ESC European Society of Cardiology
European Heart Journal - Case Reports
doi:10.1093/ehjcr/ytaa496

CASE REPORT
Heart failure

Effusive-constrictive cholesterol pericarditis: a case report

Simran Shergill *, James Davies , and Naomi Cairns

Cardiology Department, South Warwickshire NHS Foundation Trust, Lakin Road, Warwick CV34 5BW, UK

Received 9 June 2020; first decision 21 July 2020; accepted 18 November 2020

For the podcast associated with this article, please visit https://academic.oup.com/ehjcr/pages/podcast

Background Cholesterol pericarditis (CP) remains a rare pericardial disease characterized by chronic pericardial effusions with high cholesterol concentrations with or without the formation of cholesterol crystals. Effusions are often large and can cause ventricular compression and subsequent pericardial adhesion formation. CP can be idiopathic but has associations with rheumatoid arthritis (RA), tuberculosis and hypothyroidism.

Case summary We present a case of a 72-year-old male with a background of seropositive RA with a finding of an incidental pericardial effusion on computed tomography thorax abdomen and pelvis. Transthoracic echocardiogram demonstrated a large effusion with echocardiographic features of tamponade. On review, he was breathless with a raised venous pressure, bilateral ankle oedema, and pulsus paradoxus was present. Pericardial drainage was performed with fluid analysis demonstrating a cholesterol concentration of 8.3 mmol/L and numerous cholesterol crystal formation. Interval imaging demonstrated recurrence of the effusion with pericardial thickening and progressive constriction. He remained asymptomatic and underwent a successful pericardial window. At present, he is under close clinical outpatient surveillance with symptoms guiding a future pericardiectomy if warranted.

Discussion CP can present as an emergent situation with signs and symptoms of acute heart failure with prompt pericardiocentesis required in cases of clinical tamponade. However, the disease course is often one of chronicity with relapsing large effusions that tend to recur following drainage, with the development of pericardial constriction necessitating pericardiectomy for definitive management.

Keywords Cholesterol pericarditis • Tamponade • Effusive-constrictive pericarditis • Pericardial effusion • Pericardiectomy • Rheumatoid arthritis • Case report

Learning points

- Cholesterol pericarditis (CP) is characterized by chronic, large pericardial effusions that often reaccumulate following percutaneous drainage.
- Pericardiectomy is recommended as a safe and effective treatment for symptomatic cases of effusive-constrictive CP who have failed medical therapy.

* Corresponding author. Tel: +44 1926 495 321, Email: simran.shergill@nhs.net
Handling Editor: Hajnalka Vágó
Peer-reviewers: Monika Arzanauskaite and Arif Anis Khan
Compliance Editor: Gemina Doolub
Supplementary Material Editor: Ross Thomson

Introduction

Cholesterol pericarditis (CP) is a rare pericardial disease characterized by chronic effusions with high pericardial fluid cholesterol concentrations with or without the formation of cholesterol crystals.[1] First described in 1919 by Alexander as having a 'gold-paint' appearance[2]; effusions are often large with associated ventricular compression and subsequent pericardial adhesion formation.[3] We present a case of effusive-constrictive CP with clinical and echocardiographic features of tamponade in a patient with established rheumatoid arthritis (RA).

