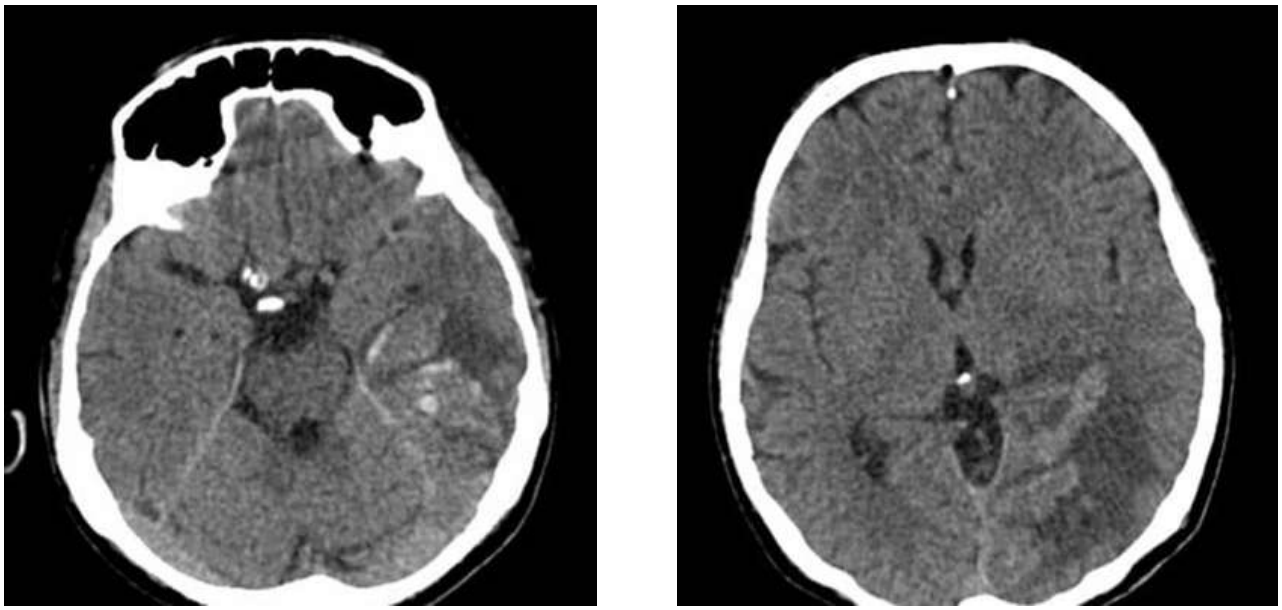

Figure 2. Contrast enhanced CT scan of brain showing hypodense mass lesion involving left posterior parietal, temporal and occipital regions with multiple haemorrhagic foci and perilesional oedema

of neurological symptoms prompted us to look for infective endocarditis with further investigations. The subsequent development of other neurological symptoms such as cortical blindness resulted in neuroimaging which revealed a haemorrhagic cerebral infarct due to systemic embolisation into the posterior cerebral circulation; another embolic complication of endocarditis. Cortical blindness was the only residual neurological deficit that persisted in our patient. Ophthalmology opinion was sought and it was concluded as having permanent damage to visual cortex, which carries a poor prognosis.

Meningitis, primarily due to Enterococcus spp. infection is very rare, but it is a common organism causing infective endocarditis. Although meningitis as a complication of endocarditis is well known, only a few cases of Enterococcus endocarditis complicated with meningitis have been reported, highlighting the rarity of the case.(4) The synergistic combination of penicillin and aminoglycosides is the cornerstone of treatment of Enterococcus infections. Generally, a prolonged course of antibiotics (6 to 8 weeks) is needed for successful treatment. However, the emergence of multi-drug-resistant strains pose a challenge.(5)

Conclusion

The clinician should have a high degree of suspicion for infective endocarditis in high-risk patients with atypical presentations. The possibility of infective endocarditis should be entertained in any patient with fever and neurological symptoms such as stroke or meningitis. Early diagnosis and treatment ensure a favourable prognosis. It is imperative to consider early multidisciplinary collaboration in complex and atypical presentations to optimise the patient outcome.

Declarations

Author contributions:
All authors contributed to the conceptualization and design of the study. All authors contributed to management of the patient and writing the manuscript. All authors read and approved the final manuscript.

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The authors declare that they have no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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CASE REPORT

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Fatal idiopathic giant cell myocarditis in a young male: a diagnostic and therapeutic dilemma in a resource-limited setting

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Abstract

Idiopathic giant cell myocarditis (IGCM) is a rare and rapidly progressive form of myocarditis characterised by severe myocardial inflammation, rapid deterioration and high mortality without timely intervention. We report a fatal case of a 15-year-old boy who presented with worsening dyspnoea and signs of congestive cardiac failure which rapidly progressed to cardiogenic shock. Extensive investigations including imaging, biopsies, viral and autoimmune panels excluded other potential aetiologies such as infiltrative cardiomyopathies, cardiac sarcoidosis, lymphocytic myocarditis and lymphomas. Due to the unavailability of confirmatory endomyocardial biopsy, a clinical diagnosis of IGCM was made, and immunosuppressive therapy was initiated. Despite aggressive management, the patient succumbed to the disease due to refractory heart failure and fatal arrhythmia. This case highlights the diagnostic and therapeutic challenges of IGCM, particularly in resource-limited settings, and the importance of considering IGCM in cases of fulminant myocarditis with rapid progression. Early diagnosis and advanced modalities of treatment are crucial to improve outcomes in this life-threatening condition.

Keywords: idiopathic giant cell myocarditis, fulminant myocarditis

Introduction

Rapidly progressing myocarditis/ fulminant myocarditis, is characterised by its swift onset and severe consequences, often leading to cardiogenic shock with high mortality. Fulminant myocarditis is defined as a severe inflammation of the cardiomyocytes, leading to rapid deterioration of cardiac function due to multiple aetiologies. The condition is marked by significant systolic and diastolic dysfunction, arrhythmias and an increased risk of sudden cardiac death.(1)

Giant-cell myocarditis is a rare and frequently lethal disorder of young adults. The affected often succumb due to heart failure and ventricular arrhythmia if cardiac transplantation is not performed.(2) Here we discuss the differentials that should be considered in fulminant myocarditis along with therapeutic strategies for patients with idiopathic giant cell myocarditis (IGCM).

Case presentation

A 15-year-old boy, presented with worsening dyspnoea over 1 week. He was functioning well up until the prior week when he started feeling exhausted with mild exertion. Then he gradually developed worsening abdominal distension and abdominal discomfort which brought him to the local hospital where he was suspected to have congestive

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heart failure of unknown aetiology. He did not have a history of fever, sore-throat, cough, cold, constitutional symptoms, rashes, arthritis, diarrhoea, dry eyes, dry mouth, lymph node enlargement or any other significant problem. He had a history of recurrent tonsillitis with bilateral parotitis since the age of 4 and had undergone tonsillectomy at the age of 8 years. He had no history of mumps and had received immunisation against it. However, he continued to have bilaterally enlarged parotids and was asymptomatic otherwise.

On examination the patient was tachypnoeic (rate of 32/minute) and tachycardic (120 bpm) with a saturation of 96% on room air. He had low volume pulses without pulse deficits or delays. There was no bilateral lower limb oedema. His blood pressure was normal and jugular venous pressure was elevated. He had a deviated-cardiac apex (3 finger breadths away from midclavicular line on 7th intercostal space) which was thrusting in nature, along with a parasternal heave, S3 gallop rhythm and loud P2. Abdominal examination revealed a moderate amount of free fluid with hepatic tenderness. No organomegaly or lymphadenopathy was noted. On respiratory examination, breath sounds were mildly reduced with stony dullness on percussion and reduced vocal fremitus on the right side.

Basic investigations were performed. ECG showed LBBB (Figure 1) and CXR PA (Figure 2) showed cardiomegaly with right sided pleural effusion.

The patient was found to be in severe congestive heart failure with a right-sided pleural effusion, congestive hepatopathy with moderate ascites and type 2 respiratory failure with haemodynamic instability. He was electively intubated and transferred for ICU management. Over time his cardiac function rapidly deteriorated. It worsened to the point of needing 4 inotropes in maximum tolerated doses to maintain a mean arterial pressure of 65 mmHg. Repeated 2D echocardiograms (Figure 3) revealed worsening heart failure with progressive ventricular dilatation and reduction in the ejection fraction. The investigations performed are listed in Table 1.Rapidly worsening myocarditis, cardiac function and severe ongoing cardiac myocyte necrosis (very high and rising titers of troponin I, LDH, CK) could only be explained by a clinical picture of IGCM. Therefore, a working clinical diagnosis of IGCM was entertained.Lymphocytic myocarditis, isolated cardiac sarcoidosis and infiltrative cardiomyopathies with malignancies including lymphomas which can mimic IGCM were duly excluded. The confirmatory endomyocardial biopsy and cardiac MRI were not performed due to unavailability. The patient was started on high dose intravenous methylprednisolone and rituximab along with supportive management. Within the ICU stay, while on ventilation he developed a right sided spontaneous pneumothorax following which an IC tube was inserted. Clinical status deteriorated further culminating in fatal arrhythmia and cardiac arrest.

Discussion

Our case describes a rapidly progressive and fatal case of probable idiopathic giant cell myocarditis.

Our patient deteriorated rapidly over one week due to high severity of the disease. This case posed a critical diagnostic and management dilemma throughout the course of the illness and observable delay in initiating high grade immunosuppression due to inaccessibility to confirmatory investigations like cardiac MRI and endomyocardial biopsy in a

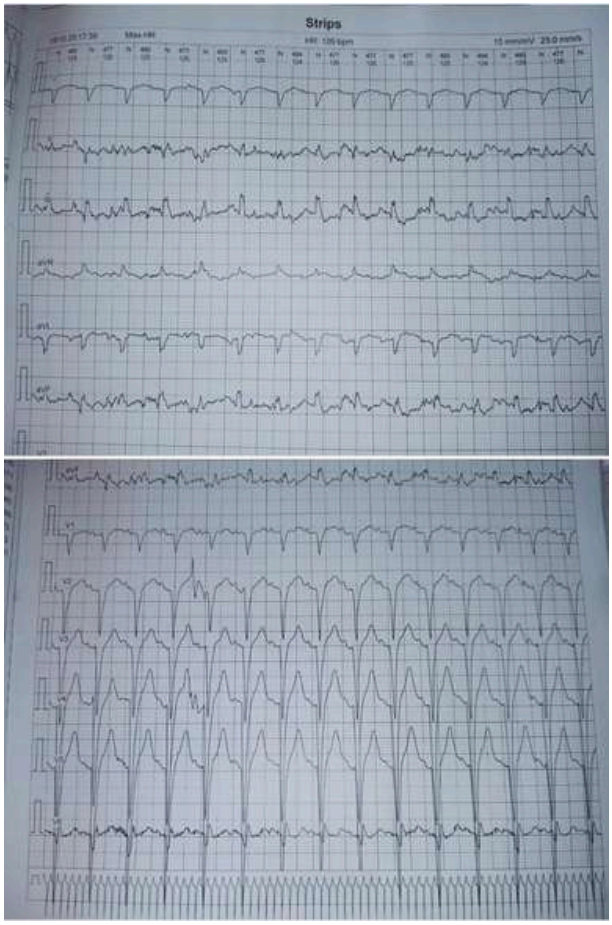

Figure 1. ECG with left bundle branch block

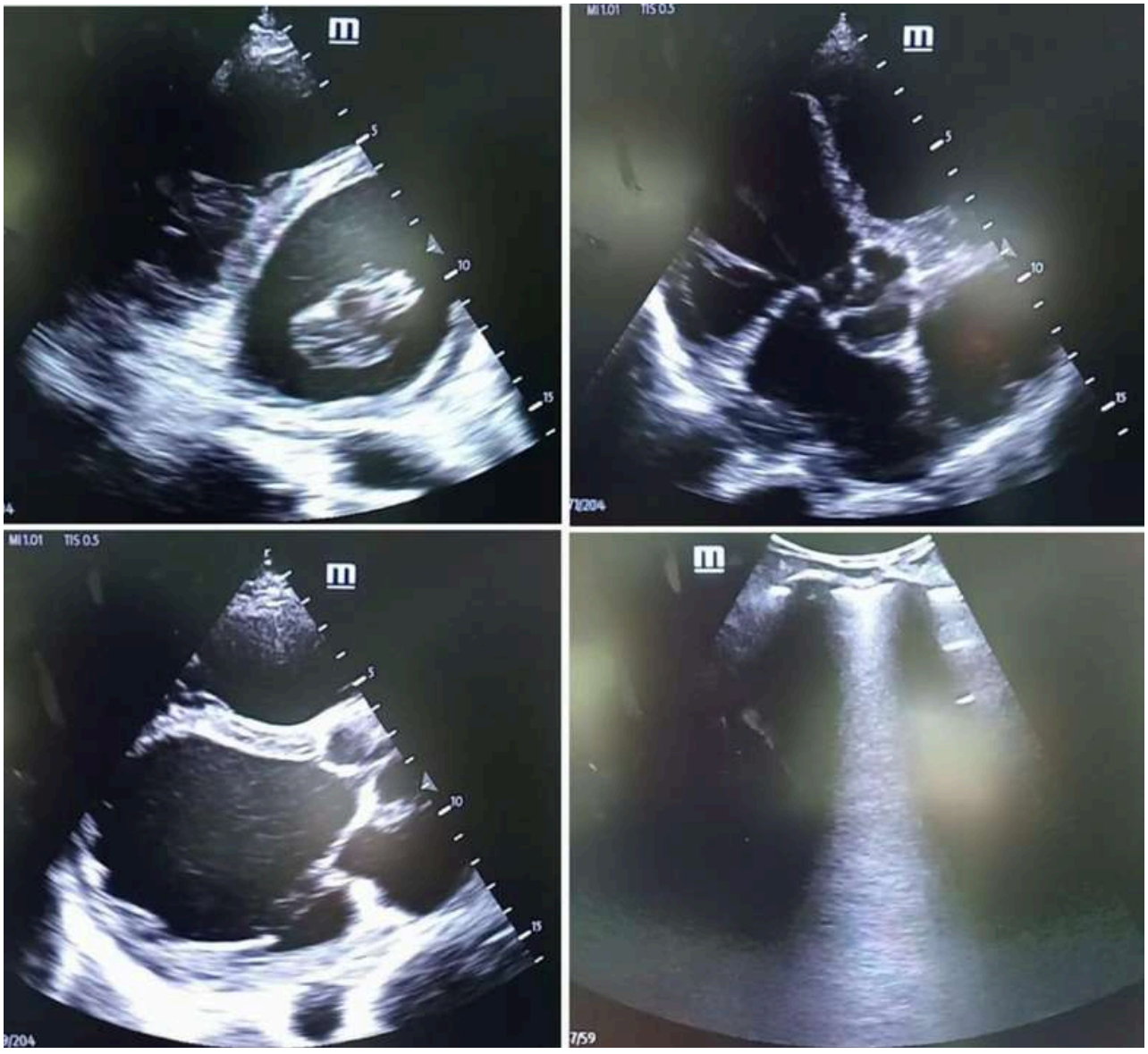

Figure 2. 2D echo views (dilated LV/LA) & B profile

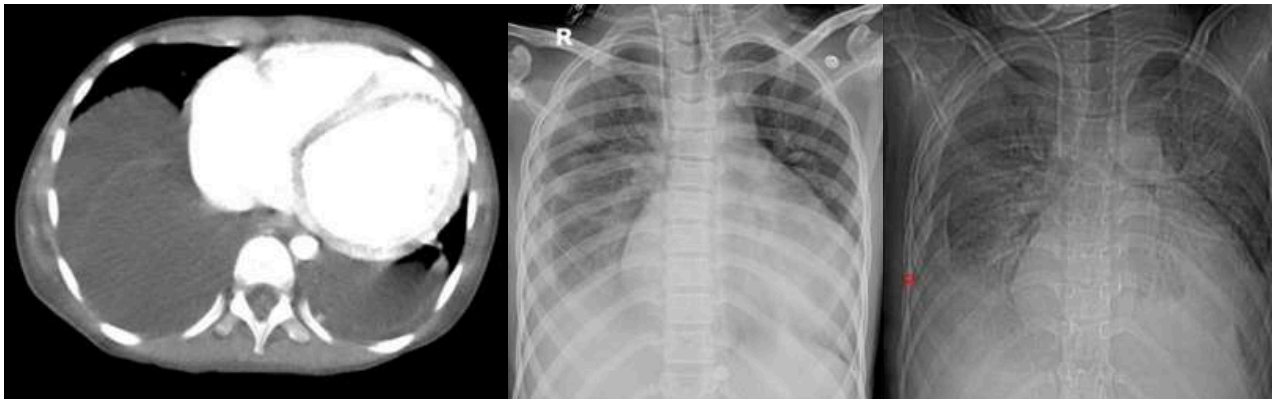

Figure 3. Chest X-ray showing dilated cardiac shadow and HRCT showing dilated thinned cardiac chambers

resource-poor setting like Sri Lanka. Diagnosing IGCM by exclusion of other causes was a significant challenge.

With expert opinion, several differentials were considered including giant cell myocarditis, lymphocytic myocarditis due to viral or autoimmune causes, isolated cardiac sarcoidosis, infiltrative cardiomyopathies (e.g., haemochromatosis and amyloidosis) and lymphoma-like malignancy-associated cardiomyopathies.

Based on the available extensive investigation panels (biochemical evidence of ongoing severe cardiac myocyte necrosis, LBBB on ECG, rapidly worsening cardiac function in serial echocardiograms with increasing inotrope dependency and dilated cardiac chambers, negative multiple biopsies for lymphoma, malignancies, infiltrative diseases and infectious agents, negative viral and autoimmune panel, absence of other systemic manifestations of a plausible multisystemic disorder) and the clinical course, a diagnosis of IGCM was made even in the absence of endomyocardial biopsy and the patient was treated accordingly with immunosuppression.

