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CASE REPORT
Cardiac imaging

Constrictive pericarditis masquerading as hepatic sequestration crisis in a patient with sickle cell disease: a case report

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Background Constrictive pericarditis is a challenging diagnosis that is easily overlooked. Worldwide, tuberculosis (TB) is the leading cause; however, in the developed countries pericarditis and cardiac surgery are common aetiologies. Medical therapy can be sufficient in specific aetiologies preventing progression of constriction and thus surgery.

Case summary A young student from Nigeria, with established sickle cell disease, presented with hepatomegaly and features of right heart failure. Following multiple investigations for hepatomegaly and pyrexia of unknown origin he was initially treated for hepatic sequestration crisis. After readmission with ongoing pyrexia, he was noted to have features of constrictive physiology on cardiac imaging. Constrictive pericarditis, secondary to TB, was suspected based on the patient's background and clinical features. He was empirically commenced on anti-TB therapy after a positive interferon-gamma release assay test; *Mycobacterium tuberculosis* was later isolated in sputum cultures. He made a successful recovery with full radiological resolution of constrictive features on follow-up cardiac imaging.

Discussion Constrictive pericarditis remains an elusive diagnosis in the context of coexisting medical problems. Revisiting the presentation and imaging helped in establishing the diagnosis. It is a potentially curable cause of diastolic heart failure with good outcomes if diagnosed and managed early. We were able to successfully manage the patient for TB constrictive pericarditis on medical therapy alone without surgical intervention.

Keywords Constrictive pericarditis • Hepatomegaly • Sickle cell disease • Tuberculosis • Case report

Learning points

- Constrictive pericarditis commonly presents with features of right heart failure including raised jugular venous pressure, peripheral oedema, and hepatomegaly. A high index of suspicion has to be maintained in the context of coexisting medical conditions so that it is not overlooked as a differential.
- Although pericardiectomy is seen as definite management, medical therapy can a be suitable alternative with good outcomes.

Introduction

Constrictive pericarditis can be an elusive diagnosis. Its rarity, long symptom-free period, non-specific symptoms, and patient's coexisting medical problems can all complicate the presentation leading to delayed or missed diagnosis.[1–3] Constrictive pericarditis can develop following any pericardial disease processes; however, in the developed world it commonly occurs following idiopathic or viral pericarditis, post-cardiac surgery, or post-radiation therapy.[4] In contrast, tuberculosis (TB) is a leading cause of constrictive pericarditis in the

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developing world with estimates suggesting 31.65 cases per 1000 person years.[5]

We describe the case of a young student from Nigeria with established sickle cell disease (SCD) who underwent multiple investigations for hepatomegaly prior to diagnosis of constrictive pericarditis secondary to TB. He made a successful recovery on medical therapy without surgical intervention. This case highlights the challenges in establishing a diagnosis of constrictive pericarditis when the presentation is complicated by coexisting medical conditions.

Timeline

Time	Events
Two weeks prior to presentation	Treated for hepatic sequestration crisis in Nigeria
Day 0	Presented with peripheral oedema and hepatomegaly
Day 3	Red cell exchange transfusion performed to treat hepatic sequestration crisis
Day 5	Discharged with planned outpatient follow-up by haematology team
Day 11	Readmitted from outpatient clinic for ongoing pyrexia
Day 17	Radiological evidence of anterior mediastinal lesion and pericardial thickening on computed tomography pulmonary angiogram
Day 21	• Further red cell exchange for hepatic sequestration • Constrictive pericarditis confirmed radiologically with cardiac magnetic resonance imaging (CMR)
Day 26	Interferon-gamma release assays positive suggesting *Mycobacterium tuberculosis* involvement
Day 32	Empirical treatment initiated for tuberculosis
Day 39	Discharged with outpatient follow-up under haematology, respiratory, and cardiology
Day 112	Sputum culture isolated *M. tuberculosis*
Day 205	Full resolution of pericardial constriction physiology on transthoracic echocardiogram and CMR

Case presentation

A 19-year-old university student presented to the emergency department with bilateral pitting oedema. Hailing originally from Nigeria, he had recently been treated there for presumed hepatic sequestration on a background of homozygous SCD. He was otherwise well and independent in activities of daily living.