Timeline

Date	Event
November 2019	Finding of an incidental encysted pericardial effusion on computed tomography thorax abdomen and pelvis.
Day 0	Transthoracic echocardiogram (TTE)—large pericardial effusion; maximum depth 38 mm with evidence of tamponade.
Admission Day 1	Patient review: dyspnoea, bilateral ankle oedema, and raised venous pressure. Pulsus paradoxus noted with electrocardiogram demonstrating low-voltage complexes.
+6 h	Pericardiocentesis with 400 mLs of dark haemoserous fluid drained.
Day 3	TTE—small rim of effusion and pericardial drain removed. Cholesterol pericarditis confirmed with high fluid cholesterol concentration and crystal formation.
Day 7	TTE—reaccumulation of pericardial fluid; 18 mm anterior to right heart. Discharged with planned surveillance echocardiograms.
Day 20	TTE—new features of constriction and mid-diastolic right ventricular collapse. Admitted for clinical review.
Admission Day 20–24	Patient asymptomatic. Raised venous pressure with no ankle oedema. Computed tomography thorax demonstrated thickened pericardium of 4.8 mm. Referred for pericardial window.
1 month	TTE—ongoing constrictive features with prominent septal bounce and hepatic vein diastolic flow reversal. Patient remained asymptomatic.
3 months	Pericardial biopsy and window performed at regional cardiothoracic centre.
Present day	Symptom surveillance in the cardiology outpatients.

Case presentation

A 72-year-old Caucasian male under investigation for macroscopic haematuria underwent a computed tomography thorax abdomen and pelvis and was found to have an incidental encysted pericardial effusion (*Figure 1*). Past medical history included seropositive RA managed on anti-tumour necrosis factor α (TNFα) therapy for over 7 years. Additionally, he had a previous surgically excised rhabdomyosarcoma, exogenous steroid-related adrenal suppression, and benign bladder polyps. He was an ex-smoker with a 100-pack year history and there was a strong family history of malignancy in both his parents. Medication history on admission included weekly etanercept injections and hydrocortisone 20 mg o.d.

Urgent transthoracic echocardiogram (TTE) demonstrated a large pericardial effusion (*Figure 2*) with a small right ventricular (RV) cavity and impaired long-axis systolic function. There was evidence of right atrial systolic and RV mid-diastolic free-wall collapse with a dilated and non-compliant inferior vena cava (Supplementary material online, *Video S1*). Given the concerning features of tamponade, he was admitted for urgent clinical assessment and management.

On questioning, he reported mildly increased shortness of breath on exertion with no associated chest pain or orthopnoea. On examination, his wrists demonstrated ulnar deviation with chronic swan neck and boutonnière deformities of the digits, but no active synovitis. Venous pressure was elevated to the mid-neck with mild pitting oedema to the ankles. Heart sounds were quiet with no added sounds and lung fields were clear. Blood pressure on arrival was 142/89 mmHg with a 11 mmHg systolic fall on inspiration. A 12-lead electrocardiogram demonstrated right axis deviation, anterior Q-waves, and low voltage complexes (*Figure 3*).

He underwent urgent pericardial drainage via the subxiphoid approach under ultrasound guidance. The drain was easily inserted without complication and 400 mLs of dark haemoserous fluid was drained. TTE confirmed resolution of the RV free-wall collapse and his pulse waveform had recovered. Pericardial fluid analysis demonstrated an elevated cholesterol count of 8.3 mmol/L (normal; 0.5–1 mmol/L) (*Table 1*). No malignant cells were present on microscopy but numerous cholesterol crystals, foamy xanthomatous macrophages, and giant cells were seen. Extended blood profile during admission showed a total cholesterol of 5 mmol/L (normal; <4 mmol/L) and a new diagnosis of type II diabetes with a haemoglobin A1c of 122 mmol/mol (normal: <42 mmol/mol).

The diagnosis of CP was made and TTE conducted 48 h later demonstrated a small rim of pericardial fluid with the drain subsequently removed. Colchicine 500 μg b.i.d. was commenced, and a urology consult was obtained given the self-limiting episode of haematuria; no definite evidence of malignancy was identified on review of the imaging. TTE prior to discharge (4 days following drain removal) demonstrated recurrence of the effusion; 18 mm anterior to the right heart with no free-wall collapse and a preserved RV longitudinal systolic function (Supplementary material online, *Video S2*). Symptomatically the patient had improved and was discharged with planned surveillance TTEs.

Two weeks later, he attended for a repeat TTE which demonstrated a stable effusion size but new RV free-wall late-diastolic collapse and mild constrictive features with inspiratory septal flattening and pericardial thickening (Supplementary material online, *Video S3*).