Myocarditis presents in a spectrum from being subclinical to sudden death. Fatal myocarditis, frequently associated with unexpected and acute onset death, has an approximate incidence of 0.15 cases per 100,000 individuals in the population. This condition is most prevalent among infants and young adults, though it can occur in any age group.(3) Autopsy studies reveal that diffuse myocarditis accounts for less than 2% of sudden deaths in adults. (3) Clinically, myocarditis typically manifests as heart failure that develops and spans over days to weeks. (2,3)

IGCM is characterised by rapid progression and significant inflammatory infiltrates in the myocardium, often leading to fatal outcomes within weeks to months of symptom onset.(2) IGCM typically presents with symptoms of acute heart failure and arrhythmias.

Diagnosing IGCM can be complex due to the absence of specific macroscopic changes in the heart. Histological examination is crucial, yet it may not always correlate with clinical severity, complicating the diagnosis.(4) Autopsy findings often reveal an enlarged heart with inflammatory infiltrates, including lymphocytes and multinucleated giant cells. (5,6) The final outcomes of IGCM are usually undesirable, with many patients succumbing within weeks to months without immunosuppressive therapy and cardiac transplantation.(2,4)

Early recognition and intervention are critical, as the condition can mimic other forms of myocarditis, leading to misdiagnosis. Therefore, we discuss differentiating the mimics, such as isolated cardiac sarcoidosis, lymphocytic myocarditis and infiltrative cardiomyopathies, based on available literature.

Lymphocytic myocarditis typically presents with symptoms of heart failure, chest pain, and arrhythmias, following a viral illness. ECG commonly shows non-specific ST-segment changes and arrhythmias. Echocardiograms might show left ventricular dysfunction and regional wall motion abnormalities along with elevated troponin levels. Causative viral genome is usually detected.(2,7) The most common aetiology includes viruses such as SARS-CoV-2 and influenza A, which can trigger severe inflammatory responses in the myocardium.(8,9) While lymphocytic myocarditis is often viral in origin and may resolve with supportive management, giant cell myocarditis is more aggressive and frequently requires urgent intervention, including heart transplantation.(2)

In isolated cardiac sarcoidosis (CS) progression is usually chronic with arrhythmias and conduction blocks (e.g., AV block). Cardiac MRI and FDG-PET are critical diagnostic tools, revealing patchy enhancement and inflammation. However, similar patterns in both conditions make differentiation challenging. GCM often exhibits more extensive right ventricular involvement in some cases.(10,11) Echocardiography cannot reliably distinguish between them. Non-caseating granulomas are the histological hallmark of CS, but the presence of significant necrosis in GCM is disproportionate to the granulomatous inflammation seen in CS. GCM typically presents with higher levels of cardiac biomarkers such as troponins and natriuretic peptides, unlike CS.(12-14)

In infiltrative myocarditis, symptoms can be more insidious, broader in range and less acute, with less severe heart failure and fewer arrhythmias, along with less pronounced elevations in cardiac biomarkers. ECG changes are often less specific and may not indicate acute ischaemia. Low-voltage QRS complexes are seen, but this is not a uniform finding. Echocardiogram findings may be less severe, with preserved ejection fraction in some cases. While GCM is a severe and rapidly progressive condition requiring aggressive treatment, infiltrative types of

Table 1. Investigations (normal values mentioned within brackets)

Investigations	Results
Haematology	Hb: 10.1 g/dL (13.0–17.0 g/dL for males) MCHC: 32 g/dL (32–36 g/dL) MCH: 27 pg (27–33 pg) MCV: 85.6 fL (80–100 fL) RDW-CW: 13.7% (11.5–14.5%)HCT: 25.9% (40–50%) Platelets: 87 × 10^9/L (150–400 × 10^9/L) WBC: 13.88 × 10^9/L (4.0–11.0 × 10^9/L) [(N): 78% (L): 13% (M): 4% (E): 0.1%] Reticulocyte count: 2.1 % Direct Coombs test: Negative
Liver function tests	AST: 157 → 2220 IU/L (10–40 IU/L) ALT: 290 → 2114 IU/L (7–56 IU/L) Total Bilirubin: 39 µmol/L (3–17 µmol/L) Direct Bilirubin: 26.7 µmol/L (<3.4 µmol/L) Alkaline Phosphatase (ALP): 90 IU/L (44–147 IU/L) Gamma-GT: 70 IU/L (8–61 IU/L) Total Protein: 5.63 g/dL (6.0–8.3 g/dL) Albumin: 2.9 g/dL (3.5–5.0 g/dL) PT/INR: 1.1 APTT: 32s
Inflammatory markers	CRP: 0.5 → 5.0 mg/L (<5 mg/L) ESR: 12 mm/1st hour (<20 mm/1st hour) Procalcitonin: 0.05 (Sepsis unlikely)
Renal function tests, electrolytes & pancreatic enzymes	(Na^+): 141 mmol/L (135–145 mmol/L) (K^+): 4.5 mmol/L (3.5–5.0 mmol/L) (Ca^{2+}): 1.8 mmol/L (2.1–2.6 mmol/L) (PO_4^{3-}): 1.1 mmol/L (0.8–1.4 mmol/L) (Mg^{2+}): 0.8 mmol/L (0.7–1.1 mmol/L) Serum creatinine: 68.2 µmol/L (62–106 µmol/L) Blood urea: 50.8 mg/dL (10–50 mg/dL) Serum amylase: 93 IU/L (30–110 IU/L)
Arterial blood gas (ABG) on admission to ICU	pH: 6.7 (7.35–7.45) PCO_2: 58.2 mmHg (35–45 mmHg) PO_2: 45 mmHg (80–100 mmHg) HCO_3^-: 10.0 mmol/L (22–26 mmol/L) Lactate: 11.1 mmol/L (0.5–2.2 mmol/L)
Cardiac markers	Troponin: 678 → 3700 ng/L (<14 ng/L) Creatine kinase (CK): 2237 IU/L (38–174 IU/L) LDH: 2600 IU/L (140–280 IU/L)

Table 1. Investigations (normal values mentioned within brackets) continued...

Investigations	Results
Lipid profile, endocrinology, tumour markers and other investigations	Serum Ferritin: 42 µg/L (30–400 µg/L) Triglyceride: 154 mg/dL (<150 mg/dL) LDL: 39 mg/dL (<100 mg/dL) HDL: 31 mg/dL (Normal: >40 mg/dL) Total Cholesterol: 83 mg/dL (<200 mg/dL) FBS (Fasting Glucose): 116 mg/dL (<100 mg/dL) Serum Cortisol (9 AM): 1330 nmol/L (171–536 nmol/L) TSH: 1.266 mIU/L (0.4–4.0 mIU/L) Beta-HCG: 8.28 mIU/mL (<5.5 mIU/mL) Alpha-Fetoprotein: 1.7 IU/mL (<7.1 IU/mL)
Peripheral blood picture/smear	Normochromic normochromic + hypochromic microcytic cells, toxic neutrophil changes, mild thrombocytopenia, otherwise normal
Histopathological investigations	BM Aspiration Biopsy: Reactive bone marrow, no evidence of infiltration or hematological malignancies, PAS Stain negative. Trephine Biopsy: Reactive bone marrow Lymph node biospy: Reactive lymph nodes, no evidence of infiltration Parotid gland FNAC: No abnormal cells noted Parotid gland biopsy: No evidence of infiltration, chronic parotitis likely. No granulomas seen. Abdominal fat pad biopsy: Congo red stain negative.
Imaging	HRCT: bilateral axillary lymphadenopathy, congestive cardiomyopathy with secondary pulmonary edema and evidence of pulmonary hypertension, gross ascites noted. No other significant mediastinal or intraabdominal lymph nodes seen. USS abdomen: gross ascites, liver & spleen normal in architecture, bowel wall edema noted. USS parotid: chronic sialadenitis noted
Cardiac assessment	Inward Holter: Normal study. No premature ventricular complexes noted. 2D Echo: Severe global hypokinesia with EF 30%, Dilated LA & LV, RA/RV not dilated, TRPG 60 (Severe pulmonary hypertension, Grade 2/3 MR & TR, No pericardial effusion, Repeat 2D Echo: EF 20% with severely impaired Biventricular systolic dysfunction

Table 1. Investigations (normal values mentioned within brackets) continued...

Investigations	Results
Viral panel	SARS Corona Virus RNA: Negative Influenza A & B RNA: Negative Adenovirus PCR: Negative Enterovirus PCR: Negative CMV IgM, IgG, EBV IgM, IgG, NS1 Ag, Dengue IgM, IgG, Mumps IgM, IgG: Negative HIV Ag: Negative HIV 1 & 2 Antibodies: Negative Hep Bsag, Hep A IgM, Hep C IgM, IgG: Negative
Autoimmune panel	ANA: Negative Anti ds DNA: Negative C3/C4 levels: Normal Rheumatoid Factor: Negative
Other investigations	Pleural effusion aspirate: transudative, VDRL: Negative Leptospiral IgM, IgG: Negative Mycoplasma Ag: Negative UFR [Protein: 1+, pus cells: few, red cells: Nil] Serum protein electrophoresis: Normal Urine Bence Jones proteins: Negative Serum Free Light Chain Assay: Normal Kappa/lambda ratio

myocarditis might reveal a broader spectrum of clinical presentations and less acute findings.(15)

Diffuse lymphoma involving the cardiac muscles is increasingly reported. Cardiac involvement has been described in Hodgkin's and non-Hodgkin's lymphoma in various cases. Extranodal lymphomas are widely recognised in conditions with impaired immunity such as HIV/AIDS or immunosuppression post transplantation. This was excluded clinically and by multiple negative tissue biopsies.(16)

Current treatment modalities for IGCM primarily focus on immunosuppressive therapies, which have shown significant efficacy in managing this condition. Corticosteroids such as prednisone and methylprednisolone are commonly used, with some cases demonstrating complete remission with monotherapy.(17) Combination therapy of corticosteroids with agents like rituximab, cyclosporine, and tacrolimus enhances treatment efficacy, leading to improved transplant-free survival rates.(18,19) Emerging evidence suggests that rabbit anti-thymocyte globulin (rATG) might improve the morbidity and mortality in severe GCM cases, and its use may be warranted in preventing the necessity for heart transplantation. Patients treated with regimes consisting of multiple immunosuppressive agents including rATG, showed significant recovery and remained transplant-free for extended periods.(20) However, the response to immunosuppression is variable, and cardiac transplantation is often necessary, although there is a risk of disease recurrence in the graft.(2)

Conclusion

This case highlights the diagnostic and therapeutic challenges of managing IGCM, a rare and rapidly fatal condition in a resource-limited setting. Despite the absence of a definitive diagnosis through endomyocardial biopsy, a meticulous clinical approach and exclusion of potential mimics guided our diagnosis and management with an observable delay.

Despite the aggressive medical management, due to the high severity of the illness and unavailability of emergency cardiac transplantation facilities in the country, the patient succumbed. This case signifies the critical need for early recognition, extensive diagnostic investigations, and aggressive treatment modalities, including immunosuppression and cardiac transplantation to improve outcomes in this devastating disease.

Declarations

Author contributions:
Conceptualization: Dr Risly NMM; case management: Dr Risly NMM, Dr Fonseka PD, Dr wijekoon VD, Dr N Athauda, Manuscript; drafting: Dr Risly NMM, Dr Sahana JF; critical review and final approval:Dr N Athauda, Dr Jayasinghe IK

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The authors declare no conflicts of interest.

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Consent and ethical consideration statement:
Informed consent was obtained from the patient for the publication of this case report and any accompanying images. All ethical considerations were adhered to in accordance with institutional guidelines.

Data availability statement:
The data supporting the findings of this case report are available from the corresponding author, upon reasonable request. Due to patient confidentiality and privacy concerns, detailed data may be shared in a de-identified format where appropriate and with relevant ethical approval.

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CASE REPORT

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Bilateral Moyamoya disease resulting in anterior circulation stroke: first case report in Sri Lanka

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Abstract

Bilateral Moyamoya disease is a rare vascular cause of young onset ischaemic stroke, characterised by progressive narrowing of the cerebral vessels. We present a case of a 28-year-old Sri Lankan man with a unilateral headache presenting with sudden onset of expressive aphasia without face, arm or leg weakness. Magnetic resonance imaging revealed evidence of multiple infarctions involving both left and right middle cerebral territories. The diagnosis was made based on the magnetic resonance angiography, which demonstrated the absence of supra clinoid segments of bilateral middle cerebral arteries (MCA) and the presence of significant collateral formation which are typical of Moyamoya disease. He was commenced on low dose aspirin, high intensity statin and speech therapy. He had a favourable outcome. Although a genetic component is commonly associated with Moyamoya disease, no such family history was identified and immunological, infectious, haematological, vascular, or congenital syndromes were not found. This is the first case of bilateral Moyamoya disease reported from Sri Lanka.

Keywords: Moyamoya disease, ischaemic stroke

Introduction

Moyamoya is an uncommon progressive cerebrovascular condition with female preponderance (female to male ratio around 2:1) that may lead to ischaemic stroke or intracerebral haemorrhage in children and adults.(1, 2) Moyamoya disease (MMD) is more prevalent in East Asian countries. The highest incidence is among the Japanese population with a positive family history compared to other populations, which is around 10 to 15 percent of cases. This strongly suggests a genetic aetiology.(3) There are many causative or syndromic conditions associated with MMD. The gold standard diagnostic investigation is cerebral angiography. The steno-occlusive areas in MMD commonly affect the brain bilaterally, but there have been documented cases of unilateral involvement as well.(2, 4) The index case is a young Sri Lankan man who presented with a unilateral headache, later developed ischaemic infarcts involving both middle cerebral artery (MCA) territories, and eventually diagnosed with bilateral MMD based on radiographic evidence.

Case presentation

A 28-year-old man presented to the emergency department of a teaching hospital, with isolated expressive aphasia upon awakening. He did not have a history of psychosis, mood disorder, substance abuse or trauma to the head.

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Two weeks prior to admission, he had been evaluated for headache and bilateral hand numbness which had lasted for three weeks. The headache had been right sided, gradual in onset, continuous, aching in nature and worse at night. The headache was not associated with vomiting, aura, photophobia and phonophobia and responded to analgesics. There was no weakness associated with bilateral hand numbness. He had been investigated with brain imaging (CT brain, non-contrast) and blood investigations which were reported to be normal and discharged when his symptoms improved. He did not have a history suggestive of cardiac illness, arrhythmias, features of connective tissue disorders, hypoglycemic episodes, hyperviscosity symptoms, amaurosis fugax, blood transfusion, sexual promiscuity or recreational drug abuse. He also denied any family history of vascular, haematological or connective tissue disorders.

His general examination was normal. His GCS was 11/15 with expressive aphasia (he was able to understand the words, respond back to commands and able to communicate with others by texting or writing notes). The rest of the neurological and other systemic examinations were unremarkable. Table 1 summarises the investigations performed.

Noncontrast computed tomography revealed a dense vessel in the left temporal region and an infarction in the temporo-parietal region. Contrast enhanced cerebral angiogram revealed a short segment narrowing in M1 segment of left MCA. However, the M2 segment and distal branches of the left MCA appeared normal. Smaller diameter of the supraclinoid part of the right MCA favoured a hypoplastic right internal carotid artery (ICA) in the supraclinoid region. The right MCA and anterior cerebral artery (ACA) appeared normal. There were no abnormalities in the posterior circulation. Magnetic resonance imaging (MRI) of the brain revealed multiple infarcts involving both left and right middle cerebral territories (a large infarction involving the left insular cortex, lentiform nucleus, cortical and subcortical regions of the left sylvian fissure and small infarcts seen in the corona radiata of the same side and a few similar infarcts were seen in the right lentiform nucleus and corona radiata) (Figure1). Magnetic resonance arteriogram (MRA) revealed absent supraclinoid segments of the right ICA, right MCA and the left ICA with a reformed left MCA. Absence of bilateral supraclinoid ICA with abnormal revascularisation in the region were compatible with Moyamoya disease (Figure 2).