Vital signs on admissions were blood pressure 105/60 mmHg, heart rate 80 b.p.m, respiratory rate 21 b.p.m, oxygen saturation 96% on ambient air, and temperature 36.2°C. Focused examination revealed scleral icterus, vesicular breath sounds, massive non-tender hepatomegaly, inguinal lymphadenopathy, elevated jugular venous pressure with Kussmaul's sign, and bilateral pitting oedema up to the scrotum. Laboratory investigations noted patient to be anaemic, haemoglobin 76 g/L (125–180 g/L), with elevated lactate dehydrogenase 411 U/L (<225 U/L) and reticulocyte count 343×10^9/L ($25–85 \times 10^9$/L). His liver profile was abnormal with bilirubin 82 µmol/L (<21 µmol/L), alkaline phosphatase 260 U/L (20–130 U/L), and alanine aminotransferase 57 U/L (<41 U/L). C-reactive protein was elevated to 94 mg/L (<1 mg/L) with white cell count of 11.5×10^9/L ($4–11 \times 10^9$/L). An electrocardiogram showed sinus rhythm with T wave inversion in precordial leads V1–V4. Chest radiograph (CXR) revealed cardiomegaly with a right-sided pleural effusion (*Figure 1*).

An ultrasound of the abdomen excluded portal vein thrombosis but confirmed a large echogenic liver extending into the left upper quadrant. Furthermore, a computerized tomography (CT) of the abdomen noted hepatomegaly extending down to the iliac crest. Consistent with these features, the patient was treated for hepatic sequestration crisis and underwent red cell exchange transfusion. He was also commenced on broad spectrum antibiotics for pyrexia with no clear foci of infection. He was discharged after symptomatic improvement and a period of apyrexia with planned follow-up and investigation including transthoracic echocardiogram (TTE).

Unfortunately, he shortly represented for ongoing pyrexia. Initial investigations failed to identify an infective focus. Investigations for pulmonary complications of SCD included a CT pulmonary angiogram which showed no evidence of pulmonary embolism. However, it identified an anterior mediastinal soft tissue lesion with lymphadenopathy and a thickened pericardium raising suspicion for constrictive pericarditis. TTE did show features of constriction physiology with a significant global pericardial thickening, septal bounce, and tethered myocardial contraction, but unfortunately full assessment for pericardial constriction was not done at the time (*Figure 2*). Further assessment with a cardiac magnetic resonance imaging (CMR) confirmed pericardial thickening with signs of inflammatory constrictive pericarditis including dilated vena cava, septal bounce, and interventricular interdependence (*Table 1*).

Based on the patient's background, non-resolving pyrexia, imaging features, and persistent hepatomegaly, a diagnosis of constrictive pericarditis, most likely secondary to TB, were strongly suspected. Whilst awaiting results of cultures, empirical treatment for TB was initiated based on positive interferon-gamma release assays. Although hepatic sequestration may have had a role to play in this patient's initial presentation, constrictive pericarditis secondary to TB was considered the unifying diagnosis. He was discharged with anti-TB medications (rifampicin 600 mg, isoniazid 300 mg, pyrazinamide 1500 mg, ethambutol 800 mg) with a view to pericardiectomy, if he failed to respond to medical therapy. Shortly after discharge, sputum cultures isolated *Mycobacterium tuberculosis* confirming the hypothesis. He made a successful recovery on anti-TB therapy (4 months intensive phase followed by 3 months of continuation phase) with full resolution of pericardial thickening and a reduction in hepatomegaly

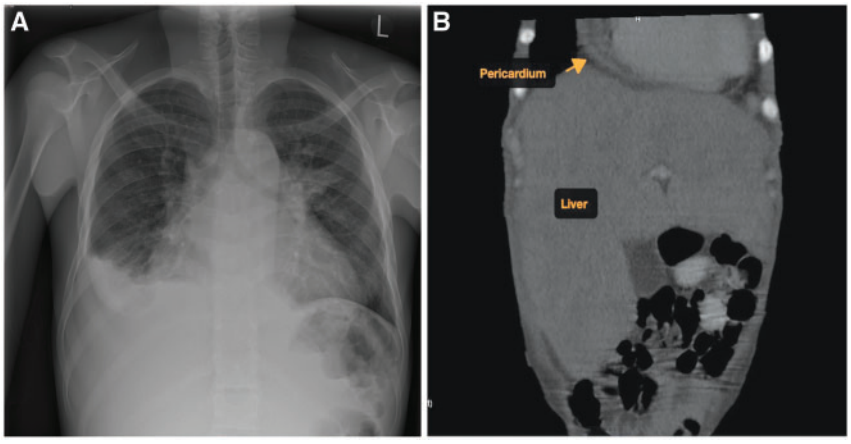

Figure 1 Initial investigations at presentation. (*A*) Chest radiograph demonstrating cardiomegaly with moderate pleural effusion on the right lung. (*B*) A computed tomography scan demonstrating massive hepatomegaly; a thickening pericardium can be partially seen.

