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Concurrent tuberculous pericarditis and lung adenocarcinoma presenting with cardiac tamponade

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Mycobacterium tuberculosis (MTB) infection and lung malignancies are both important causes of pericardial effusion (PE), particularly in developing nations such as South Africa. They are each associated with significant morbidity and mortality and pose several public health challenges for the region. This case study discussed a 58-year-old man who presented acutely with a large PE complicated by cardiac tamponade. Pericardial fluid analysis was positive for TB and further cytopathological evaluation revealed metastatic lung adenocarcinoma. Dual diagnoses are rare; however, considering the rising incidences of lung cancer and its predisposition for infectious diseases, this may be under-reported in TB endemic regions. This case highlighted the importance of considering other causes of PE that may aggravate presentation, leading to life-threatening cardiac tamponade. Further research is needed to understand the impact of rising cancer incidences and ongoing burden of infectious diseases in sub-Saharan Africa.

Contribution: The insights of this case study include the paucity of data surrounding diagnosis and treatment of lung cancer in non-smokers available for South Africa. The current data that are available is for the developed world only. Some evidence incidence might be related to exposure of biofuels, which has significance for our local population and requires more exact research.

Keywords: pericardial effusion, cardiac tamponade, tuberculosis, effusive pericarditis, lung carcinoma.

Case presentation

A 58-year-old male, human immunodeficiency virus (HIV)-negative, nonsmoker presented acutely to the authors' emergency unit with respiratory distress. He reported a 7-day history of progressive shortness of breath, fatigue and chest pain. On further systemic enquiry, he had a long-standing (> 3 months) history of dry cough, unintentional weight loss and loss of appetite. His background medical history was remarkable for dermatomyositis, hypertension, dyslipidaemia, Type 2 diabetes and morbid obesity, with a poor baseline status. He resided permanently in a care facility because of both social and medical reasons.

On presentation, he was acutely distressed with a blood pressure of 106/79 mmHg, heart rate of 118 beats per min, body temperature of 36.3 °C, respiratory rate of 35 breaths per min and oxygen saturation of 84% on room air. On physical examination, he had an elevated jugular venous pressure (JVP), bilateral basal lung crepitations, a displaced apex beat and soft, distant heart sounds.

Electrocardiogram (ECG) (Figure 1) showed a sinus tachycardia with premature atrial complexes, right bundle branch block and q waves in leads III and augmented Vector Foot (aVF). On the initial chest X-ray (Figure 2), there was significant cardiomegaly consistent with a large PE, with bilateral basal and right perihilar opacification. Echocardiography confirmed a massive PE requiring urgent side-room pericardiocentesis. Approximately 1500 mL of haemorrhagic fluid was drained, which was sent for chemistry, microscopy and cytology while a pericardial catheter was left *in situ*. A further 430 mL of haemorrhagic fluid was aspirated the following day, and the catheter was removed.

Table 1 lists the results of initial investigations. The pericardial fluid contained a red cell count of 1.621×10^{12}/L and a nucleated cell count of 5.820×10^{9}/L. There was a predominance of lymphocytes and large, atypical cells that were suspicious of malignant cells observed on fluid microscopy. The fluid chemistry showed protein of 49 g/L, albumin of 26 g/L, lactate dehydrogenase of 1620 U/L and adenosine deaminase (ADA) of 51.3 U/L. Microbiological analysis of the pericardial fluid was GeneXpert polymerase chain reaction (PCR) positive for