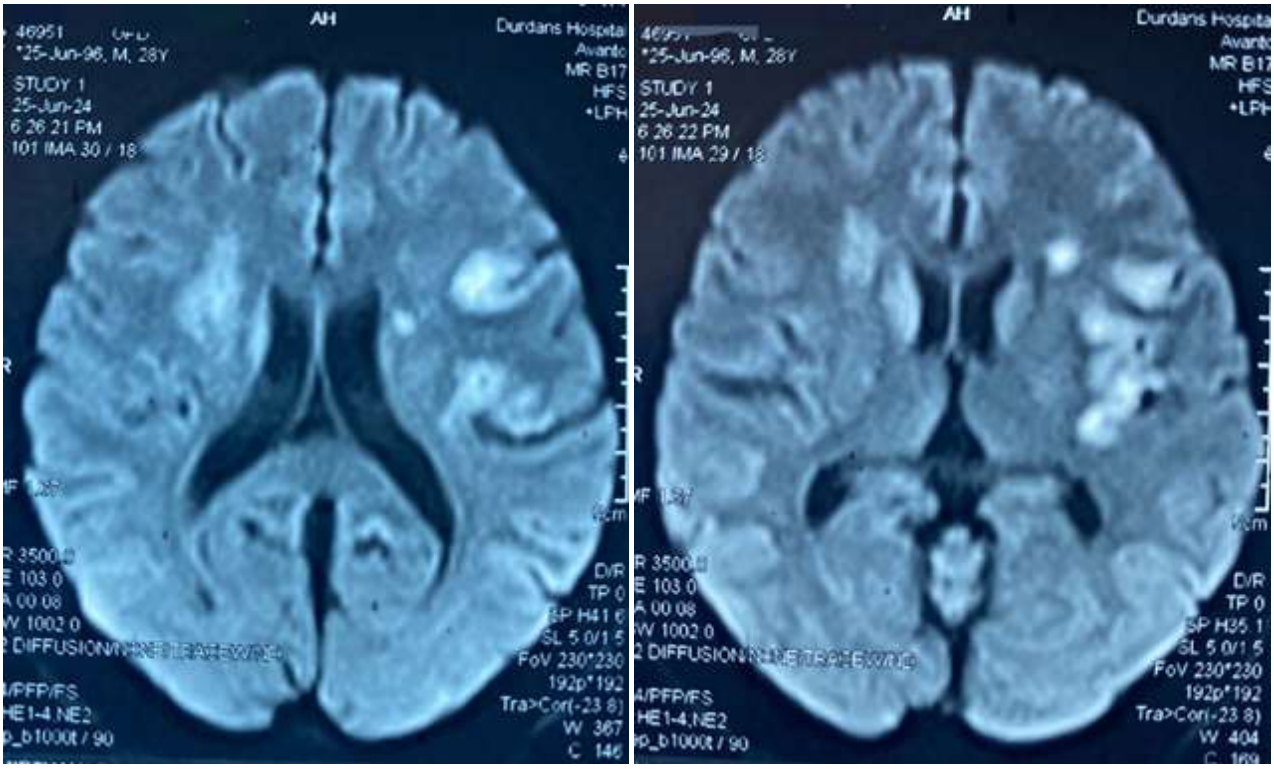

Figure 1. Magnetic resonance imaging revealed multiple infarcts involving both left and right middle cerebral territories

Table 1. Summary of investigations

Investigation (unit)	Patient parameter	Reference value
White blood cell count (×10^3/uL)	12	4-11
Haemoglobin (g/dL)	15.4	11.0-15.0
Mean corpuscular volume (fL)	84	80.0-100.0
Platelet count (×10^3/mm^3)	353	150-450
Blood picture	No abnormal cell lines	
Erythrocyte sedimentation rate (mm/1st hour)	10	<10
C-reactive protein (mg/dL)	3	<6
eGFR (mL/kg/1.73m^2)	127	
Serum sodium (mmol/L)	138	136-145
Serum potassium (mmol/L)	3.9	3.5-5.1
Serum total calcium (mmol/L)	2.24	2.12-2.62
Aspartate transaminase (U/L)	32	15-37
Alanine transaminase (U/L)	49	12-78
Serum bilirubin (mg/dL)	0.7	0.2-0.8
Alkaline phosphatase (U/L)	50	46-116
Serum albumin (g/L)	42	34-50
Serum globulin (g/L)	35	22-48
International normalised ratio	1.07	1.08
Activated partial thromboplastin time (sec)	31.5	27-42
ANA (AU/mL)	27	0-40
Urine full report	Normal	
Lupus anticoagulant screen(ratio)	1.17	0.8-1.2
Cardiolipin-IgM antibody (MPL U/mL)	1.3	<5
Cardiolipin-IgG antibody (GPL U/mL)	2.5	<10
Beta 2 glycoprotein-IgM antibody (U/mL)	4.2	<10
Beta 2 glycoprotein-IgG antibody (U/mL)	5.8	<10
Fasting blood sugar (mg/dL)	104	<126
HbA1c (%)	5.4	
24-hour Holter monitoring	Normal	

Table 1. Summary of investigations (continued...)

Investigation (unit)	Patient parameter	Reference value
Transthoracic echocardiogram	Normal systolic and diastolic function with no intra-atrial septal abnormality and no evidence of intracardiac thrombus	
Chest radiograph	Normal	
Doppler scan of the neck vessels	No evidence of a thrombus/plaque	
Total cholesterol (mg/dL)	188	
Triglycerides (mg/dL)	89	
HDL-C (mg/dL)	46	
LDL-C (mg/dL)	124	
VLDL-C (mg/dL)	18	
CHO/HDL-C ratio	4.1	
TSH (uIU/mL)	1.108	0.4-4.0

HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; VLDL-C: Very-low-density lipoprotein cholesterol; CHO/HDL-C Ratio: Total cholesterol to HDL ratio; TSH: Thyroid-stimulating hormone

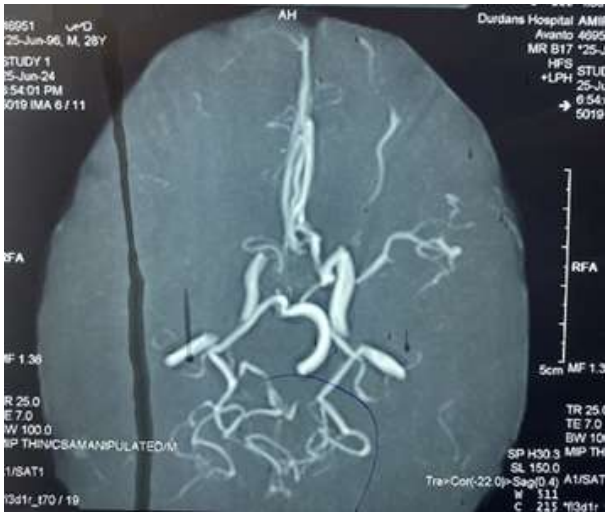

Figure 1. Magnetic resonance arteriogram revealed absence of bilateral supraclinoid middle cerebral arteries and the presence of significant collateral formation

He was observed for the preceding few days and subjected to specialised investigations. He was discharged with oral aspirin 75 mg nocte and atorvastatin 40 mg nocte and a schedule for speech therapy. During the immediate follow-up clinic visit, his speech showed mild improvement with the ability to name objects and form simple sentences. The patient currently shows appreciable recovery.

Discussion

Moyamoya disease is an uncommon aetiology for ischaemic stroke and is characterised by progressive narrowing of large intracranial arteries associated with formation of small vessel collaterals. The term "moyamoya" is a Japanese word which means hazy, like a puff of smoke in the air and has been coined because of the characteristic smoky appearance produced by small vessel collaterals on angiography.

According to the available literature, the aetiology of MMD is closely linked to genetic factors, but the actual aetiology is not known. However, no familial inheritance pattern has been discovered, which is similar to our case. There are many causative or syndromic conditions associated with this disease including diseases mainly affecting arteries around the circle of Willis such as cranial trauma, brain

tumours, meningitis, atherosclerosis, radiation therapy to the base of the brain, other viral or bacterial infections (e.g., leptospirosis, human immunodeficiency virus [HIV] and Cutibacterium acnes) and haematological conditions such as sickle cell disease, Fanconi anaemia, homocystinuria and hyperhomocysteinaemia, factor XII deficiency, essential thrombocythemia and protein S deficiency. Additionally autoimmune conditions like systemic lupus erythematosus, polyarteritis nodosa and post infectious vasculopathy, Graves' disease; anti phospholipid syndrome, pulmonary sarcoidosis, and type 1 diabetes mellitus (DM), are also found to have associations with MMD. There are reported cases of MMD in patients with congenital syndromes such as Alagille syndrome, Down syndrome, Marfan syndrome, neurofibromatosis type 1, Prader-Willi syndrome, pseudo xanthoma elasticum and tuberous sclerosis.(1,3) No such associations were observed in the index case.

The expression of Moyamoya and the age at presentation are influenced by regional and ethnic differences which result in varying clinical presentations.(3) MMD can present as ischaemic stroke, transient ischaemic attack, intra cerebral, intra ventricular and subarachnoid haemorrhage, seizures and headache and other uncommon manifestations like dystonia, chorea or dyskinesia. It can be found incidentally in asymptomatic patients as well. Our patient, initially presented with a unilateral headache which is common in patients with Moyamoya. The commonly associated headache phenotype is Migraine. However, other headaches such as tension-type headache and cluster headache have also been reported. Headache can be due to irritation of the meningeal nociceptive fibers expanding to neovascularisation.(1,3)

MMD commonly presents as ischaemic strokes and transient ischaemic attacks. In the United States a retrospective analysis of a case series revealed, among the 31 adults with MMD who presented with ischaemic symptoms, stroke was prevalent in 61% where border-zone pattern of infarction was the predominant pattern.(5) Hemiparesis or speech impairment predominated ischaemic symptoms, reflecting the predilection for stenosis of the anterior cerebral circulation. It is worth noting that our patient had expressive aphasia with no weakness and was found to have multiple infarcts involving both MCA territories. Though MMD presents commonly with ischaemic symptoms, intracerebral haemorrhagic complications of MMD contribute to a significant clinical burden which is more common in adults than children. Ischaemic damage to the brain in MMD can infrequently manifest as seizures.

The characteristic angiographic appearances of bilateral stenoses affecting the distal ICA (or other vessels of the proximal circle of Willis) along with the presence of prominent collateral vessels are the identified features for diagnosis of MMD. Additionally, digital subtraction angiography is typically required to guide management. Considering the patient's clinical presentation, lack of traditional risk factors for stroke, neurological examination findings, radiological findings and exclusion of other possible differential diagnoses according to the 2021 diagnostic criteria, the diagnosis of Moyamoya disease is justified. Early recognition of this uncommon cerebrovascular condition is crucial for appropriate management and timely intervention to prevent recurrence of stroke. MMD is mainly treated via open surgical methods as medical therapies have shown to be ineffective in halting progression and neurointerventional endovascular surgery has been unsuccessful in stenting the stenotic segment up to date.

Surgical options include direct and indirect cerebrovascular bypass. Connecting a blood vessel from outside the brain to a vessel inside the brain to reroute blood flow around an artery that is narrowed, blocked, or damaged is a direct method of revascularisation. The superficial temporal artery to MCA is the most common bypass procedure, which may achieve instant improvement in blood flow. The superficial temporal artery, temporalis muscle or the dura is placed in direct contact with the brain surface, with the expectation that vessels will eventually grow into the brain and improve blood supply, is an indirect method of revascularisation. Direct bypass would be the best option for those presenting with an ischaemic event. The patients who had surgical revascularisation and the patients who received conservative management were compared in two meta-analyses which revealed that the patients in the surgical group had a reduced risk of stroke compared to the conservatively managed group.(6,7) Surgery was associated with a reduced rate of haemorrhage during follow-up (5% vs. 19%) and the trend towards reduction in the rate of ischaemic stroke (10% vs. 14%); pooled odds ratio [OR] was 0.71 (95% CI: 0.5-1.1). In children who have smaller vessels which are less suitable for direct anastomosis, the choice of surgery is the indirect method.(8,9) Since our patient did not consent for surgery, he was managed conservatively with antiplatelet (aspirin) and statin (atorvastatin) therapy, coupled with speech therapy.

For all patients with MMD including asymptomatic or symptomatic ischaemic-type, long-term aspirin as antiplatelet therapy has been recommended for secondary prevention. The natural history of MMD tends to be progressive in children and adults.(10, 11) Progressive neurological deficits and poor outcome were reported in 50 to 66 percent of untreated patients in a long-term follow-up prospective study. (12, 13) The progression rate and extent however, varies substantially between populations.

Conclusion

This is the first case of bilateral MMD reported in Sri Lanka. It is a rare, progressive cerebrovascular disorder where early diagnosis and treatment are crucial to prevent severe complications such as ischaemic stroke, transient ischemic attack, or intracranial haemorrhage. While the exact cause remains unknown, advancements in genetic research and imaging technology have improved understanding and management of the disease. Treatment options, including surgical revascularisation procedures like direct or indirect bypass surgeries, have significantly enhanced outcomes, reducing the risk of recurrent strokes and improving quality of life. Long term care and monitoring are essential for individuals with MMD to manage symptoms and maintain neurological function. Ongoing research continues to offer hope for better diagnostic methods, treatment, and a potential cure in the future.

Declarations

Conflicts of interest:
The authors declare no conflicts of interest.

Funding:
None

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CASE REPORT

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Protein C and antithrombin III deficiency in an elderly patient presenting with pulmonary embolism

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Abstract

Pulmonary embolism is a life-threatening condition, which if not detected and treated timely may lead to death. It is usually a consequence of deep vein thrombosis, which itself may occur due to several risk factors like prolonged immobilisation, surgery, long haul flights, obesity, previous or family history of thrombosis, intravenous drug abuse, oral contraceptive pills and conditions like antiphospholipid syndrome, paroxysmal nocturnal haemoglobinuria or myeloproliferative disorders. In the background of recurrent thrombosis since childhood, once the common causes are excluded, natural anticoagulant deficiencies like protein C, protein S or antithrombin III deficiency are considered. Here we present a case of a 72-year-old man with multiple comorbidities, presenting with cough, breathlessness and features suggestive of aspiration pneumonia. Despite treatment his condition worsened and further investigation revealed sub-massive pulmonary embolism due to protein C and antithrombin III deficiency, a rare occurrence in this age group. The patient did not have any other common risk factors for thrombosis. To the best of the authors' knowledge this is the first reported case of such dual anticoagulant deficiency presenting only with pulmonary embolism in an elderly patient, which may have developed due to severe inflammatory state. However, after the initiation of anticoagulant therapy his condition gradually improved with resolution of symptoms and thrombus on follow-up imaging. This case highlights the importance of considering natural anticoagulant deficiency in elderly when common risk factors of clotting are excluded and also focuses on the diagnostic challenges along with therapeutic strategies employed in managing this case.

Keywords: pulmonary embolism, protein C deficiency, antithrombin III deficiency

Introduction

Pulmonary embolism (PE), characterised by blockage in the pulmonary arteries, typically results from a thrombus forming in a systemic blood vessel, often in the deep veins of the lower extremities. In Western nations, the incidence of PE in the general population ranges from 60 to 120 cases per 100,000 annually, with an in-hospital mortality rate of 14% and a 90-day mortality rate of 20%.(1) In an Asian study involving 696 patients PE-related mortality was 5.6%.(2) The challenge of diagnosing PE persists due to its nonspecific symptoms, resulting in less than 10% of initially evaluated patients receiving confirmation of the condition.(3) Consequently, it is often underdiagnosed, posing a significant risk of mortality if left untreated. This underscores the necessity for ongoing suspicion and immediate therapy for PE. Such assertions have fueled a state of hyper-vigilance surrounding its diagnosis.(3,4)

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As a patient gets older, the diagnosis accuracy declines. When concomitant conditions such as bronchopneumonia, asthma, chronic fibrosing pulmonary processes or chronic obstructive pulmonary disease (COPD) are present, diagnosis might be challenging.(5) PE usually originates from the deep veins of the legs, most commonly the calf veins but there are some other important contributory risk factors.(1) Well-known risk factors include aging, smoking, being obese, having a personal or family history of venous thromboembolism (VTE) as well as recent surgery, trauma, hospitalisation or prolonged immobilisation. (6) There are some hereditary factor deficiencies which can cause a prothrombotic state such as Protein C (PC), Protein S (PS), Antithrombin (AT) III which are naturally occurring coagulation inhibitors. (7) PC, a glycoprotein synthesised in the liver, relies on vitamin K for its activation. Activated protein C (aPC) exerts its anticoagulant effect by degrading coagulation factors Va and VIIIa which are crucial for the activation of factor X and the generation of thrombin. Deficiency of PC disrupts the fine equilibrium between procoagulant and anticoagulant proteins, tipping the scales towards a heightened risk of clot formation.(8) AT III is a natural anticoagulant that deactivates enzymes like thrombin and clotting factors IXa, Xa, XIa, and XIIa. The risks of both arterial and venous thrombosis increase in individuals lacking antithrombin.(9) In this case report, we discuss a case of PE in an elderly patient due to PC and AT III deficiency.

Case presentation

A 72-year-old, bed-ridden patient on a nasogastric tube, presented with low grade fever, productive cough and sudden onset of shortness of breath which progressively increased and got aggravated on lying flat but improved when propped up. He had a history of Parkinson's disease, ischaemic heart disease, hypertension and ischaemic stroke with right sided hemiparesis 2 years back following which he was bed-ridden. The nasogastric tube was inserted to maintain nutrition following drowsiness after an episode of acute gastroenteritis two weeks prior to the current presentation. His cough was productive with moderate sputum production, which was clear in colour. There was no diurnal variation of his symptoms. On examination, he had bilateral lower limb swelling. He had a respiration rate of 24 breaths/min, pulse rate of 118 beats/min, temperature of 99.5oF and blood pressure of 125/85 mmHg. The jugular venous pressure (JVP) was not elevated and his SpO2 was 94% on oxygen 2L/min. His GCS was 14/15. Auscultation findings only revealed crepitations in the middle zone of the left lung. His chest X-ray is shown in Figure 1A.

The patient was diagnosed to have aspiration pneumonia based on clinical findings and investigations (Table 1). He was managed accordingly with 2 litres/min oxygen and broad-spectrum antibiotics. However, the patient's shortness of breath progressively increased with a sudden rise in oxygen demand up to 15 litres/min through a non-rebreathing mask. His blood pressure dropped to 80/50 mmHg but there was no deterioration in his chest x-ray and auscultation findings. A previously done spiral computed tomography (CT) scan of the brain revealed moderate generalised cerebral atrophy and intracranial atherosclerotic disease (ICAD).

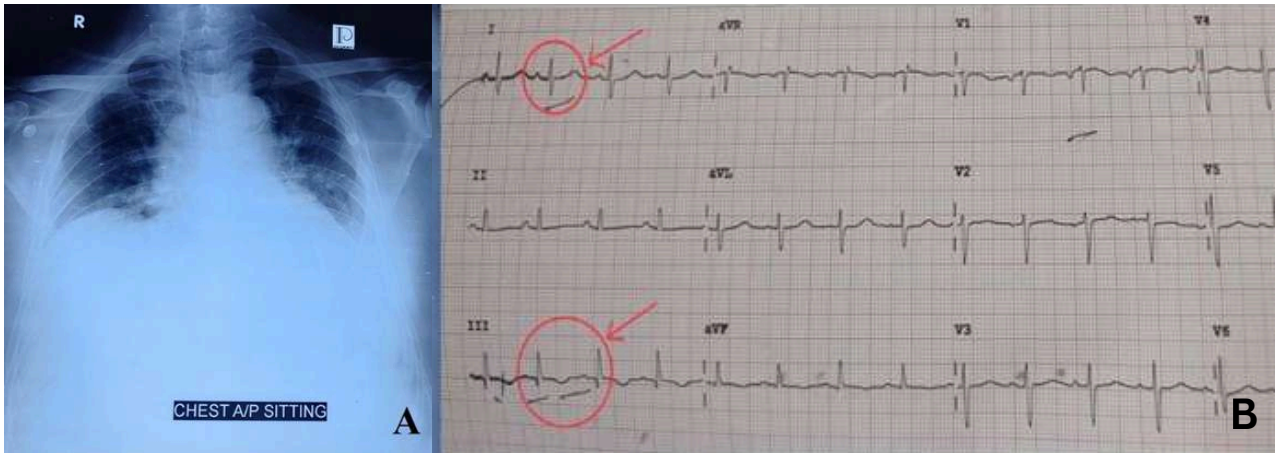

Figure 1. Chest X-Ray & ECG during admission. (A) Chest X-ray posteroanterior view (supine position) showing non-homogeneous opacity in the left upper, middle and lower zones. (B) ECG showing sinus tachycardia with S1Q3T3 pattern (indicated by the arrows)

Table 1. Investigations on admission

Investigation	Result	Normal range
White blood cell count ($\times 10^9$/L)	21.46	4-10
Platelet count (K/µL)	180	150-410
Haemoglobin (g/dL)	13.50	13-17
Erythrocyte sedimentation rate (mm/1st hour)	102	0-10
C reactive protein (mg/L)	103	<5.00
Procalcitonin (ng/mL)	0.12	<0.05
Alanine amino transferase (U/L)	102	Up to 41 (Male), Up to 33 (Female)
Serum creatinine (mg/dL)	1.11	0.70-1.20
Blood urea (mg/dL)	32.90	16.60-48.50
Serum albumin (g/dL)	3.11	3.50-5.20
Serum calcium (mg/dL)	8.78	8.80-10.60
N-terminal pro b-type natriuretic peptide (NT-proBNP) (pg/mL)	8894.00	<125
Troponin I (ng/mL)	0.716	0-0.034

As the oxygen demand was disproportionate to the auscultation and x-ray findings, an ECG was done which showed sinus tachycardia with S1 Q3 T3 pattern (Figure 1B). His echocardiography showed dilatation of the right atrium (RA) and right ventricle (RV) with right ventricular dysfunction, pulmonary artery systolic pressure (PASP) of 60 mmHg and ejection fraction of 62%. His D-dimer levels were elevated to 6.03 microgram/mL (<0.50 microgram/mL). Diagnostic CT pulmonary angiogram (CTPA) was performed which revealed acute occlusive PE involving bilateral main pulmonary arteries and branches. (Figure 2). Duplex study of bilateral lower limbs had no evidence of deep vein thrombosis (DVT).