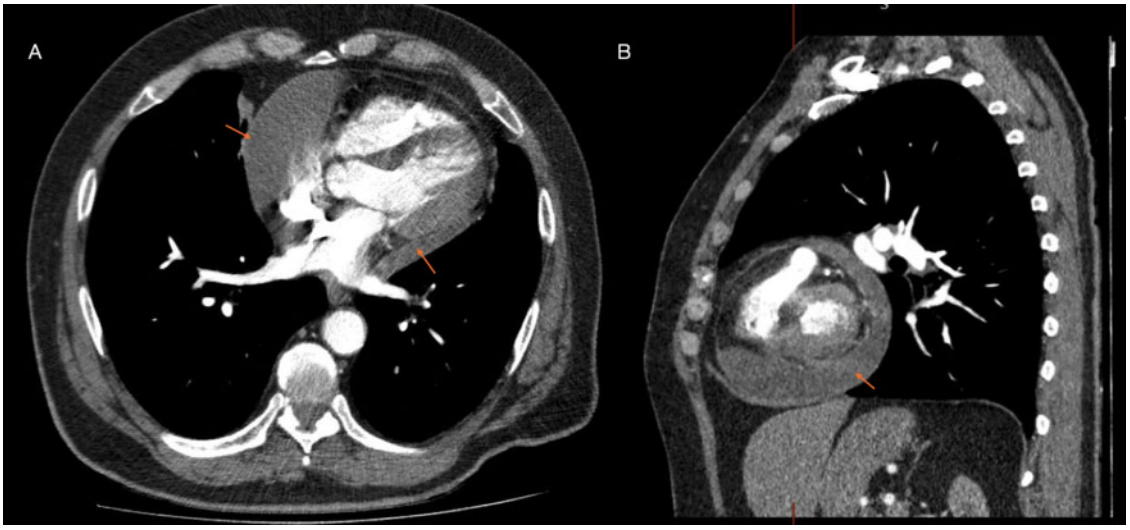

Figure 1 Contrast enhanced computed tomography thorax abdomen and pelvis in arterial phase with soft tissue windowing demonstrating the incidental encysted pericardial effusion (arrowed) in axial plane (*A*) and sagittal plane (*B*).