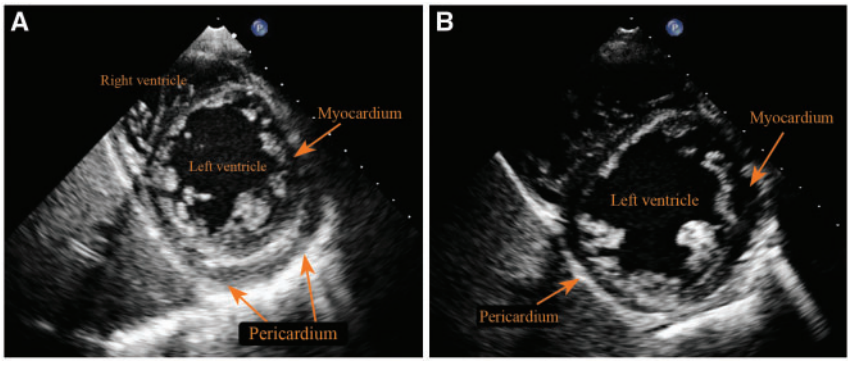

Figure 2 Transthoracic echocardiogram before and after treatment. (*A*) Short axis view of the heart depicting thickened pericardial layer. (*B*) Repeat echocardiogram in short axis view, Day 83 after discharge, showing significantly improved pericardial layer.

at Day 167 post-discharge (*Figure 3*). At his most recent review, 1 year and 9 months after admission, he was discharged from clinic with no further planned follow-up.

Discussion

Constrictive pericarditis is the encasement of the heart due to fibrosis or calcification with resultant impaired diastolic function. It is a challenging diagnosis with patients often undergoing multiple investigations prior to appropriate management; in some cases it is only diagnosed after death.[1] Indeed, the presenting features of constrictive pericarditis can mimic other causes including lung and liver disease. Hepatic involvement is observed in 10–40% of SCD crises and hepatomegaly can be a common presenting feature.[6] In our case, the patient was treated for hepatic sequestration crisis initially but on reflection had features of constrictive pericarditis.

The European Society of Cardiology (ESC) recommends that all patients with suspected constrictive pericarditis should undergo a CXR and a TTE; these modalities are readily available and non-invasive.[4] The CXR features include pericardial calcification and pleural effusion.[4] The diagnostic features of constrictive pericarditis on TTE is well established in the literature and restrictive ventricular filling a key characteristic.[7] Nonetheless, diagnosis based on imaging alone can be difficult if the clinical narrative does not raise suspicion for constrictive pericarditis. Although a standard TTE can comment on systolic dysfunction or valvular disease, a 'constrictive pericarditis protocol' focusing on ventricular septum, mitral annular/inflow velocities, and variation in the hepatic vein profile maybe necessary.[8] In our case, the initial TTE was performed without full assessment for pericardial constriction and only after retrospective review of the images, by an imaging specialist, was constrictive pericarditis considered as a unifying diagnosis. Respiration-related ventricular septal shift is the

Table 1 Relevant radiological investigations with pertinent findings in chronological order

Investigations	Findings
CXR (*Figure 1*)	• Cardiomegaly; cardiothoracic ratio 66% • Right sided moderate pleural effusion
US Abdomen	• Hepatomegaly extending into the left upper quadrant • Normal flow direction in portal vein • Normal flow in the hepatic artery and hepatic vein
CT Abdomen (*Figure 1*)	• Massive hepatomegaly extending down to iliac crest • Marked thickening of the pericardium
TTE (*Figure 2*)	• Normal left ventricular systolic function; ejection fraction 58% • Grade II diastolic dysfunction • Respiratory variation in ventricular filling • Marked pericardial thickening
CMR (*Figure 3*)	• Marked pericardial thickening • Increased signal and late gadolinium hyperenhancement of the pericardium • Homogenous soft tissue in left anterior mediastinum 6 x 4.9 cm that is insinuated around anterior surface of pulmonary artery and aortic arch; in continuum with thickened pericardium • Consolidation in upper lobe left lung

CMR, cardiac magnetic resonance imaging; CT, computed tomography; CTPA, CT pulmonary angiography; CXR, chest radiograph; MRI, magnetic resonance imaging; TTE, transthoracic echocardiogram; US, ultrasound.