Subsequently, we diagnosed the patient with submassive PE and initiated conservative treatment. Simultaneously, given the life-threatening nature of this condition, we conducted a thorough evaluation to identify any underlying causes of PE. To exclude all potential factors, a coagulation profile was performed (Table 2). It was done on the second day after diagnosing PE by Sysmex automated coagulation analyzer CS-1600 which uses a multi-wavelength detection system, allowing for a variety of measurement principles, including those used for chromogenic assays and immunoturbidity. The hypercoagulability tests revealed reduced levels of PC and AT III activity, while PS and homocysteine levels were within normal limits.

In the evaluation of the causes of PC and AT III deficiency, we ruled out malignancy by testing for tumour markers. Except for prostate specific antigen (PSA) which was 7.03 ng/mL (<4.00 ng/mL), all other markers; alpha fetoprotein, CA 19-9, CA 15-3, and carcinoembryonic antigen (CEA) were normal.

Following the diagnosis of submassive PE, we initiated treatment with unfractionated heparin (starting at a bolus dose of 80 IU/kg IV followed by a continuous infusion rate of 18 IU/kg/hr for three days). Subsequently, warfarin was introduced on the second day of unfractionated heparin therapy, leading to the onset of haematuria and notable changes in laboratory parameters; prothrombin time increased to 49 seconds (12-17 seconds), activated partial thromboplastin time extended to 62 seconds (28-36 seconds) and international normalised ratio was elevated to 4.13 (target 2-3). Warfarin was stopped and switched to a regimen consisting of enoxaparin sodium, which is a low-molecular-weight

Table 2. Coagulation profile

Investigation	Result	Normal range
Antithrombin III (%)	33.5	75-125
Protein C activity, plasma (%)	50	70-130
Protein S activity, plasma (%)	59	60-130
Homocysteine (µmol/L)	12.14	5.00-15.00
Factor V activity (%)	115.30	50-150

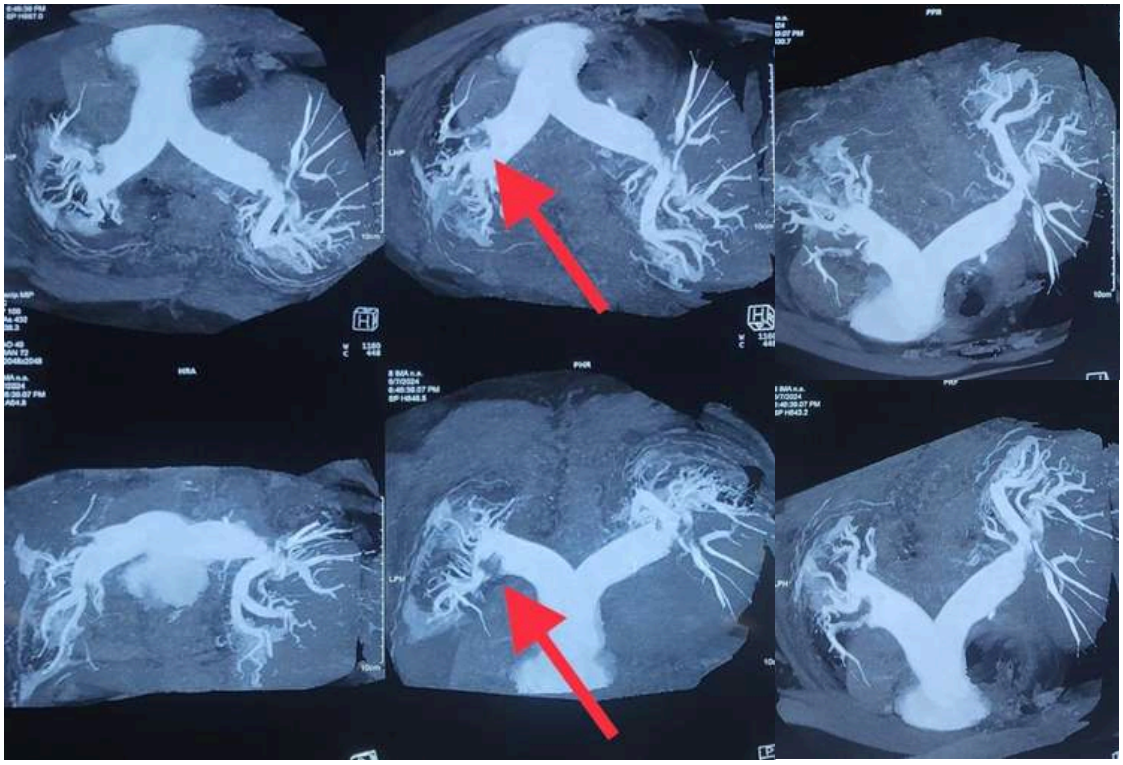

Figure 2. CTPA after admission showing acute occlusive PE involving bilateral main pulmonary arteries & branches.

heparin (LMWH), at a dosage of 40 mg subcutaneously twice daily for 5 days. Following this, rivaroxaban, a direct factor Xa inhibitor, was initiated with a loading dose of 15 mg twice daily for 3 weeks, followed by a maintenance dose of 20 mg once daily. The patient was additionally administered 3 units of fresh frozen plasma due to the unavailability of purified PC concentrate and AT III concentrate in our country. His breathlessness gradually improved, and his oxygen requirements returned to normal. After 48 hours of stability without oxygen support, an ECG (Figure 3) was done which showed resolution of its acute changes. Echocardiography revealed resolution of right ventricular dysfunction and decreased PASP (42 mmHg). Chest X-ray also showed improvement (Figure 3). Following 7 days of treatment with rivaroxaban, the patient was discharged without any reported adverse events. He continued taking medication at home for one month. There were no thrombosis related symptoms at the follow-up appointment after a month.

The patient was advised to continue medication for three months. Repeat echocardiography on his follow-up visit showed no dilation of the right atrium and right ventricle. D-dimer level was normal (0.48). Repeat CTPA showed resolution of PE (Figure 4). PC activity became 107% and AT III was 133%, which were within normal limits. Rivaroxaban 15 mg was switched to apixaban 2.5 mg per oral twice daily due to its lower risk of major bleeding while exhibiting comparable efficacy in preventing systemic embolism.(10)

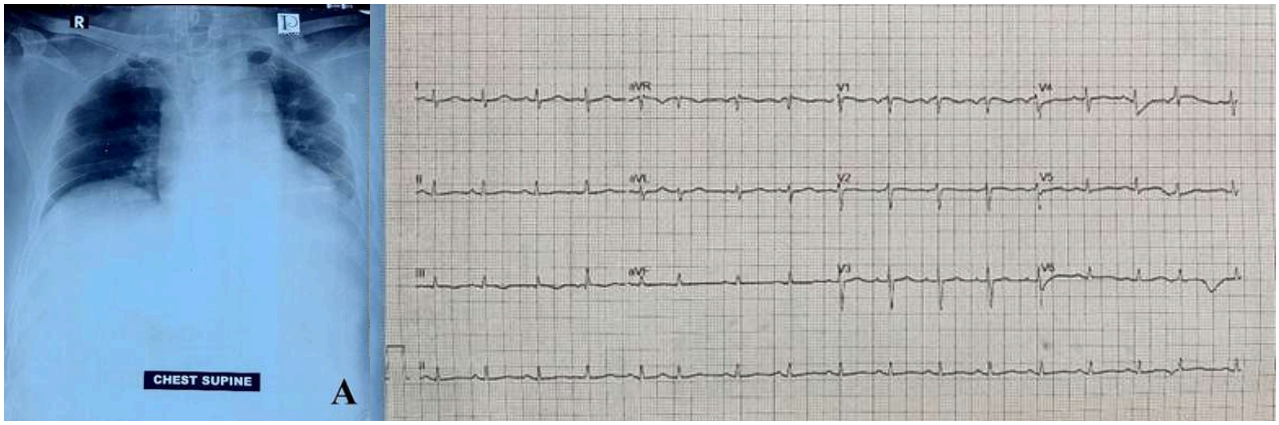

Figure 3. Normal ECG & improved chest x-ray at discharge

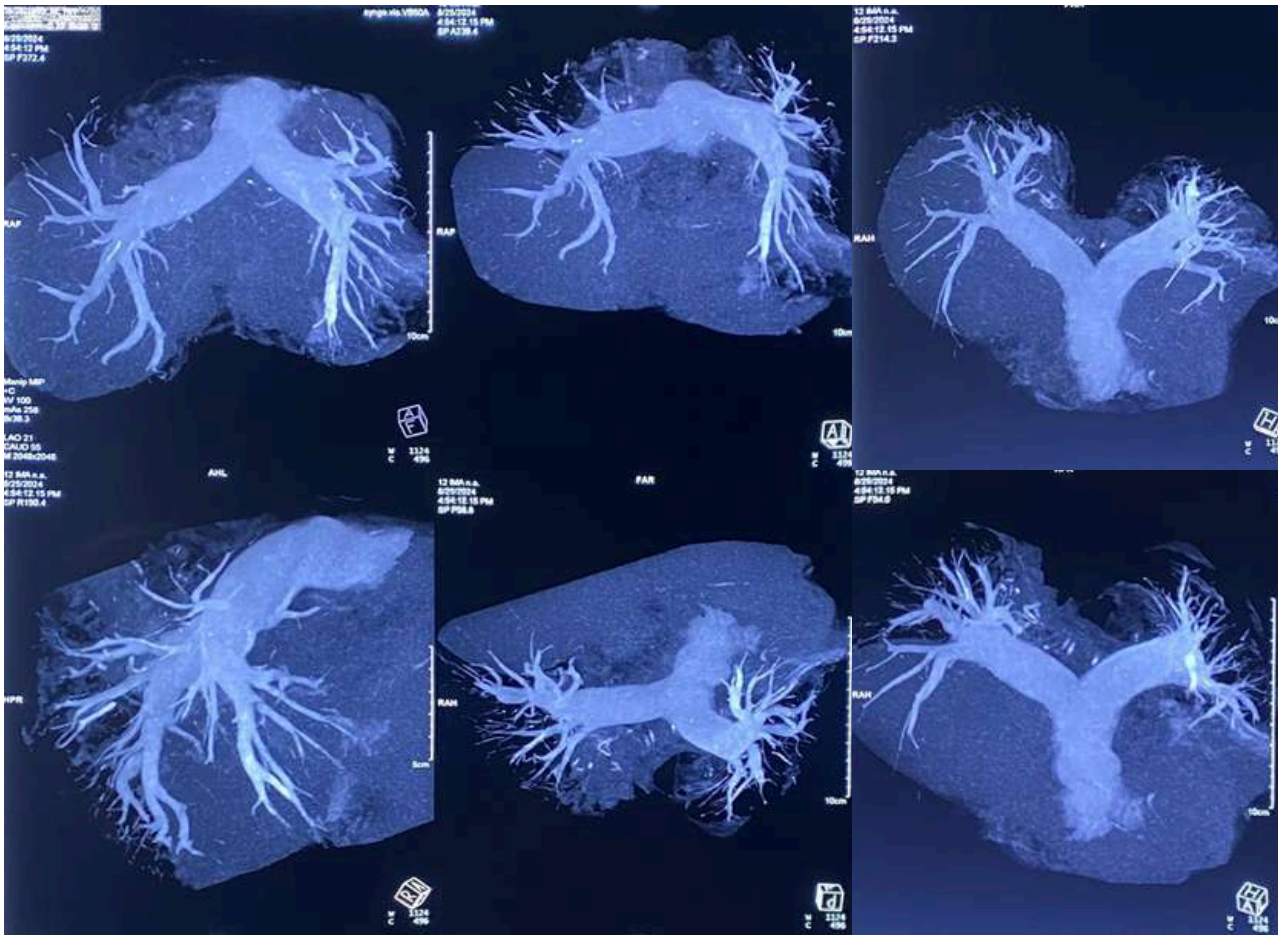

Figure 4. CTPA after 3 months showing resolution of thrombus

Discussion

PC deficiency, determined solely by plasma levels, occurs in approximately 1 in 200 to 1 in 500 individuals in the general population. However, many of those affected do not exhibit symptoms throughout their lives.(11)

The diagnosis of AT III deficiency requires family screening and excluding pathological conditions that lead to impaired synthesis, such as liver disease or treatment with vitamin K antagonists (e.g., warfarin). It also involves investigating potential causes of AT III loss, such as renal failure/nephrotic syndrome, and considering factors that might deplete AT III, such as disseminated intravascular coagulation (DIC).(12)

Reflecting on this case, we observed that PE developed in this elderly patient not due to a common risk factor, but rather because of dual natural anticoagulant deficiency, which is exceptionally uncommon at this age. Clinical findings which lead to suspicion of PE were decreasing oxygen saturation, fall of blood pressure (systolic <100 mmHg), heart rate over 118 beats/min along with Well's score being more than 4. We identified the patient to have an intermediate risk submassive PE and managed accordingly. Treatment protocol for submassive PE includes fibrinolysis, catheter assisted embolectomy, surgical embolectomy and inferior venacaval filter insertion.(13) PE ranks as the third leading cause of death among hospitalised patients. Therefore, clinical, radiological and laboratory findings, along with bleeding risk assessment should be considered together to guide therapeutic decision-making.(14)

Thrombolysis was not warranted due to the diagnosis of submassive pulmonary embolism. We managed the patient with LMWH and warfarin initially and later switched to direct acting oral anticoagulant (rivaroxaban) when haematuria developed. Studies suggest that direct acting oral anticoagulants are clearly non-inferior to vitamin K antagonist (warfarin) therapy in the treatment of acute symptomatic VTE. (15) We suspected DVT was the cause of PE in this patient as he was bedridden for some time. However, the duplex study did not reveal any evidence of DVT. We found that his PE was due to dual anticoagulant deficiency (PC & AT III). PC deficiency can occur congenitally, or it can be acquired. Acquired PC deficiency can result from inflammatory or infectious conditions, liver disease, malignancies, chemotherapy, disseminated intravascular coagulation, and inadequate vitamin K levels or the use of vitamin K antagonist medications.(16) In our patient, malignancy, liver disease and DIC were excluded.

Current management of severe PC deficiency involves administering exogenous PC through either fresh frozen plasma or preferably purified PC concentrate (ceprotin or protexel), alongside oral anticoagulant therapy to manage and prevent thrombosis.(17) As purified PC concentrate or AT III concentrate is not available in our country we chose to administer fresh frozen plasma and used heparin since it stimulates antithrombin III activity.(18)

Given our early diagnosis and prompt initiation of treatment, we anticipated a complete resolution of this condition. We have also planned to continue treatment for six months, with frequent follow-up appointments during this period.

The prevalence of protein C and antithrombin III deficiencies in the general population is 0.2% to 0.4% and 0.02% to 0.2%, respectively.(19) Acquired deficits are known to occur in people with severe infections, disseminated intravascular coagulation (DIC), and other disorders listed above, albeit it is challenging to pinpoint their precise prevalence. Acquired Protein C and Antithrombin III deficiency together is not a precise, well-defined statistic and the combined prevalence of both abnormalities is a rarity.

Based on a review of numerous case reports, atypical VTE has been observed in numerous individuals purely as a result of a single natural anticoagulant deficit, such as either Protein C, Protein S, or Antithrombin III. The majority of them are mainly hereditary deficiencies that affect young people. However, there has never been a case report of an elderly individual developing acquired dual anticoagulant deficiencies that eventually led to pulmonary embolism.

Conclusion

The diagnosis of PE is elusive and once diagnosed it is important to look for the cause. When all the common risk factors of thrombosis are excluded, it is imperative to look for natural anticoagulant deficiency even in elderly. To the best of the authors' knowledge this is the first reported case of dual anticoagulant deficiency presenting with PE. This case report provides an insight to other clinicians in diagnosing and treating this rare condition.

Declarations

Author contributions:
All authors were involved in the management of the patient and all authors contributed to the conception, writing, and editing of the case report.

Conflicts of interest:
The authors stated that there is no conflict of interest in this study.

Funding:
This study received no external funding.

Ethics approval and consent to participate:
The case report has been submitted for Ethical Board Review and approved as ethically sound report. Ref no: PMC/Ethicalrc/2024/036

Consent and ethical consideration statement:
Informed written consent was taken from the parents of the patient to publish details relevant to the disease and management.