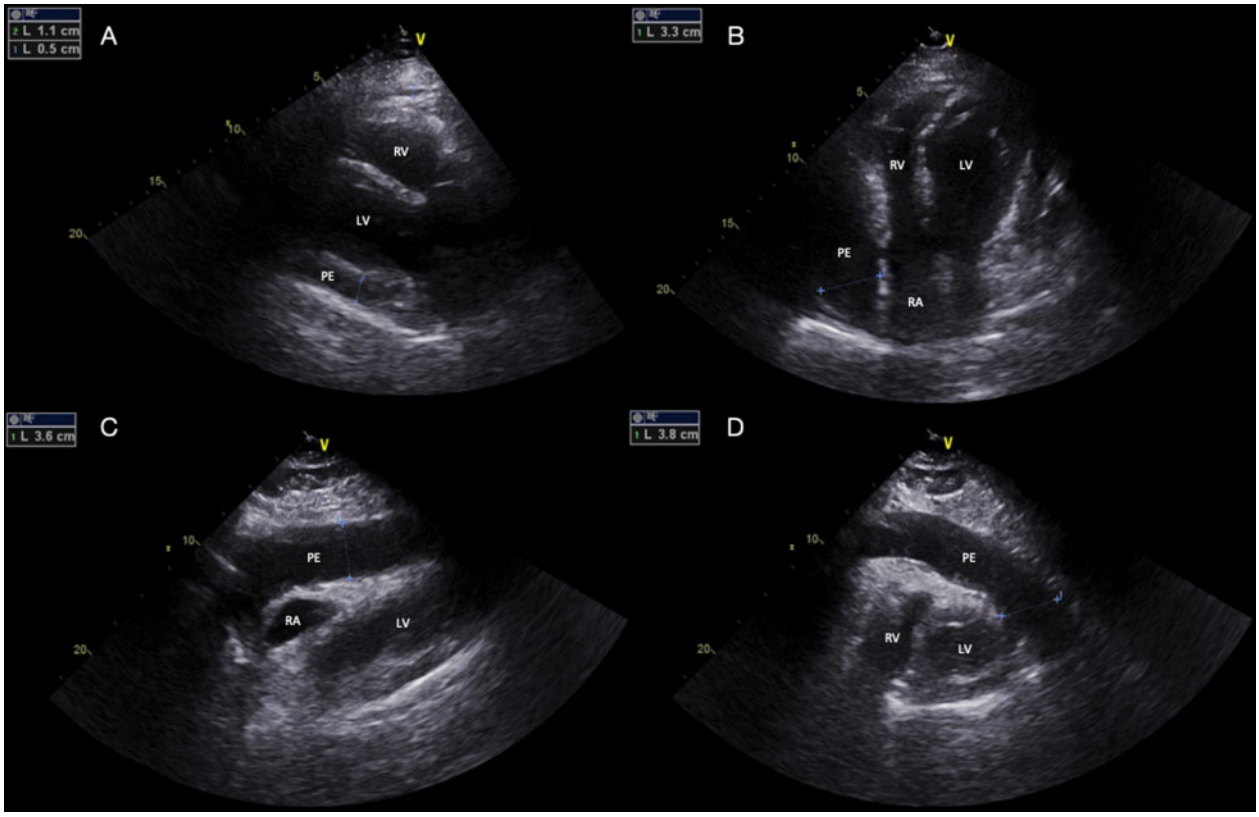

Figure 2 Transthoracic echocardiogram demonstrating the large pericardial effusion dimensions. (*A*) Parasternal long-axis with 11 mm posterior to the left ventricle. (*B*) Apical four-chamber with 33 mm anterior to right atrium. (*C*) Subcostal window with 36 mm anterior to right ventricle. (*D*) 38 mm apically in subcostal SAX.