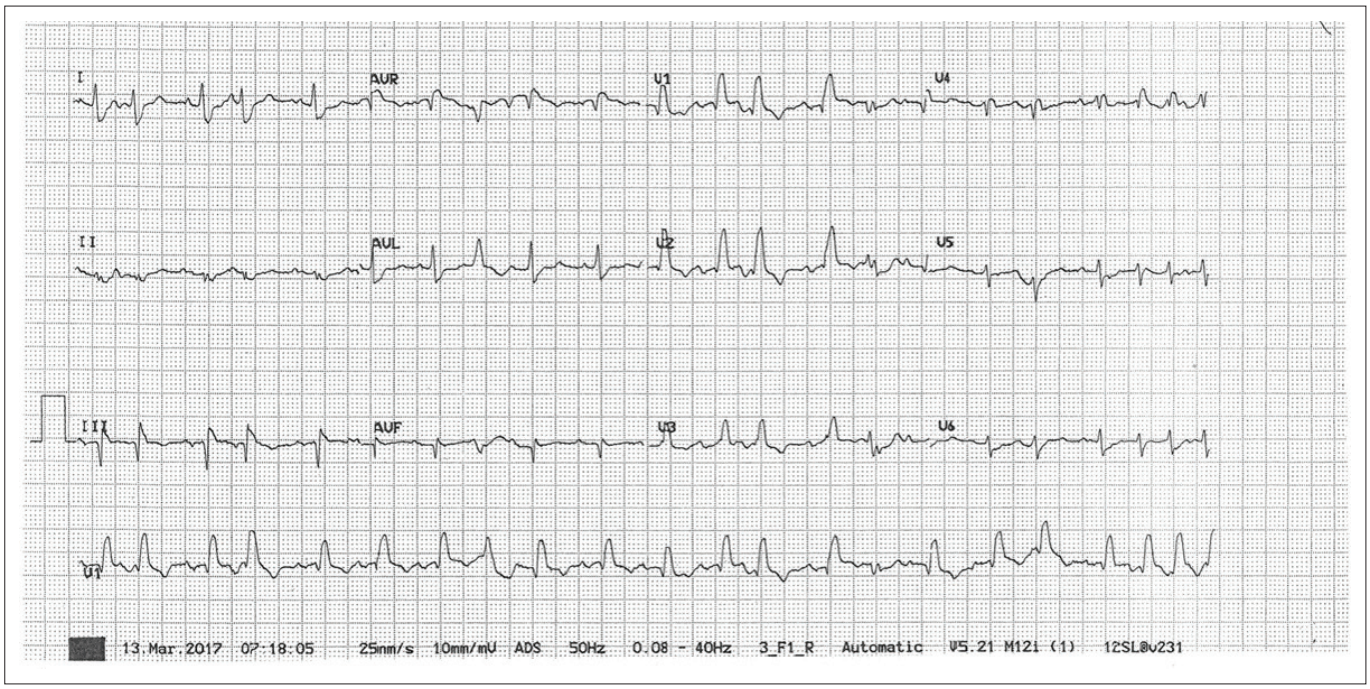

FIGURE 1: Electrocardiogram on presentation of cardiac tamponade.

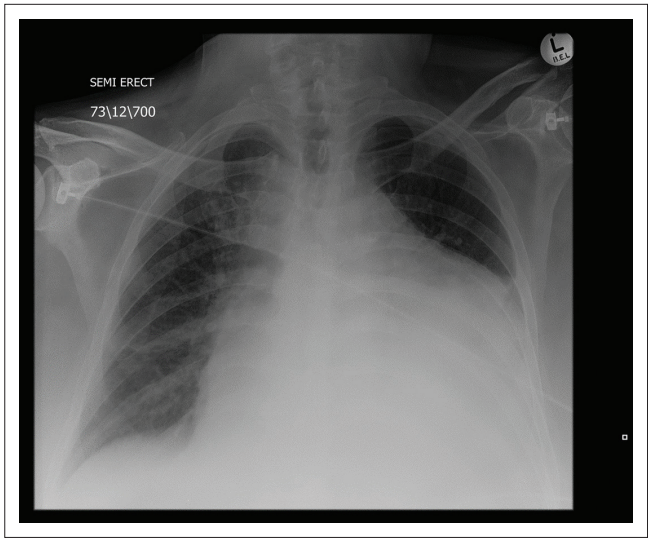

FIGURE 2: Chest X-ray on presentation showing increased cardiothoracic ratio.

TABLE 1: Initial laboratory serum values.

Diagnostic test	Serum value
White cell count	13.8
Haemoglobin	12.0
Mean corpuscular volume	92.8
Red cell distribution width	15.6
Platelet count	200
Sodium	135
Potassium	3.6
Urea	9.7
Creatinine	70
eGFR	> 60
Calcium (corrected)	2.23
Magnesium	0.68
Phosphate	0.77
C-Reactive protein	141
Troponin T	72
HbA1c	7.8%
Beta-human chorionic gonadotropin	< 1
Alpha foetoprotein	2.2
Prostate-specific antigen	0.23
Cancer antigen 125	486
Cancer antigen 19-9	1

eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin.

tuberculosis (TB), sensitive to rifampicin. The bacterial culture of the aspirated pericardial fluid showed no growth after 2 days.