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CASE REPORT

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Haemophagocytic lymphohistiocytosis secondary to invasive pseudomonas infection

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Abstract

Haemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening genetic condition in children or a secondary disease in adults. The inherited form of HLH is caused by defects in lymphocytes, involving both autosomal recessive and X-linked patterns. In contrast, secondary or acquired HLH typically arises in response to infections, autoimmune diseases, or lymphoid cancers, possibly, in genetically susceptible individuals. The exact mechanisms of secondary HLH remain unclear, and the condition often goes unrecognized and untreated. Here we discuss a case of pyrexia of unknown origin in an elderly south-Asian woman, complicated with HLH triggered by invasive pseudomonas infection. This case highlights the challenges in diagnosis, treatment and identifying the aetiology of HLH.

Keywords: pyrexia of unknown origin, haemophagocytic lymphohistiocytosis, secondary HLH, *Pseudomonas* infection

Introduction

Haemophagocytic Lymphohistiocytosis (HLH) is an aggressive and life-threatening syndrome of excessive immune system activation. The aetiology of HLH may be classified as genetic (primary) and acquired (secondary). It often affects infants, but also occurs in children and adults of all ages. Over the past two decades, secondary forms of HLH have been increasingly reported in adults.(1) The incidence of gram-negative bacillaemia associated HLH is low (2.39%), but it has a high mortality (43.75%) and *Pseudomonas aeruginosa* accounts for 1.55%.(2) HLH is characterised by an excessive, inappropriate activation of histiocytes and/or T-lymphocytes, leading to elevated serum cytokine levels and accumulation of activated immune cells in target organs, resulting in a persistent immune response and tissue damage. The underlying factor is a defect in the perforin-mediated cytotoxic functions of CD8+ T-cells and reduced NK-cell activity.(3) Secondary form of HLH occurs sporadically, usually triggered by infections, malignancies, autoimmune diseases, or immune deficiencies.(3,5) Diagnosing HLH can be challenging and often mistaken for conditions like sepsis, metabolic disorders, or immune deficiencies, which leads to delayed or missed diagnosis. HLH can progress rapidly and become life-threateningif not diagnosed and treated timely. The mainstay of treatment is steroids and eliminating the trigger, which should be initiated promptly to prevent irreversible damage.

Case presentation

A 69-year-old woman diagnosed with diabetes mellitus, hypertension, bronchial asthma and dyslipidaemia presented with a one-month history of

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intermittent high-grade fever with chills associated with nausea, reduced appetite, generalised weakness, malaise and right hypochondrial pain. Nine days prior to the current admission she had been treated for acute gastroenteritis. She denied respiratory or urinary symptoms and there was no history suggestive of autoimmune connective tissue disorders or any other infections. There was no family history of chronic diseases or malignancies. On admission, she was pale and mildly dehydrated but not tachypnoeic. Her body temperature was 39.8°C and blood pressure was 100/60 mmHg with a heart rate of 116 beats per minute. Respiratory rate was 14 per minute and few coarse-crepitations were heard over the right lower zone on auscultation. Abdominal and Nervous system examinations were unremarkable. There was no lymphadenopathy, ankle oedema and rashes.

Initially full blood count showed bi-cytopenia which progressed to pancytopenia. Serum creatinine levels were elevated with hyponatraemia, denoting acute renal impairment. Elevated ESR and CRP indicated a widespread inflammatory response. Hyperferritinaemia and hyper-triglyceridaemia were noted (Table-1). Liver and thyroid functions were normal except for marginally elevated aspartate aminotransferase and a deranged coagulation profile. With the given results, possible bacterial infection was suspected and IV cefotaxime 1 g thrice

Table 1. Investigation summary

Investigation	Reference range	20/07/2024	30/07/2024	11/08/2024	23/08/2024
White blood cell (10^9/L)	4-10	2.78	3.06	2.74	6.42
Neutrophil (%)	50-70	49.1	73.3	72	82.3
Lymphocyte (%)	20-40	33.9	11.5	15	10.4
Haemoglobin (g/dL)	11-15	8	7.7	8.9	9.3
MCV (fL)	80-100	85.4	84.4	87	88.1
MCH (pg)	27-34	28.1	28.1	28.2	28.6
Platelets (10^9/L)	150-450	169	172	80	200
ESR (mm/1st hour)	<20	120	90		20
CRP (mg/L)	0-3	37.3	58	122.4	12.8
Serum creatinine (mmol/L)	49-90	160	120	137	124
Serum sodium (mmol/L)	136-145	132	133	128	130
Serum potassium (mmol/L)	3.5-5.1	4.7	4.5	4.3	4
INR	0.8-1.2	1.75	1.55		
PT (s)	9-12	18.2	16.3		
APTT (s)	24-34	32.5	20.3		
Serum ferritin (ng/mL)	11-264	717	974	1680	
Triglyceride (mmol/L)	<1.7	3.42	2.71		2.72

MCV-mean corpuscular volume, MCH- Mean hemoglobin concentration, CRP-C-reactive protein, ESR-Erythrocyte sedimentation rate, PT-Prothrombin time, APTT-Activated partial thromboplastin time, INR-International normalizing ratio

daily and oral azithromycin 500 mg daily were started empirically after sending blood and urine for culture. Initial cultures, serological tests for autoimmune disease, screening for venereal diseases, melioidosis, malaria and chronic granulomatous diseases were unrewarding. Ultrasound scan of the abdomen showed hepatosplenomegaly with porta-hepatis and multiple para-aortic lymph nodes (largest-1.3 cm). The blood picture showed anaemia of chronic disease and serum protein electrophoresis was consistent with chronic inflammation. 2D-echocardiography showed normal ejection fraction with no features of infective endocarditis. Elevated procalcitonin level (0.399 ng/mL) was suggestive of persistent bacterial infection. Considering her clinical deterioration, antibiotics were escalated to IV piperacillin-tazobactam 4.5 g thrice daily. CECT-CAP showed hepatosplenomegaly and multiple para-aortic lymphadenopathy. Bone marrow aspirate showed reactive marrow with histiocytes increased in number and activity with very few haemophagocytes.

Laparoscopic biopsy of supra-pancreatic lymph node showed an intense immunoblastic reaction and vague collection of histiocytes with atypical population of large cells, related to HLH, even though definite haemophagocytosis was not seen (Figure-1). All cultures were negative except bone marrow, which isolated pseudomonas species and the antibiotic was switched to meropenem.A diagnosis of HLH was made. Intravenous dexamethasone 24 mg daily (10 mg/m^2/d) was started and tapered off by half every two weeks. She improved both clinically and biochemically following which she was switched to oral steroids. She was discharged with a tapering regime of steroids and followed-up. She had a full recovery and was followed up in her routine clinic.

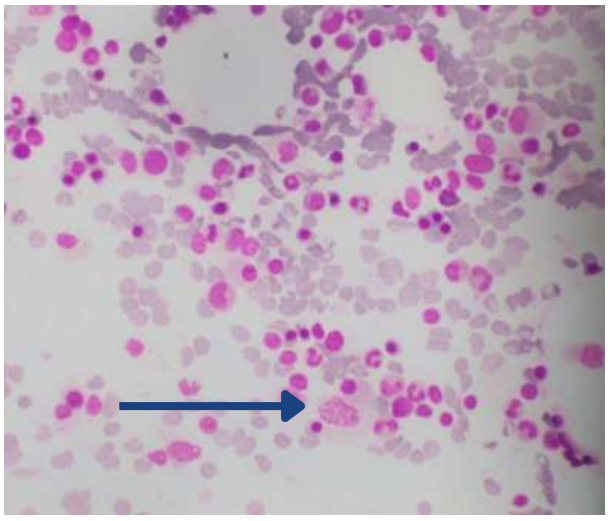

Figure 1. The blue arrow denotes vague collection of histiocytes with atypical population of large cells in supra-pancreatic lymph node

Discussion

Haemophagocytic lymphohistiocytosis is an immune-mediated inflammatory response to various infections, immune disorders, and malignancy. HLH triggers cytokine storms, and the bone marrow shows lymphohistiocytic reaction and macrophagic haemophagocytosis. Gram-negative bacillaemia-associated-HLH is very rare but can be life-threatening. The clinical presentation of HLH is highly variable, which may delay or lead to misdiagnosis. The HLH-2004 diagnostic criteria-initially developed for children was commonly being used for adults as well.(1) But according to updated HLH-2024 criteria, HLH can be diagnosed if there is a known genetic mutation or if at-least 5 of 7 criteria are met. The H-score is developed to estimate the likelihood of HLH in adults by considering parameters such as, immunosuppression, fever, splenomegaly, triglyceride, ferritin, aspartate transaminase, fibrinogen levels, cytopenias and evidence of haemophagocytosis in bone marrow aspirate. A score of ≥250 indicates 99% probability of HLH, whereas ≤90 suggests a probability of <1%.(4,6) Given the patient's clinical presentation and a rise in serum ferritin from 717 ng/mL on day-1 to 1680 ng/mL on day-21, the focus shifted to other hyperferritinaemic syndromes such as Still's disease, catastrophic antiphospholipid syndrome, sepsis, and macrophage activation syndrome. Based on clinical and laboratory findings, these conditions were ruled out, and secondary HLH due to pseudomonas infection was considered as 6 out of 7 HLH diagnostic criteria were met; fever, splenomegaly, cytopenia, hypertriglyceridaemia, hyperferritinaemia, haemophagocytosis in lymph node with Pseudomonas species isolated in bone-marrow culture. The calculated H-score showed a 93-96% probability of HLH. Initial clinical presentation suggested sepsis of unknown focus with minimal evidence of haemophagocytosis in bone marrow which delayed the diagnosis. Though bone-marrow was not convincing enough to make the decision, lymph node biopsy supported the diagnosis of HLH in our case.

Pseudomonas causing HLH is exceedingly rare. HLH should be suspected, in the case sepsis with unknown focus or PUO not responding to empirical treatment. Early diagnosis remains challenging

because of its rarity, nonspecific presentations and variable laboratory findings. Timely diagnosis and prompt treatment is vital to improve the prognosis and prevent life-threatening complications.(7) Treatment focuses on targeting the primary pathology and supportive care. Drugs commonly used in the management of HLH are corticosteroids, intravenous immunoglobulin, and etoposide. Allogenic stem cell transplantation is reserved for refractory cases, CNS involvement and for patients with HLH gene mutations.

Conclusion

HLH is an aggressive and life-threatening syndrome of excessive immune system activation characterised by uncontrolled activation and proliferation of cytotoxic T-lymphocytes and histiocytes that secrete large amounts of inflammatory cytokines. Gram-negative bacillaemia associated-HLH is very rare but has a high mortality. HLH should always be considered when faced with a perplexing clinical presentation, particularly in cases of fever and cytopenias with evidence of persistent inflammation or those refractory to medical treatment. Highlighting the diagnostic challenges of HLH, requires careful clinical, biochemical and imaging correlation with continuous monitoring. This case emphasises the importance of maintaining a high index of suspicion for HLH to recognise the condition early and initiate prompt treatment to improve prognosis.

Declarations

Author contributions:
All authors contributed to the conceptualization and design of the study, contributed to the acquisition of data, conducted the data analysis, contributed to data interpretation and writing the manuscript. All authors read and approved the final manuscript.

Conflicts of interest:
The authors declare that they have no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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CASE REPORT

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Illustrative case series of intra-abdominal abscesses - a radiological viewpoint

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Abstract

Intra-abdominal abscesses (IAA) may commonly arise following complicated gastrointestinal tract infections and, on occasion, from infections within the urinary system. Many of these IAA arise as a consequence of post-surgical complications. These abscesses have a substantial risk of morbidity and mortality. It is crucial to diagnose and treat them to minimise these adverse outcomes promptly. Radiological modalities play a vital role in diagnosing, localising, and detecting associated complications of IAA, as sometimes other investigations can be less reliable and non-specific. Radiological techniques such as ultrasound scans (USS), contrast-enhanced computed tomography (CECT), and even magnetic resonance imaging (MRI) are immensely helpful in diagnosing these conditions. These imaging tools guide clinicians in determining the most appropriate patient management strategies. In this article, we compile a case series involving tubo-ovarian abscess, appendicular abscess, diverticular abscess and infected walled-off pancreatic necrosis, delineating characteristic radiological features which aid in their diagnosis.

Keywords: intra-abdominal abscesses, tubo-ovarian abscess, appendicular abscess, diverticular abscess, infected walled-off pancreatic necrosis

Introduction

Abscesses are localised collections of pus buried in a tissue, an organ, or a confined space. They are one of the morphological forms of acute inflammation.(1) Abscesses can occur in any site of the body, including the brain, soft tissues, lungs, and intra-abdominal and pelvic organs.(2) Intra-abdominal abscesses (IAA) are classified as intraperitoneal vs retroperitoneal, spontaneous vs post-operative and primary vs secondary.(3) IAA commonly arise following infections of the gastrointestinal tract and occasionally following infections from the urinary system. Post-surgical IAA account for about 70% of IAA.(4) Intra-abdominal infections are likely to get complicated by spreading beyond the primary organ of infection, forming abscesses. Abscesses commonly occur in patients with comorbidities such as diabetes mellitus, intravenous drug abuse and immunosuppression, including those with HIV infection.(5-8) IAA have a substantial risk of increased morbidity and mortality. Hence, a high index of suspicion, close follow-up and improved methods for early diagnosis are mandatory.(9) In the prompt diagnostic workup, radiological modalities such as ultrasound scans (USS), contrast-enhanced computed tomography (CECT) and magnetic resonance imaging (MRI) are vital.(9) Four such cases of intra-abdominal abscesses are described in this article, paying particular attention to characteristic radiological features in the diagnosis.

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Case 1

A 43-year-old woman presented with pelvic discomfort, fever and reduced appetite persisting for three weeks. She also reported vaginal discharge and pain during intercourse over the preceding two weeks. The physical assessment identified a tender, cystic mass about 6 cm in size in the left adnexa, with notable cervical motion tenderness. Laboratory analysis revealed elevated inflammatory markers, including a c-reactive protein (CRP) of 62 mg/dL. Ultrasound imaging detected a well-defined cystic lesion containing dense material, corroborated by contrast-enhanced computed tomography (CECT) findings (Figures 1a and 1b), which confirmed a unilocular fluid collection adjacent to the uterus. She underwent a laparoscopic hysterectomy with bilateral salpingo-oophorectomy and adhesiolysis, followed by intravenous and oral antibiotics with full recovery.

Case 2

A 35-year-old woman presented with six days of high fever, right lower abdominal pain, nausea and vomiting. Examination revealed fever and right iliac fossa tenderness with guarding. Laboratory findings showed a neutrophil leukocytosis and CRP of 82 mg/dL. Ultrasonography (USG) demonstrated a localised fluid collection, confirmed on CT as an 8.7 cm x 6.4 cm x 6.2 cm thick-walled abscess with gas locules adjacent to the caecum (Figures 2a and 2b). The abscess was drained via an ultrasound-guided pigtail catheter and intravenous antibiotics were given. She recovered fully and was discharged on day six with oral antibiotics. An interval appendicectomy was performed seven months later.

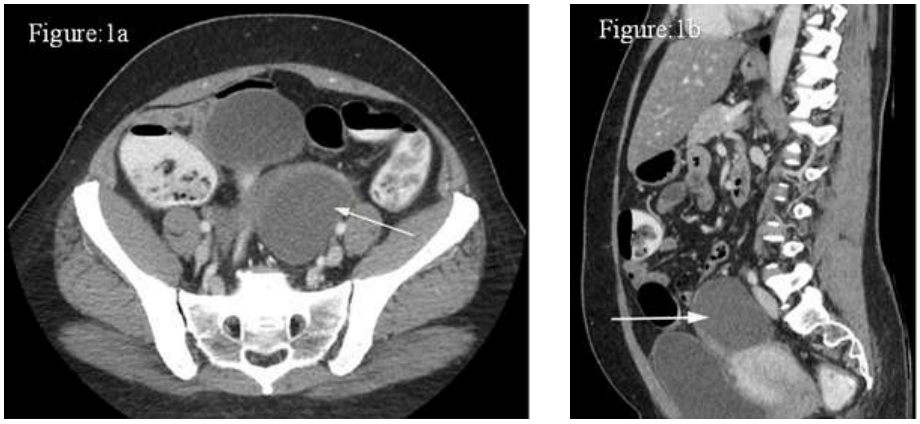


Figure 1a and 1b. Axial and sagittal contrast-enhanced CT scan of the abdomen revealing a left-sided moderate size tubo-ovarian abscess (white arrows) with a small amount of pelvic free fluid.

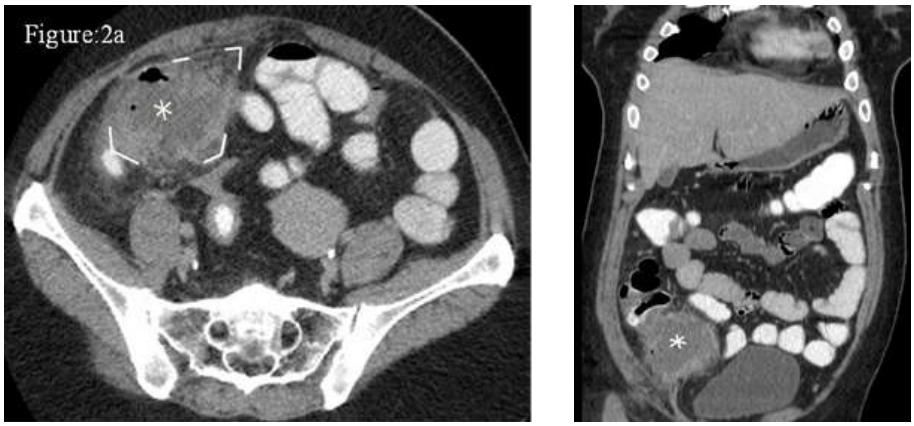


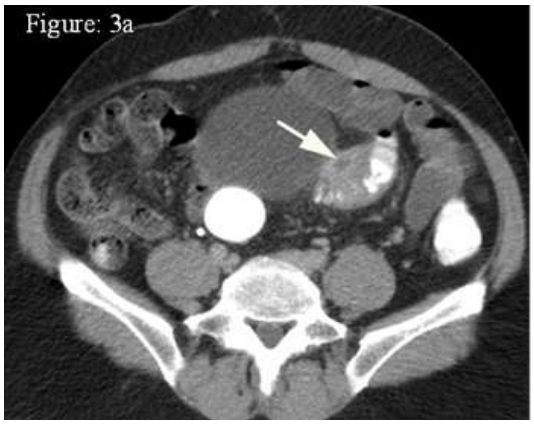
Figure 2a and 2b. Axial and sagittal contrast CT scan of the abdomen demonstrating a moderate-size appendicular abscess (asterisk)

Case 3

A 62-year-old man presented with one week of left lower quadrant pain, low-grade fever and altered bowel habits. Examination revealed localised tenderness without guarding. Laboratory findings showed leukocytosis, mild anaemia and elevated CRP (69.2 mg/dL). Ultrasound revealed a small pelvic fluid collection near the sigmoid colon with inflamed perilesional fat. CECT with rectal contrast confirmed a pericolic abscess (1.0 cm × 1.3 cm × 1.5 cm) and sigmoid wall thickening (Figures 3a and 3b), consistent with diverticulitis (Hinchey classification, stage Ib). He was treated conservatively with intravenous antibiotics and made a full recovery within a week.