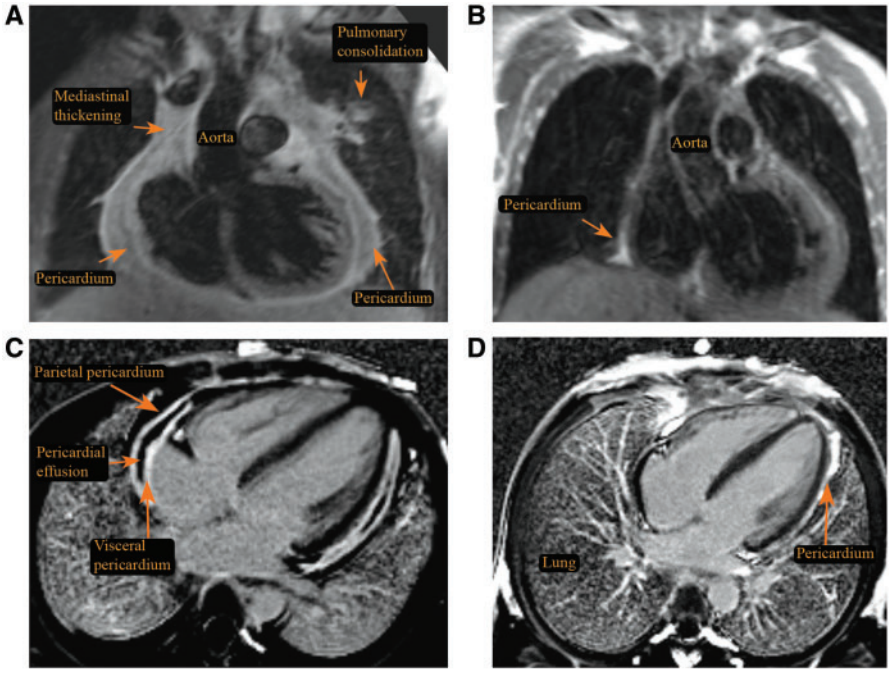

Figure 3 Cardiac magnetic resonance imaging before and after treatment. (*A*) Cardiac magnetic resonance imaging showing thickened pericardium in continuum with mediastinal thickening. (*B*) Cardiac magnetic resonance imaging after treatment, at Day 167 post-discharge, depicting resolution of pericardial thickening. (*C*) Late gadolinium hyperenhancement showing thickening of all layers of pericardium with small pericardial effusion. (*D*) Cardiac magnetic resonance imaging after treatment, at Day 167 post-discharge, with no significant late gadolinium hyperenhancement.

most sensitive finding on TTE and it was observed upon review.[7] This occurs as a result of the unyielding pericardium which forces the ventricular septum to adjust to maintain cardiac output; where the ventricular septum shifts towards the left in inspiration and towards the right in expiration allowing increased right ventricular filling. CT/CMR is not required for diagnosis but can offer more information to support the diagnosis as in this case. Although imaging and clinical features of constrictive pericarditis were present, the absence of a strong clinical suspicion of constrictive pericarditis along with coexisting SCD meant that constrictive pericarditis was initially overlooked as a diagnosis.

The ESC recognize that medical therapy does play a role in managing specific aetiologies (e.g. TB) as well as transient constrictive pericarditis.[4] To date, there is no randomized controlled trial looking at early pericardiectomy vs. surgery for patients with failed medical therapy. Pericardiectomy is the gold standard for chronic constrictive pericarditis; however, it is associated with significant mortality and morbidity.[9,10] Our patient improved on anti-TB medications alone with radiological resolution of constrictive pericarditis approximately 5 months after discharge.

Conclusion

Constrictive pericarditis is a challenging diagnosis in the context of coexisting medical problems. Our patient was initially thought to have hepatic sequestration crisis but on reflection had features of constrictive pericarditis. Revisiting the presentation and cardiac imaging with a high index of suspicion allowed us to diagnose and initiate appropriate medical treatment for tuberculous constrictive pericarditis preventing progression of constriction and thus surgery.

Lead author biography

Dr Zafraan Zathar, BMBS BSc, graduated from University of Southampton, UK. During his medical school he intercalated in Medical Science with Surgery and Anaesthesia at Imperial College London where his research looked at endomicroscopy for use in breast cancer surgery. He completed his Foundation Programme at Sandwell and West Birmingham NHS Trust during which he developed an interest in cardiology. He has published and presented at various forums as well as winning prizes for his quality improvement projects. He hopes to pursue a career in cardiology and continue his academia alongside his clinical commitments.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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