Despite pericardial fluid drainage, commencement of antituberculous treatment and initiation of corticosteroids, the patient remained distressed with poor oxygen saturation. His condition continued to deteriorate over the following week, with a repeat chest X-ray (Figure 3) showing a hilar mass and bronchial tapering highly suspicious of a malignancy and a persistent but improved cardiomegaly suggesting residual PE. Subsequent cytopathological analysis of the pericardial fluid confirmed cells with morphology consistent with metastatic carcinoma in favour of lung adenocarcinoma. No immunohistochemical studies were carried out. In the light of his advanced disease and echo evidence of posterior re-accumulation of pericardial fluid (Figure 4), planned malignancy staging was deferred for referral to cardiothoracic surgery for a palliative pericardial window; however, the patient demised shortly thereafter.

Discussion

Pericardial effusion (PE) is a commonly occurring medical condition with clinical manifestations ranging from incidental small effusions to large, life-threatening cardiac tamponade.[1,2] Early identification of the underlying aetiology has major therapeutic and prognostic implications; however, the aetiologies of PE are diverse and vary

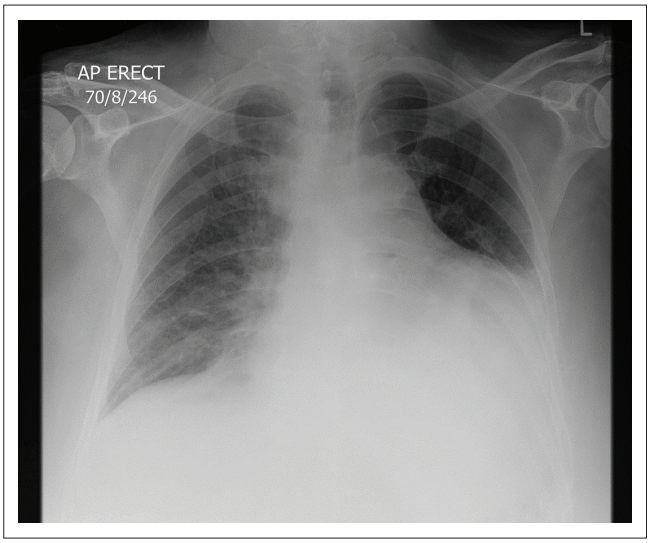

FIGURE 3: Repeat chest X-ray showing recurrent pericardial effusion.

according to geographical location.[3] In the developing world, TB is the offending agent in most cases, further driven by the HIV pandemic in regions such as sub-Saharan Africa. In the Western world, cases of PE are more likely to be idiopathic because of postviral infection or malignancy related.[4] However, the disease landscape in Africa is changing, with cancer death rates on the continent now surpassing TB, acquired immunodeficiency syndrome (AIDS) and malaria combined and an expected 85% increase in cancer incidence predicted in sub-Saharan Africa by 2030.[5,6] As such, malignancy-related PE will become more prevalent, and early identification and diagnosis are critical.

Tuberculous pericarditis (TBP) remains a severe form of extrapulmonary TB. In the HIV-infected population, TB is the cause of PE in the overwhelming majority of patients and often associated with more aggressive disease as a result of disseminated TB infection.[7] The presentation of TBP may be variable, and often nonspecific systemic symptoms such as fever, fatigue, night sweats and weight loss are the primary complaint.[8] Definitive TBP diagnosis has posed several challenges, particularly in high-burden areas where inexpensive rapid testing is needed. Pericardial fluid culture is the most widely used diagnostic tool; however, results are dependent on the bacillary yield, which may be affected in concomitant HIV infection.[9] A two-test approach with Xpert MTB/Rif followed by either biochemical tests for ADA or interferon-gamma (IFN-γ) offers high sensitivity and specificity where there is diagnostic uncertainty.[10,11] Still, in resource-limited settings where advanced testing is restricted, TBP may be difficult to distinguish from several other important causes of PE. As such, in regions with a high TB burden, clinicians often start anti-TB treatment empirically,[12] despite some evidence to suggest higher associated morbidity and mortality with empiric therapy.[13] In South Africa, where TB is still the leading cause of PE and prevalence rates of up to 70% have been reported,[14] other potential aetiologies may be neglected. In addition, in developing nations where cost effectiveness dictates investigative capacity, the diagnosis of TBP is sometimes a presumptive one.[15]

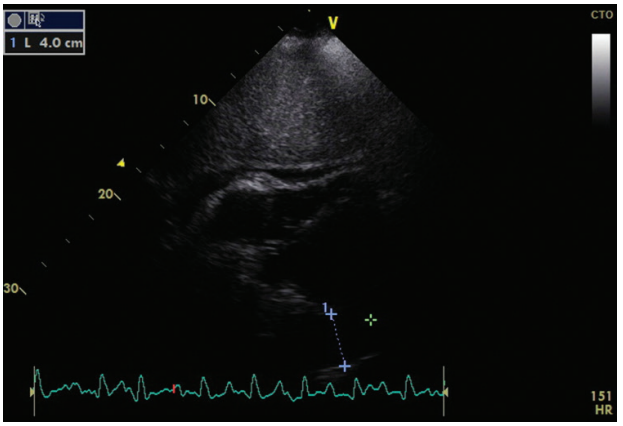

FIGURE 4: Echocardiography image of re-accumulation of pericardial fluid posteriorly.