Case 4

A 42-year-old man with alcohol abuse and uncontrolled diabetes presented with generalised abdominal pain, high fever and weight loss. He had a history of recurrent pancreatitis. Examination revealed hypotension, abdominal guarding, and tenderness. Laboratory findings showed leukocytosis, thrombocytosis, and mild amylase elevation. USG and CECT showed multiple intercommunicating fluid collections near the pancreatic tail with gas locules and air-fluid levels, consistent with infected walled-off pancreatic necrosis (WOPN) (Figures 4a, 4b). He underwent ultrasound-guided aspiration, saline irrigation, and pigtail drainage, and made a full recovery after an extended stay in the intensive care unit and a surgical ward.



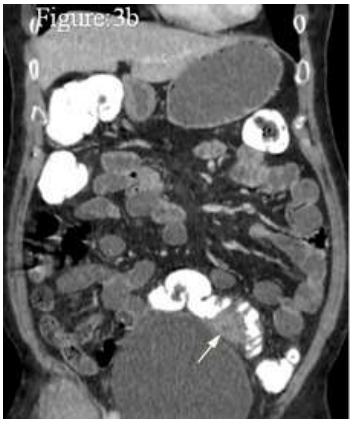
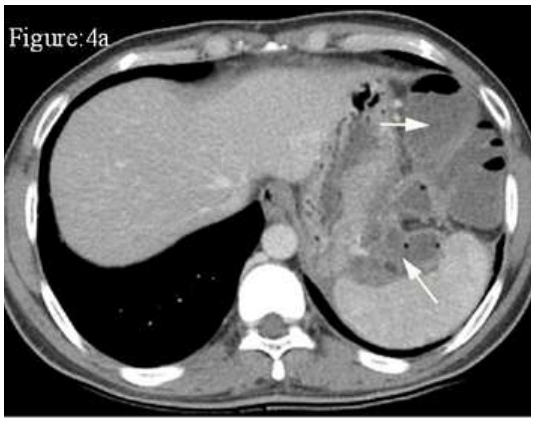


Figure 3a and 3b - Axial and sagittal contrast-enhanced axial CT scans of the abdomen showing a mesosigmoid diverticular abscess (Hinchey classification, stage Ib) (white arrows). The inflammatory mass appears adherent the urinary bladder wall.



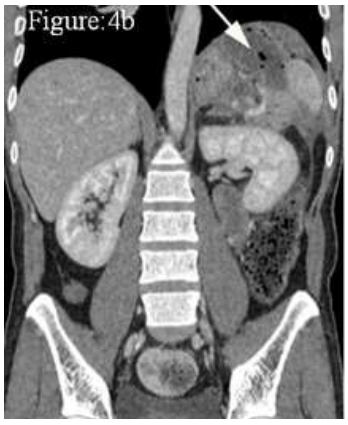


Figure 4a and 4b - Axial and sagittal contrast-enhanced axial CT scans of the abdomen show an ill-defined intercommunicating infected pancreatic pseudocyst at the splenic hilar region (white arrows) extending superiorly and inferiorly

Discussion

IAA are diverse and carry high mortality and morbidity if timely diagnosis and treatment are not instituted.(4,9) However, clinical features and basic blood investigations are nonspecific and imaging plays a pivotal role in their diagnosis.(4,10,11) In addition, image-guided interventions enable microbiological sampling for definitive aetiological diagnosis with a specific ABST pattern directing targeted antibiotic therapy.(12)

Tubo-ovarian abscess:

A tubo-ovarian abscess (TOA) is a complex pelvic inflammatory disease typically seen in premenopausal women, resulting from ascending polymicrobial infection from the upper genital tract.(13,14) It presents as a walled-off inflammatory mass involving the fallopian tube and ovary.(14)

Transvaginal (TVS) or transabdominal ultrasound is the preferred first-line imaging modality due to its availability, non-invasiveness, and high sensitivity (93%) and specificity (98%).(14,15) USG typically shows a complex adnexal cystic mass with thick, irregular walls and coarse internal echoes, often representing pus with cellular debris. The transvaginal examination may better delineate the lesions and exhibit pelvic tenderness over the affected adnexal area.(16)

In uncertain or complex presentations, CECT is valuable, particularly when ultrasound findings are equivocal, or complications are suspected. CECT may reveal unilocular or multilocular cystic lesions with heterogeneous content, thickened walls, and perilesional fat stranding.(17,18) Internal gas locules are rare but reliable indicators for TOA.(19) Identifying a pus-filled fallopian tube with an enhanced thick wall facilitates distinguishing TOA from a neoplastic lesion or endometrioma.

Magnetic Resonance Imaging (MRI) offers superior soft-tissue characterisation and can differentiate TOA from other adnexal masses, such as endometriomas and dermoid cysts. On MRI, TOAs generally appear hypointense on T1-weighted and hyperintense on T2-weighted sequences, with restricted diffusion on DWI and intense wall enhancement with gadolinium.(19)

Laparoscopy remains the gold standard for diagnosis and treatment, especially when image-guided drainage is not feasible. In our case, surgery was preferred due to poor access to percutaneous intervention, and the patient recovered fully postoperatively.

Appendicular abscess:

An appendiceal abscess (AA) is a localised inflammatory collection that typically develops following perforation in acute appendicitis, occurring in 2–6% of cases.(20,21) Diagnosis primarily relies on USG and CECT. Ultrasonography is often the first-line imaging modality, particularly in resource-limited settings, paediatric populations and during pregnancy, with reported sensitivity ranging from 56–94% and specificity from 47–95%.(22) Typical sonographic findings include an ill-defined hypoechoic fluid collection with internal debris, thickened walls and surrounding echogenic fat.(22) Additional findings may include communication between the abscess and the appendiceal lumen, air within the appendiceal wall and decreased or absent tenderness with transducer compression.(23)

CECT offers superior diagnostic accuracy, with a sensitivity of 98–100% and specificity of 91–99%.(24) It clearly defines the abscess as a thick-walled fluid collection in the right iliac fossa, often containing gas locules or appendicoliths.(24) CECT is also superior in evaluating complications such as periappendiceal adhesions, fat stranding, and mass effect on adjacent bowel loops.(25)

For abscesses larger than 4 cm, image-guided percutaneous drainage (e.g., pigtail catheter placement) is preferred over immediate surgical intervention. This approach reduces overall costs and postpones surgery in critically ill patients.(26) It also facilitates delayed, elective interval appendectomy, as illustrated in the case presented.

Diverticular abscesses:

Diverticular abscesses (DA) are localised inflammatory collections that develop adjacent to the colon as a complication of diverticulitis.(27) Clinical examination and laboratory findings are significantly inaccurate in defining many aspects of diverticular disease. Therefore, imaging plays a crucial role in the detection and characterisation of DA.(28)

Historically, barium enema was used in diagnosis, but it has poor sensitivity and specificity compared to modern imaging techniques and is not recommended in acute settings.(28,29) Ultrasonography, being non-invasive, accessible, and

free of radiation, is particularly valuable in younger individuals and premenopausal women. It also assists in image-guided therapeutic procedures and ongoing monitoring.(30) On ultrasound, DA often appears as a fluid-filled cystic structure with internal echogenic debris and scattered air locules, usually positioned near the site of maximal tenderness.(30)

CECT, particularly with rectal contrast, remains the preferred modality for diagnosing diverticulitis and associated abscesses. It offers excellent sensitivity (up to 97%) and near-perfect specificity (approaching 100%).(31) In addition to confirming the diagnosis, CECT allows for disease staging. The modified Hinchey classification, proposed by Kaiser et al. in 2005, categorises disease severity based on CECT findings and serves both prognostic and therapeutic purposes.(32) Building on this, Sartelli et al. introduced a simplified CT-based system in 2015 that considers patient comorbidities and clinical stability to guide treatment.(33)

According to this model, diverticular abscesses under 4 cm can be managed with antibiotics, while image-guided percutaneous drainage is recommended for abscesses more than 4 cm. A surgical approach is proposed for more complicated cases such as those with pneumoperitoneum.(33)

MRI, though less frequently used, can be helpful in specific situations, especially for younger patients or those requiring repeated imaging. It has shown a sensitivity of 94% and specificity of 88% for diagnosing acute diverticulitis, with higher accuracy observed in younger individuals.(34)

Infected walled-off pancreatic necrosis:

The revised Atlanta classification provides a clearer framework for differentiating complications of acute pancreatitis, including acute peripancreatic fluid collections, pancreatic pseudocysts, acute necrotic collections and walled-off pancreatic necrosis (WOPN).(35) Cross-sectional imaging based on this new classification avoids the confusion in terminology used over the last 20 years.(36) Pancreatic pseudocysts (PPC) are defined as localised, enzyme-rich fluid collections encased in a fibrous wall without epithelial lining, typically occurring in 10–20% of patients following acute pancreatitis.(37) Walled-off pancreatic necrosis is an encapsulated pancreatic or peripancreatic collection containing necrotic tissue debris and occurs in 1–9% of patients with acute pancreatitis.(38) While both sterile and infected collections can occur, infection is more frequently associated with necrotic collections.(39) Infected WOPN is linked to a substantial risk in mortality, estimated between 30% and 39%, highlighting the importance of early detection and appropriate intervention.(40) Apart from deteriorating signs of infection, objective assessment of the collection with imaging is vital. An ongoing infection due to gas-forming organisms can be suspected if gas locules or air-fluid levels are seen on CECT. However, the presence of gas-forming organisms can be reliably obtained using fine needle aspiration (FNA) of the collections and cultures of organisms. Imaging features more suggestive of WOPN than PPC include larger lesion size, irregular or thickened walls, fat-density debris, multiple septations and pancreatic tissue irregularities.(41) Necrotic components of the infected collection are better identified on ultrasonography and T2W MRI than on CECT.(41) Ultrasonography and CECT are essential during guided FNA and inserting an image-guided pigtail catheter where indicated.(42)

In the case discussed here, multiple interconnecting collections with dense internal debris and gas were detected. The diagnosis was confirmed through ultrasound-guided FNA, and the patient was successfully treated with active aspiration and passive pigtail catheter drainage.

The presented cases demonstrate the critical role of choosing appropriate imaging techniques tailored to specific clinical situations. Key considerations include disease complexity and resource availability. Table 1 summarises the advantages and common applications of ultrasound, CT and MRI in evaluating different intra-abdominal abscesses.

Conclusion

In conclusion, ultrasonography serves a crucial role as the primary imaging modality in diagnosing a variety of intra-abdominal abscesses. CECT abdomen and MRI better characterise the diagnosis. Imaging-guided interventions in intra-abdominal abscesses play an essential role in managing these patients, which significantly reduces the morbidity and mortality.

Declarations

Author contributions:
SRS -formulated the concept, designed the review, conducted the literature review, and wrote and edited the manuscript. PDA -literature review and contributed to manuscript writing. All authors read and approved the final manuscript.

Table 1. Comparative radiological evaluation of intra-abdominal abscesses, modalities strengths and clinical applications

Features	USS Advantages	CT Advantages	MRI Advantages	Typical Use Case
Tubo-ovarian abscess(TOA)	First-line for adnexal evaluation; 93% sensitivity and 98% specificity; transvaginal USS enhances detection	Better for complex cases (multilocular abscesses, gas locules, fat stranding). Enhanced walls and septations are well visualised.	Superior tissue characterisation. Distinguishes TOA from endometrioma.DWI shows diffusion restriction	Start with USS; CT if inconclusive; MRI for equivocal cases or differentiation from endometrioma
Appendicular Abscess	The initial modality (56–94% sensitivity); identifies fluid collections, and echogenic fat. Low-cost, portable.	Gold standard and 98-100% sensitivity and 91–99% specificity.It shows wall enhancement, gas locules, and appendicoliths.	Limited to pediatric/pregnant patients where radiation avoidance is critical.	USS first in resource-limited settings.CT for confirmation and guided drainage.
Diverticular Abscess	Non-invasive; good in young or premenopausal patients; used in follow-up.Shows pericolic collections with debris	Imaging of choice; sensitivity up to 97%, specificity 100%; allows Hinchey staging; detects distant abscesses, fistulae, or perforation.	Emerging role (94% sensitivity)Useful for characterisation; better in younger patientsor repeated imaging needs.	CT is first-line; USS for follow-up, radiation-sensitive cases, staging or drainage.
Infected Walled-off pancreatic necrosis	Detects internal debris, guides drainage; and identifies septations better than CT.Bedside utility in ICU setup.	Best for confirming gas locules, extent, and differentiating pseudocyst vs necrosis	Best for necrotic tissue characterisation; no radiation; excellent for follow-up	CT for initial diagnosis and interventional planning; MRI for complex or equivocal cases

Declarations

Conflicts of interest:
The authors declare that they have no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics approval:
This radiology review did not require ethical approval as it involved a retrospective analysis and reviewing of existing patient investigations and records, with all patient identifiers carefully removed to ensure anonymity; additionally, all DICOM images were de-identified and are available upon reasonable request, upholding privacy and confidentiality standards.

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CASE REPORT

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Concurrent multiple myeloma and gastrointestinal amyloidosis presenting as chronic gastritis refractory to treatment

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Abstract

We present a rare case of concurrent multiple myeloma and gastrointestinal (GI) amyloidosis with jejunal and duodenal involvement masquerading as chronic gastritis with poor response to treatment in a 65-year-old woman. Oesophagogastroduodenoscopy and biopsy identified amyloid deposition while serum protein electrophoresis revealed monoclonal gammopathy. Subsequent bone marrow aspiration confirmed the diagnosis of multiple myeloma with clonal plasma cells of 45%. This case highlights the rare presentation of multiple myeloma and GI amyloidosis with jejunal and duodenal involvement, masquerading as chronic gastritis with poor treatment response.

Keywords: amyloidosis, gastrointestinal amyloidosis, multiple myeloma, chronic gastritis

Introduction

Amyloidosis is a rare disorder characterised by the extracellular deposition of abnormal, insoluble, fibrillar proteins in various tissues and organs. This leads to the distortion of tissue architecture and function. Amyloidosis can be broadly classified into systemic or localised forms.(1) Systemic amyloidosis occurs in various forms, such as primary, secondary, hereditary, related to haemodialysis and senile systemic amyloidosis. Amyloidosis affecting the gastrointestinal (GI) tract causing noticeable symptoms is uncommon ranging from 1-2%.(2) Clinical manifestations of GI amyloidosis can be general or specific such as tiredness, dizziness, loss of appetite, weight loss, abdominal pain, vomiting, diarrhoea, bloating, reflux symptoms and gastrointestinal bleeding.(1,3) Amyloidosis has been observed in multiple myeloma (MM) with an incidence ranging from 8 – 43% in literature.(4) However, GI amyloidosis as the first manifestation of MM is extremely rare with only a limited number of cases.(5)

Case presentation

A 65-year-old woman with diabetes mellitus (DM), hypertension and ischaemic heart disease (IHD) for 8 years, presented with epigastric burning sensation and intermittent vomiting which progressively worsened over 6 months and had poor response to acid suppression therapy. She also complained of loss of appetite and unintentional weight loss of 8-10 kg for the same duration.

Glycaemic control was satisfactory and except for IHD, there were no macrovascular or microvascular complications of diabetes. The patients' epigastric pain did not radiate to the back. She did not have a

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history suggestive of autonomic neuropathy, yellowish discolouration of eyes or pale stools. There was no melaena, altered bowel habits, dysphagia or evening pyrexia. There was no history of tuberculosis (TB) or family history of solid organ or haematological malignancies. She had reached menopause at 54 years of age with no episodes of post-menopausal bleeding. Clinical features suggestive of multiple myeloma such as bone pain, sinister backache or pathological fractures were not demonstrated.

On examination she was thinly built with a BMI of 17.2 kg/m^2. Mild pallor was noted with no fever or icterus. Bilateral pitting lower limb oedema up to midcalf was present without periorbital oedema or ascites. Skin rashes or lymphadenopathy were not detected. She was haemodynamically stable. Cardiovascular, respiratory, abdominal and neurological examinations did not reveal any murmurs, organomegaly or peripheral neuropathy.

Two oesophagogastroduodenoscopies (OGD) were performed within 6 months of symptom onset considering the need to exclude gastric malignancy. Histology revealed chronic gastritis which was treated with Helicobacter pylori eradication therapy followed by a long course of proton pump inhibitors (PPI) and antacids. Lack of treatment response prompted a third OGD, 6 months later, which showed nodular thickening of the duodenal mucosa. Biopsy samples were taken and further histological evaluation confirmed amyloid proteins. Serum Protein Electrophoresis (SPEP) was performed on suspicion of AL amyloidosis which yielded a monoclonal gammopathy. Bone marrow biopsy confirmed the diagnosis of multiple myeloma (MM) with clonal plasma cells reported as 45% (Table 1). However, resource constraints limited further evaluation with immunohistochemistry. Definitive treatment was commenced with bortezomib, thalidomide, dexamethasone and supportive remedies consisting of PPI and antiemetics.

Discussion

Amyloidosis affects various tissues and organs due to buildup of abnormal and misfolded proteins that accumulate extracellularly.(5) There is higher prevalence among males and older individuals, typically around 63 years.(1) AL amyloidosis, linked to plasma cell dyscrasias and AA amyloidosis, associated with chronic inflammatory conditions, are contributors to amyloidosis(6). Reduced renal clearance of beta-2 microglobulin (B2M) in end stage renal disease patients undergoing dialysis and apolipoprotein E in Alzheimer's disease are implied in the pathogenesis of amyloidosis.(7) The association of amyloidosis and multiple myeloma (MM) ranges from 8-43%.(4) A review by Hu et al. identifies 12 cases with symptomatic GI amyloidosis as the initial manifestation of multiple myeloma.(6) This article adds to literature as the only such case reported from Sri Lanka.(8)

Skin, renal and cardiac involvement is frequent in AL amyloidosis, with GI complications being comparatively rare, occurring in 3–8% of cases.(10) Among them, studies indicate 98% to be asymptomatic.(11) A case series of 769 patients with primary systemic amyloidosis showed that only 1% of individuals had symptomatic GI amyloidosis confirmed by biopsy.(9)

Cowan et al. observed that unintentional loss of weight was the most common (45%) clinical feature in symptomatic GI amyloidosis as observed in our patient.(12) Additionally, vomiting, diarrhoea and upper GI bleeding in the form of melaena and haematochezia have been recorded.(12-15) The finding of a gastric mass or gastric retention suggestive of malignancy have also been documented in literature.(13,16). Chronic gastritis and dyspeptic symptoms have been reported in GI amyloidosis with an incidence of 33%.(12)

Histology samples have yielded the highest diagnostic results for GI amyloidosis in the duodenum at 50%, followed by the stomach at 44%, colon at 32%, oesophagus at 12%, and rectum at 8% with jejunal involvement considered to be extremely rare.(10) CECT imaging of our patient was suggestive of jejunal involvement but was not confirmed histologically due to limited facilities.

The pathogenesis of GI involvement in amyloidosis is broadly divided into mucosal or neuromuscular infiltration. The extent of mucosal infiltration varies based on the type of amyloid deposition. AL amyloidosis affects the muscularis mucosa, submucosa and muscularis propria, creating protrusions that cause symptoms resembling bowel obstruction. In addition, AA amyloidosis primarily impacts the mucosa, resulting in erosions and presenting as diarrhoea and malabsorption.(1) Amyloid protein deposition in the neuromuscular layer can affect intrinsic neural networks, termed as the submucosal and myenteric plexus, resulting in irregular peristalsis and impaired motility.(1)

Table 1. Diagnostic evaluation

Laboratory parameter	Result	Reference
White blood cells (10^9/L)	5.56	4 - 11
Haemoglobin (g/dL)	9.8	11- 13
Platelets (10^9/L)	334	150- 450
Albumin (g/L)	25	35- 52
Total protein (g/L)	65	70-83
Urea (mmol/L)	3.5	2.8- 7.2
Creatinine (micromol/L)	42.1	74- 110
Sodium (mmol/L)	138.3	136- 146
Potassium (mmol/L)	4.5	3.5- 5.1
Albumin corrected calcium (mmol/L)	2.07	2.06- 2.60
Lactate Dehydrogenase (U/L)	233.6	125- 243
Erythrocyte sedimentation rate (mm/1st hour)	65	
Aspartate transaminase (U/L)	11.2	<50
Alanine transaminase (U/L)	7.2	<50
C-reactive protein (mg/dL)	5	0-5
Urine full report	Protein - trace	
Urine Protein/Creatinine Ratio (mg/mmol)	89.4	20- 200
Serum lactoferrin/calprotectin	negative	
Thyroid stimulating hormone (mIU/L)	1.5	0.5- 5
OGD (3rd)	Nodular duodenal mucosa with prominent lacteals and denuded mucosa	
Histopathology	Duodenal mucosa containing an eosinophilic material that is suggestive of amyloid (Facilities for amyloid subtyping was not available)	
Contrast enhanced computed tomography (CECT) of abdomen	Diffuse sub-mucosal oedema of proximal jejunum and D2-D4 of duodenum associated with para-aortic and mesenteric lymph nodes.	
Blood picture	Features of mixed deficiency anaemia and moderate amount of rouleaux formation	
Serum protein electrophoresis	Monoclonal band in gamma region with “M band” concentration 10g/L	
Bone marrow biopsy	>25% of clonal plasma cells present	
Echocardiogram	Ejection fraction 55%- 60%, no evidence of cardiac amyloidosis	

To investigate AL amyloidosis, it's essential to conduct both serum and urine tests to detect monoclonal light chains using immunoelectrophoresis and immunofixation. Additionally, assessment of bone marrow aspirate is necessary to quantify plasma cells and confirm the presence of monoclonal light chains. Endoscopic examination with biopsy is confirmatory, but patients may need push-enteroscopy or capsule endoscopy to identify lesions specifically in the jejunum.(3) This was not performed due to resource constraints. The gold standard for diagnosing amyloidosis involves observing the distinct green birefringence under polarised light when tissue biopsy is stained with Congo red.(3)

Treatment for amyloidosis is tailored to the specific type and severity of the condition. In the case of AL amyloidosis, chemotherapy is necessary and in some instances, haematopoietic stem cell transplantation may be recommended to eliminate abnormal plasma cell clones. The treatment of AA amyloidosis depends on managing the underlying inflammatory condition to diminish disease progression.(12) AL amyloidosis involving the GI system tends to have a poor prognosis with a median survival of approximately 6.3 years. This prognosis is influenced by malnutrition, intestinal bleeding, pseudo-obstruction due to impaired intestinal movement, and although infrequently, perforation.(11) The primary focus of treatment continues to be supportive measures for GI symptoms. However, surgical intervention becomes imperative in situations involving life-threatening haemorrhage, obstruction, or perforation.(3,7)

Conclusion

This case highlights the rare presentation of multiple myeloma and GI amyloidosis with jejunal and duodenal involvement, masquerading as chronic gastritis with poor response to treatment. We emphasise the need to maintain a high index of suspicion for GI amyloidosis while reiterating the need for early diagnosis and prompt evaluation in the context of poor prognosis associated with simultaneous occurrence of the above.

Declarations

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All authors contributed to the conceptualization of the case study. KEC and CKP contributed to the acquisition of data. KEC and CKP contributed to writing the manuscript which was supervised and reviewed by ATM and NF. All authors read and approved the final manuscript.

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CASE REPORT

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Acute inferior ST-segment elevation myocardial infarction as an initial presentation of acute pancreatitis leading to multiorgan dysfunction

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Abstract

Acute myocardial infarction associated with acute pancreatitis is an uncommon occurrence where both share inflammation as a commonality. Though, the precise mechanism behind this association remains unclear, systemic inflammatory response syndrome (SIRS) may play a role. We present a case of acute inferior myocardial-infarction with complete heart block managed with thrombolysis, later diagnosed to have acute severe pancreatitis and multiorgan dysfunction which posed a major diagnostic and therapeutic challenge. It is vital to ensure the treatment of one condition does not worsen the other.

Keywords: acute inferior myocardial infarction, acute pancreatitis, multiorgan dysfunction

Introduction

The association of STEMI with acute pancreatitis has been rarely described in literature. The precise mechanism remains unknown, but could be multifactorial. Electrocardiographic abnormalities mimicking myocardial ischaemia (pseudo-infarction) have been reported in intra-abdominal conditions, including acute pancreatitis. Electrocardiographic changes involving T-wave and ST-segment abnormalities are reported in 25% of cases of acute pancreatitis but presenting as a STEMI is very rare.(1) On the other hand, STEMI as an initial presentation of acute pancreatitis is extremely rare. It is an important cause for concern and should be immediately evaluated as it demands a different approach to treatment. Although there is no standard management protocol for these situations, administration of thrombolytic agents may cause life threatening complications based on the limited studies.(2) We recommend that coronary angiography, angioplasty and stenting should be an option in these cases. Early and accurate diagnosis is crucial to ensure appropriate management and prevent potential complications.

Case presentation

A 64-year-old woman, previously diagnosed patient with diabetes mellitus, hypertension, hypothyroidism, bilateral knee-joint osteoarthritis and dyslipidaemia presented to a peripheral hospital with cardiac-type of chest pain associated with autonomic symptoms and diagnosed to have inferior-STEMI with complete heart block. She was transferred to our hospital for further management after thrombolysis. On admission, pulse rate was 78/minute, regular,

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average volume and blood pressure was 90/60 mmHg with the support of 0.3 microgram/kg/minute noradrenaline. Her precordial, respiratory, abdominal, and neurological examinations were unremarkable. Local hospital 12-leads electrocardiography showed ST-elevation in inferior leads (II, III, aVF) with reciprocal depression in leads I and aVL and repeat ECG showed complete heart block (Figure 1 and 2).

2D-transthoracic echocardiography showed regional wall-motion dysfunction of inferior wall with moderate left ventricular systolic-dysfunction. Chest X-ray was normal. Random blood sugar at admission was 338 mg/dl and optimised with subcutaneous soluble insulin. Arterial blood gas analysis was normal and urine for ketone-bodies were negative which ruled out diabetic-ketoacidosis. Troponin-I was elevated (>80 ng/ml). There was significant reduction in ST-segment with sinus rhythm after thrombolysis with tenecteplase.

She was placed on aspirin, clopidogrel, atorvastatin, enoxaparin and thyroxin with supportive care. On day two of coronary-care unit stay, she complained of severe, continuous, generalised abdominal pain radiated to the back, associated with nausea and vomiting. Abdominal examination revealed epigastric tenderness but no organomegaly or free fluids and no features of intestinal obstruction. Results of the blood investigations are shown in Table 1.

A neutrophilic leukocytosis with acute kidney injury and raised serum inflammatory markers were

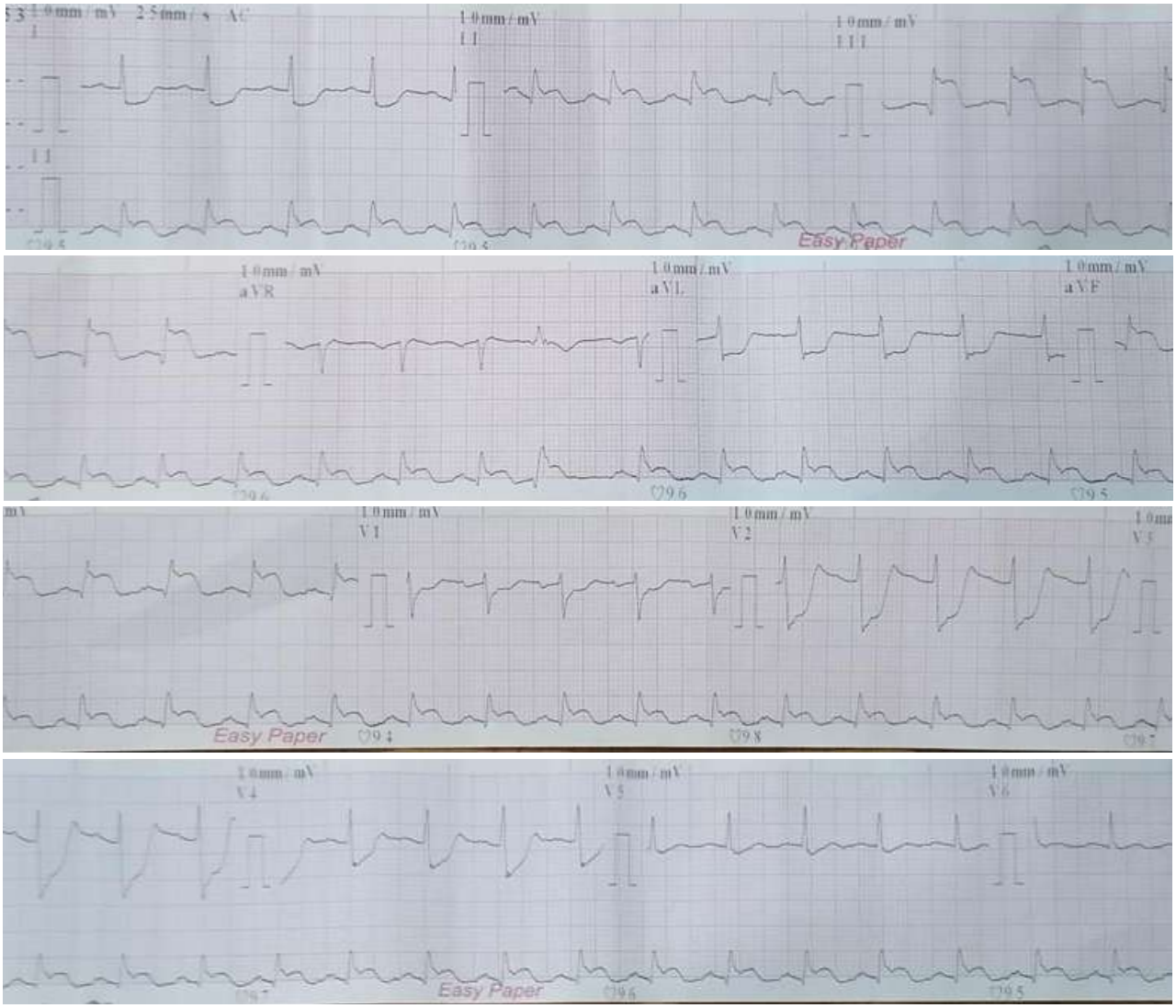

Figure 1. ST-elevation in leads II, III, aVF with reciprocal depression in leads I and aVL

observed. Liver function test was normal except for elevated transaminases possibly due to ischaemic liver injury. Serum amylase was elevated and lipase level was unavailable. Thyroid function and electrolytes including serum calcium were normal. She had low albumin level (30 g/dl) and age was above 55 years, her Glasgow-Imrie criteria scored 3points which was suggestive of high risk for severe pancreatitis. Ultrasound abdomen showed trace of free fluid in hepatorenal pouch with grade-I fatty liver. Non-contrast computed tomography of the abdomen showed a swollen pancreas with peri-pancreatic fluid and retro-peritoneal fluid suggestive of acute pancreatitis but no walled-off collection or features of perforation. The patient was managed for AMI with acute severe pancreatitis complicated with multiorgan dysfunction. She was kept nil per oral and given intravenous fluids with noradrenaline while monitoring fluid balance and vital parameters. Adequate pain relief was given with subcutaneous morphine 6 mg thrice a day given while empirical antibiotic, IV ceftazidime 1 g/thrice a day was started due to high inflammatory markers. It was later converted to IV meropenem 1g thrice a day. Serum amylase level started to drop gradually, but on the fourth day she experienced severe epigastric pain with shortness of breath. Complications of acute pancreatitis were suspected. CECT-CAP showed acute pancreatitis with focal necrosis in pancreatic-body, a CT severity index of 5 and bilateral moderate pleural effusion with passive atelectasis of lower lobes (Figure 3).

Antibiotics, thrombotic prophylaxis with enoxaparin, pain management and monitoring of vital parameters were continued and patients improved clinically and biochemically. Oral feeding was established gradually with Pancreatin with meals. Coronary angiogram showed 99% occlusion of left circumflex (LCX) artery and 90% occlusion of left anterior descending (LAD) artery with normal right coronary artery (RCA) (Figure 4).

Percutaneous coronary interventions to LCX and LAD

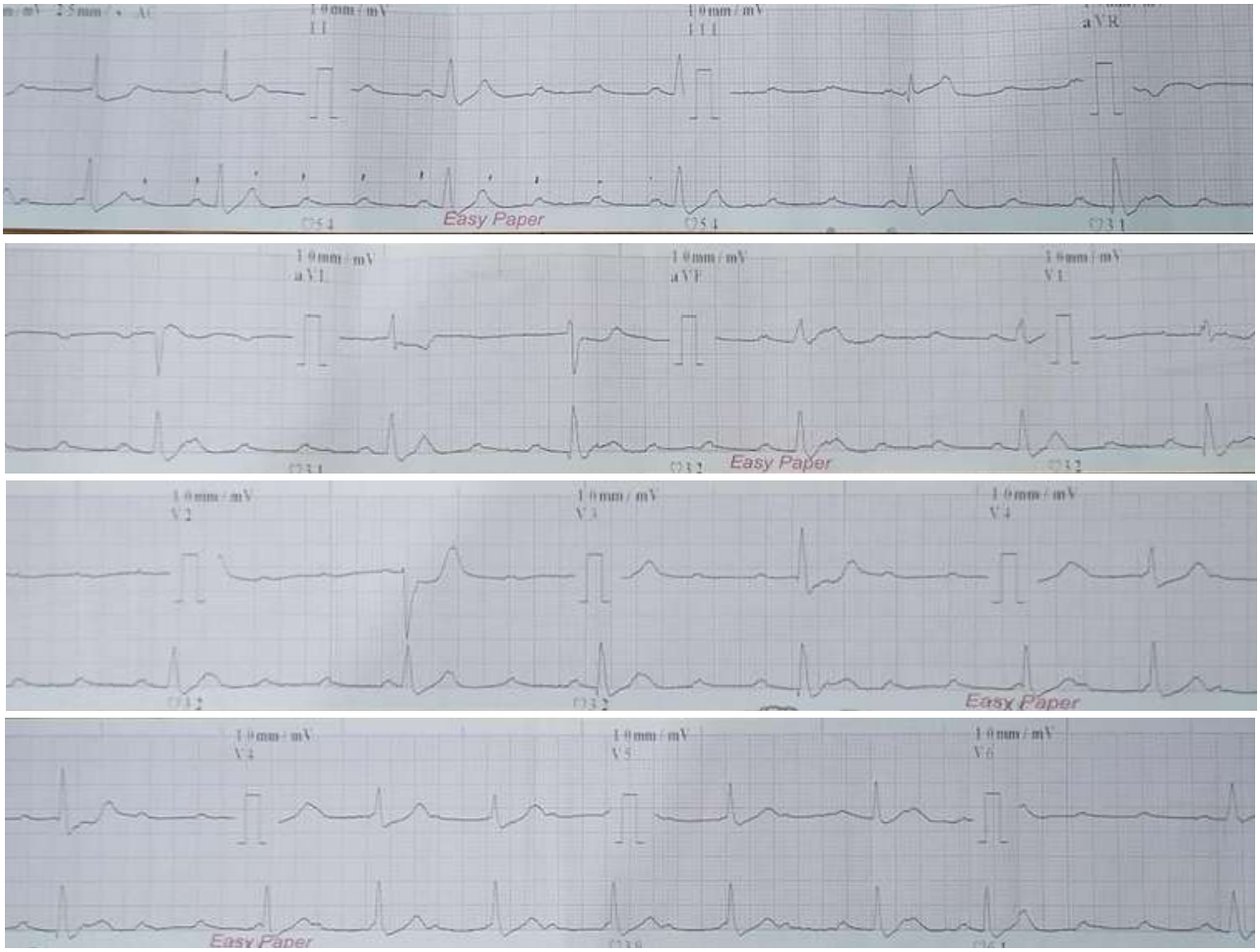

Figure 2. Complete heart block

with 3.0x15 mm and 2.75x23 mm stents were deployed respectively across the lesion. LCX and LAD had TIMI grade-4 flow. The post procedure period was uneventful. The patient was discharged from hospital on day 11 after arranging proper follow up.