In an oncology patient, there are several mechanisms by which a PE may present.[16] Four primary mechanisms are described: (1) direct extension or metastatic spread via lymphatics or blood into the pericardium, (2) complication of systemic tumour (radiation and chemotherapy toxicity), (3) opportunistic infections as a result of immunosuppression therapy and (4) derangements in renal and/or cardiac and/or liver function because of antineoplastic therapy.[16,17,18,19] Rarely is symptomatic PE or even cardiac tamponade the first manifestation of an occult malignancy.[20] In most cases, malignant disease has already been established, and the PE is a sign of disease progression, with a 5-year survival in advanced disease of almost zero.[17,21,22] Sanchez-Enrique et al. reported cardiac tamponade to be most commonly associated with malignant effusive pericarditis (MEP), more than any other diagnostic category of PE.[23] As such, a diagnosis of malignancy is an important exclusion in cases of acute pericardial disease with cardiac tamponade.[18,24]

Lung cancer is the most common cancer involving the pericardium.[16,17,23,25] Non–small cell lung cancers with an anaplastic lymphoma kinase (ALK) gene rearrangement are particularly likely to involve the pericardium or present with PE.[26] These mutations are associated with specific clinical features including younger age at diagnosis, nonsmokers and adenocarcinomas at histology. In the last decade, there have been great advances made into genetic testing and systemic therapies for molecular subgroups of patients with advanced disease.[27] In the developed world, therapies targeted at specific mutations have been developed and implemented with improved outcomes. It would be of great value to look at the genetic profiles of these tumours locally; however, there is a paucity of data for the African population, thus limiting the advancement of personalised therapy. These are important considerations locally, as lung cancer ranks as the number one cause of cancer-related deaths in South Africa.[28]

The co-existence of lung malignancies and TB infection has been well described. However, extrapulmonary manifestations of TB such as TBP and concurrent lung malignancies are more complex and less well-known. Considering the high prevalence

of both conditions in South Africa, the dual diagnosis of TBP and MEP may be underdiagnosed because of poor outcomes with limited survival data.

This case demonstrates the rare presentation of an undiagnosed metastatic lung malignancy in a nonsmoking patient, with simultaneous extrapulmonary TB presenting in cardiac tamponade. In addition, his pre-existing inflammatory condition of dermatomyositis may have put him at risk for developing a PE. There is also a known association between dermatomyositis and the development of malignancies, specifically lung malignancies in male patients.[29] Sadly, because of the advanced stage of his disease at presentation and poor baseline status, any further therapeutic intervention was limited.

South Africa is facing a 'colliding of epidemics' of smoking, TB and HIV, increasing the likelihood of concurrent lung malignancies and TBP.[28] There is some epidemiological evidence that suggests a bidirectional relationship between Lung Ca and TB, with risk for TB significantly higher in patients with lung Ca, and lung Ca risk significant in those with prior pulmonary TB.[30,31] Several gaps exist in current data surrounding cancer epidemiology and concomitant infections from developing nations, particularly from the African continent. Further research is needed in the region to guide cancer prevention strategies and local guidelines informing clinical practice and improve overall management of these patients.[32]

Learning points

- Sub-Saharan Africa faces a disproportionate burden of disease, with high rates of infectious diseases such as TB and HIV continuing and the disease burden attributable to cancer rising.
- Tuberculosis and malignancy are the commonest causes of cardiac tamponade but may present in a similarly nonspecific manner, posing several diagnostic challenges.
- Clinicians should maintain a high index of suspicion in patients with poor response to anti-TB treatment presenting with cardiac tamponade.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

K.N, S.D., Q.S.-H. and M.N contributed equally to this work.

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Ethical considerations

This research was submitted as part of a sub-study approved by the University of Cape Town Human Research Ethics Committee (HREC) (ref. no. 570/2021). Written informed consent was obtained from the patient.

Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Disclaimer

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