Table 1. Investigation summary

Investigations	Reference range	22/02/2025	23/02/2025	28/02/2025	03/03/2025
White blood cells(10^9/l)	4-10	12.46	10.54	9.76	9.34
Neutrophil(%)	50-70	73.9	83.3	79.2	74
Lymphocyte(%)	20-40	18.1	9.7	12.3	17
Hemoglobin(g/dl)	11-15	12.3	12.5	11.8	10.6
Platelets(10^9/l)	150-450	244	173	280	244
C-reactive protein(mg/l)	0-3	4.2	308	157	46
Creatinine(micromol/L)	49-90	126	72	66	59
Alanine transaminase(U/L)	16-63	468	180	113	82
Aspartate transaminase(U/L)	15-37	1293	268	121	51
Amylase(U/L)	25-115	-	1720	365	150
Troponin-I(ng/ml)	<0.12	>80	-	-	-
NT-proBNP II(pg/ml)	<300	-	-	3140	-

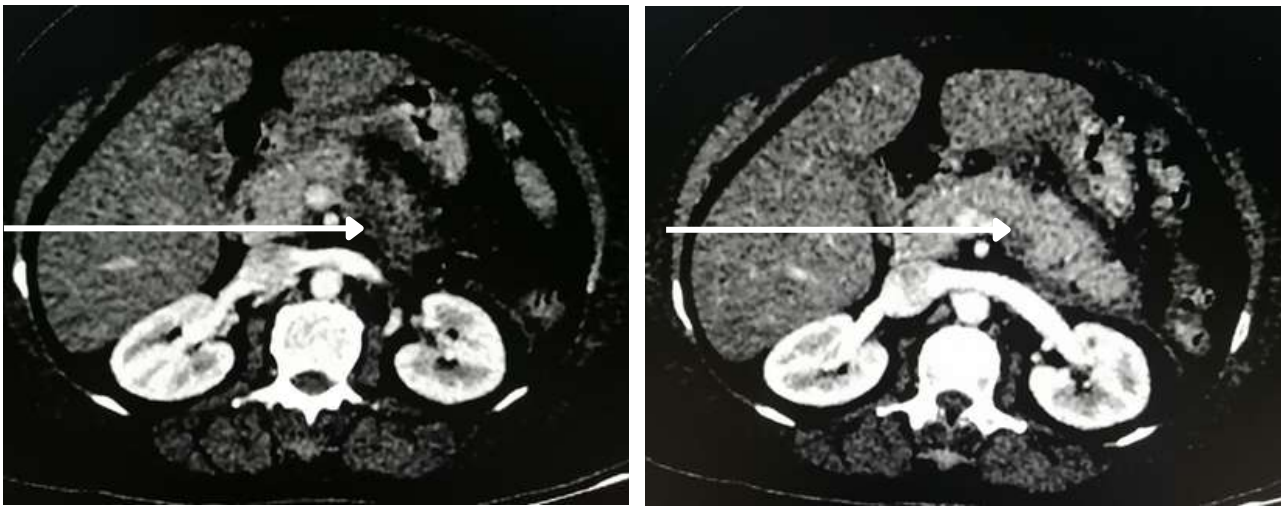

Figure 3. Abdominal computed tomography revealing diffuse pancreatic enhancement with fat stranding and focal area of hypo-enhancement in proximal pancreatic body inferiorly

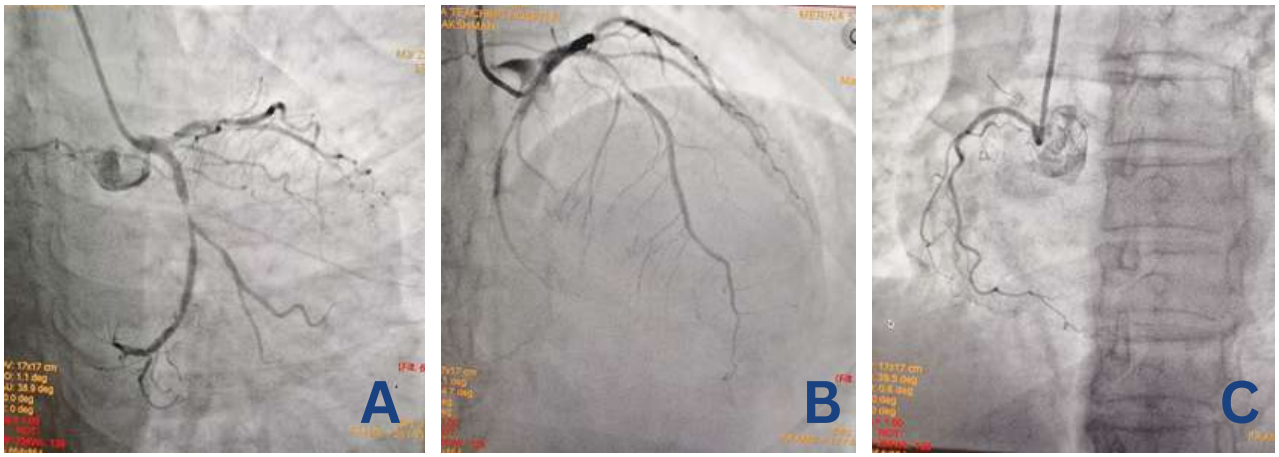

Figure 4. Coronary angiography demonstrating 99% occlusion of LCX artery (A), 90% occlusion of LAD artery (B) with normal RCA (C)

Discussion

AMI initiates an immediate inflammatory reaction, which functions to repair the heart. Besides localised inflammation in the myocardium, an increased systemic inflammatory response has been reported in patients with AMI. Indicators of systemic inflammatory response are forecasts of negative clinical outcomes, including mortality, recurrent myocardial infarction and heart failure in individuals with AMI.(3) However, acute pancreatitis initially presenting as acute myocardial infarction is extremely rare. Acute pancreatitis is an acute inflammation of the pancreas which leads to haemostatic imbalance and a temporary hypercoagulable state predisposing to thrombotic events. The similarity of certain symptoms between acute pancreatitis and AMI can lead to challenges in diagnosis. Electrocardiographic abnormalities resembling myocardial ischaemia have been documented in acute pancreatitis. Though ST-elevation in acute pancreatitis is an uncommon occurrence, ECG may exhibit arrhythmias, conduction abnormalities and variations in T-wave, QT interval and ST-segment.(4)

Many theories account for these ECG changes in acute pancreatitis including vagal reflexes, electrolyte imbalances like hyperkalaemia, hypocalcaemia, hyponatraemia and being stress-induced (Takotsubo) as well as the presence haemodynamic instability.(5) Except for being hypotensive there were no electrolyte abnormalities found in this case. Proteolytic enzymes from the pancreas, such as trypsin, may directly harm the myocyte membrane, leading to alterations in cell permeability, potential cellular necrosis and secondary electrical disturbances. These enzymes might alter platelet adhesiveness and affect the coagulation system, potentially resulting in coronary thrombosis.(6) Some research suggests an increased occurrence of cardiovascular lesions in patients with acute or chronic pancreatitis, unrelated to typical cardiovascular risk factors.(7) However, our patient had an increased risk as she was having typical cardiovascular risk factors as well. Despite angiographic or morphologic assessments in pancreatitis patients with ST-elevation showing normal coronary arteries in many instances, a cardiovascular evaluation is advised in these situations.(8) In this case, probably, RCA thrombus must have lysed due to tenecteplase given at the presentation and patient might have already had double vessel coronary artery disease as she had multiple risk factors. Acute pancreatitis associated with actual myocardial infarction is quite uncommon and familial hypertriglyceridaemia needs to be excluded in such cases.(2) Though our patient had hyperlipidaemia, she didnot fit into familial hypertriglyceridaemia category. The primary differential diagnosis of pseudo versus true-myocardial infarction is crucial as their treatment approaches vary significantly. Incorrectly given thrombolytic agents in pseudo-MI situations can lead to catastrophic consequence.(9) However,our patient had a true myocardial infarction with acute pancreatitis as a rare occurrence which posed a diagnostic and therapeutic challenge.

Management concerns encompass the selection of revascularisation treatment, the safety of antiplatelet and anticoagulant therapies, administration of

intravenous fluids, pain management and the utilisation of cardiac drugs that may possibly induce hypotension. This patient arrived with AMI and was later found to have acute severe pancreatitis with focal necrosis and improved well with intensive treatment. Although the connection between these two entities is rare, they both initiate an inflammatory cascade that leads to SIRS, a hypercoagulable state and thrombus formation which may explain this association. This patient experienced generalised abdominal pain, nausea and vomiting on the day following thrombolysis, delaying the diagnosis of pancreatitis. We emphasise that even though the occurrence of AMI as an initial presentation in acute pancreatitis is low, a straightforward blood test, serum amylase or lipase and abdominal imaging can assist in timely diagnosis if the patient exhibits relevant symptoms.

Conclusion

Coincidental symptoms of AMI and acute pancreatitis pose challenges in timely diagnosis. Although there are established treatment guidelines for AMI and acute pancreatitis, there is no standard protocol to manage the simultaneous occurrence of both conditions. The choice of revascularisation is vital and clinicians should be cautious about the safety-profile of antiplatelet and anticoagulant therapy. It requires clinical judgement to ensure that the treatment of one diagnosis does not worsen the other condition.

Declarations

Author contributions:
All authors contributed to the conceptualisation and design of the study, contributed to the acquisition of data, conducted the data analysis, contributed to data interpretation and writing of the manuscript. All authors read and approved the final manuscript.

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(1) Answer E - Squamous Cell Carcinoma

The lesion is located on the lateral aspect of the upper arm. It is a large, well-defined, irregularly shaped plaque with a hyperkeratotic and crusted surface. The central portion exhibits ulceration with eschar formation and surrounding induration, suggesting tissue necrosis. The periphery shows variable pigmentation, including hyperpigmented and hypopigmented zones, with associated scaling and signs of post-inflammatory change. The margins appear irregular with possible infiltration into surrounding tissue. Smaller satellite hyperpigmented macules are present distal to the main lesion. The color pattern is heterogeneous, with areas of reddish-brown discoloration and crusting. The lesion's location on a sun-exposed site and the morphological features raise concern for a premalignant or malignant process such as squamous cell carcinoma (SCC), especially given the central ulceration and induration. In contrast, basal cell carcinoma (BCC) typically presents as pearly or translucent nodules with rolled borders. Central ulceration may be seen in advanced cases but less keratinized. BCC is less scaly and not usually pigmented unless it is a pigmented variant.

Cutaneous anthrax typically begins as a painless papule that progresses to a vesicle, then forms a characteristic black eschar, often surrounded by marked oedema. The lesion is often painless and rapidly evolves over a few days. In contrast, the described lesion evolved slowly over 8 months, shows variable pigmentation, and has no systemic signs of toxaemia, which are common in anthrax.

Cutaneous leishmaniasis typically starts as a painless papule after a sandfly bite, evolving into a central ulcer with raised indurated margins. The lesion is usually much smaller and not hyperkeratotic or crusted to the same extent. Leishmaniasis often occurs in endemic areas and typically doesn't present with satellite macules or significant scaling.

Lupus vulgaris is a chronic form of cutaneous tuberculosis. Lesions are often reddish-brown plaques, slowly enlarging over years, commonly involving the face or neck. They show the characteristic "apple-jelly" appearance on diascopy and are often less hyperkeratotic and ulcerated. The presence of necrotic ulceration and crusting, along with the rapid progression over months, is less typical of lupus vulgaris.

(2) Answer D - Psoriasis

Multiple well-defined, discrete to coalescent plaques are noted on the anterior aspect of the shin. The lesions range in size and exhibit a violaceous to hyperpigmented hue, with several showing prominent overlying silvery-white scaling. Some plaques demonstrate evidence of lichenification, suggesting chronicity. The distribution is predominantly localised to the extensor surface. These findings are consistent with chronic plaque psoriasis.

Lichen planus classically presents with flat-topped, violaceous papules, often on the wrists, forearms, or mucous membranes, and are usually intensely itchy. Wickham striae (white reticulations) may be seen. Scaling is finer than in psoriasis, and lesions are often polygonal.

Nummular eczema presents as coin-shaped, exudative or crusted lesions often with central clearing and a weepy surface. Psoriasis plaques tend to be more chronic, with sharply demarcated, dry, scaly lesions, and more symmetry on extensor surfaces.

Prurigo nodularis is characterised by firm, discrete, itchy nodules due to chronic scratching. Typically

seen on extensor surfaces, but nodules are dome-shaped and not as scaly or coalescent as seen in psoriasis.

Tinea incognito is a fungal infection modified by corticosteroids. Lesions often have less well-defined borders, less scale centrally, and more inflammation at the periphery. Psoriasis plaques are generally more uniform with silvery-white scales.

(3) Answer B - Hypertrophic lichen planus

The image shows asymmetrically distributed dermatological lesions predominantly affecting the right lower limb. Multiple hyperpigmented, well-demarcated plaques with lichenification and scaling are evident, consistent with chronic scratching. Some lesions exhibit excoriation and areas of post-inflammatory hyperpigmentation. A few hypopigmented patches are also visible, likely representing resolving lesions or post-inflammatory changes. The left lower limb shows comparatively fewer and milder post-inflammatory alterations, with no active plaques observed. This presentation is typical of hypertrophic lichen planus (LP) with a chronic course and significant pruritus as opposed to non-hypertrophic LP which has violaceous, thick, hyperpigmented plaques. Lesions may show Wickham striae on close inspection.

Cutaneous T-cell lymphoma typically presents with patches or plaques resembling eczema or psoriasis but with slower progression. It is usually not intensely pruritic or lichenified at the onset.

Lichen simplex chronicus presents as a solitary or limited number of thickened, hyperpigmented plaques due to repeated rubbing. Hypertrophic LP is more widespread and can involve multiple sites.

Post-inflammatory hyperpigmentation refers to pigmentation changes following healing. It's not a primary lesion and lacks scaling, lichenification, or active inflammation.

Though both conditions can be itchy, psoriasis plaques are usually pink or red with silvery scales and more symmetrical in distribution.

(4) Answer B - Chikungunya infection

The woman presents with an abrupt onset of fever and joint pain lasting three days, accompanied by painful swelling of the right leg. The foot appears swollen, particularly over the dorsum and medial ankle, with shiny skin and mild erythema. These features may mimic unilateral or bilateral cellulitis. However, the combination of acute fever, arthritis, and arthralgia—especially during an outbreak—raises suspicion of chikungunya infection. Laboratory findings such as a normal white cell count and marginally low platelet count support a viral aetiology. Notably, both CRP and ESR are elevated in chikungunya fever which mimics a bacterial aetiology. During a known chikungunya outbreak, it is critical to maintain a high index of suspicion for atypical or varied manifestations of the disease.

Cellulitis typically presents as a unilateral, localised skin infection with warmth, redness, tenderness, and often systemic symptoms. However, this patient has bilateral ankle swelling, lacks marked erythema or tenderness, and has a normal white cell count, which is not typical of bacterial cellulitis.

Panniculitis refers to inflammation of subcutaneous fat, presenting as tender nodules or plaques on

the thighs or shins, and may or may not be associated with systemic symptoms. In this case, the swelling is localised to the ankles and feet, without nodules or erythematous plaques, which makes panniculitis less likely.

Gonococcal arthritis, caused by the bacteria Neisseria gonorrhoeae, often presents with migratory polyarthralgia and tenosynovitis, potentially involving multiple joints and tendons. In contrast, reactive arthritis, often triggered by infections in the urinary or digestive tract, typically manifests as an asymmetric oligoarthritis, predominantly affecting the lower limbs, and can include enthesitis.

(5) Answer B - Meningococcal septicaemia

The image displays the plantar aspect of a foot with black discoloration affecting all toes, most prominently at the distal ends, consistent with dry gangrene. The 2nd to 5th toes exhibit sharply demarcated necrosis, while the great toe is discolored but less advanced. The surrounding skin appears dry and intact, without signs of secondary infection, indicating non-wet ischaemic necrosis due to critical limb ischaemia.

Anti-phospholipid syndrome (APS) can cause thrombosis and gangrene due to hypercoagulability, but it usually presents with a history of recurrent miscarriages, arterial or venous thromboembolism, or stroke. It is rare for APS to present with acute febrile illness, hypotension, rash, and rapidly progressive peripheral gangrene. The absence of a prior thrombotic history and the acute infectious presentation argue against APS.

While rickettsial infections can present with fever and rash, peripheral gangrene is an uncommon complication. Additionally, rickettsial infections typically involve eschar formation at the inoculation site, and the rash tends to be maculopapular or petechial. Hypotension can occur in severe cases, but the extensive acral gangrene seen here is more suggestive of meningococcaemia.

Although Staphylococcus aureus bacteraemia can lead to sepsis, endocarditis, or skin/soft tissue infections, it rarely causes purpura fulminans or symmetrical peripheral gangrene. Furthermore, staphylococcal sepsis does not typically present with a widespread rash and the classical meningococcal-like haemorrhagic skin necrosis.

Thromboangiitis obliterans (Buerger's disease) is a chronic, non-infectious, inflammatory thrombotic disease usually affecting young male smokers. It typically causes chronic ischaemia of the extremities but does not present acutely with fever, rash, or hypotension. There is no infectious prodrome and no acute progression to gangrene within a few days. Hence, the acute and systemic nature of this presentation rules out Buerger's disease.

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