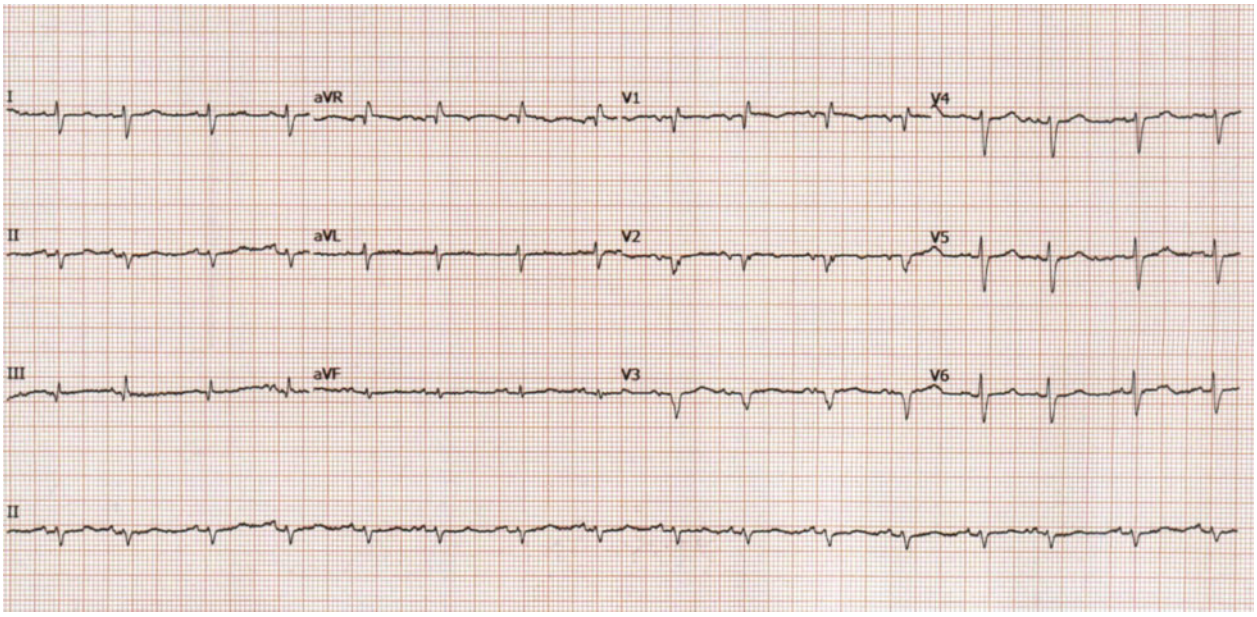

Figure 3 Admission electrocardiogram demonstrating sinus rhythm, anterior Q-waves, right axis deviation, and low voltage complexes.

Table 1

Pericardial fluid analysis	Results
Macroscopic appearance	Opaque watery brown fluid
White blood cells	Nil seen
Gram stain	Organisms not seen
Culture	No growth after 48 hours incubation
Acid fast bacilli	Negative
Glucose	11.3mmol/L
Total protein	52 g/L
Lactate dehydrogenase	Haemolysed
Cholesterol	8.3mmol/L

Computed tomography thorax demonstrated a thickened pericardium of 4.8 mm with a distorted cardiac border against the visceral pericardium suggesting a loss of compliance (*Figure 4*). On assessment, he was asymptomatic with no change in exercise capacity and haemodynamically stable with no evidence of pulsus paradoxus. Venous pressure was raised at 6 cm with no peripheral oedema. Prednisolone 30 mg o.d. was commenced alongside colchicine and he was discharged given his clinical stability. Given the constrictive features he was planned for a pericardial window.

Further surveillance TTEs demonstrated progressive constrictive features with a thickened pericardium of 5 mm posterior to the left ventricle, prominent septal bounce and dilated hepatic veins with diastolic flow reversal (Supplementary material online, *Video S4*). Ongoing echocardiographic evidence of ventricular compression was seen, yet the patient remained asymptomatic with no clinical evidence of tamponade.

Our patient underwent a pericardial window in the coming months. On table transoesophageal echocardiogram confirmed a large anterior collection with a thickened pericardium. An upper midline subxiphoid approach with a 2 cm diameter window was created. Multiple adhesions over the ventricles were noted and 300 mL of turbid yellow fluid was drained. Histopathological examination revealed a fibrotic pericardium with granulation tissue and haemosiderin deposits. He remained clinically stable and was discharged with ongoing follow-up in the cardiology clinic, with symptoms guiding a future pericardiectomy if warranted.

Discussion

In 49% of cases, CP tends to be idiopathic, whilst other cases have been attributed to RA, tuberculosis, and hypothyroidism.[4,5] Less commonly associations exist with renal polycytosis, heart failure, myocardial infarction and metastatic carcinomas.[4,5] In our clinical case, no evidence of malignancy was identified; making his RA, although quiescent the most likely underlying aetiology. A diagnostic aid in CP is the finding of pericardial fluid cholesterol levels greater than 1.8 mmol/L; significantly more than standard 0.5–1 mmol/L with associated cholesterol crystal formation on microscopy.[6] In our case, the clinical course, elevated pericardial cholesterol concentration and cholesterol crystals on histopathological examination allowed the diagnosis to be made.

During first presentations of CP, patients tend to develop signs and symptoms of heart failure with fatigue, dyspnoea, and chest pain predominating. The disease course is one of chronic, large effusions[7] that accumulate slowly over time, often allowing them to be haemodynamically well tolerated by the patient. As seen in our case, prompt pericardiocentesis is required in cases of clinical tamponade but

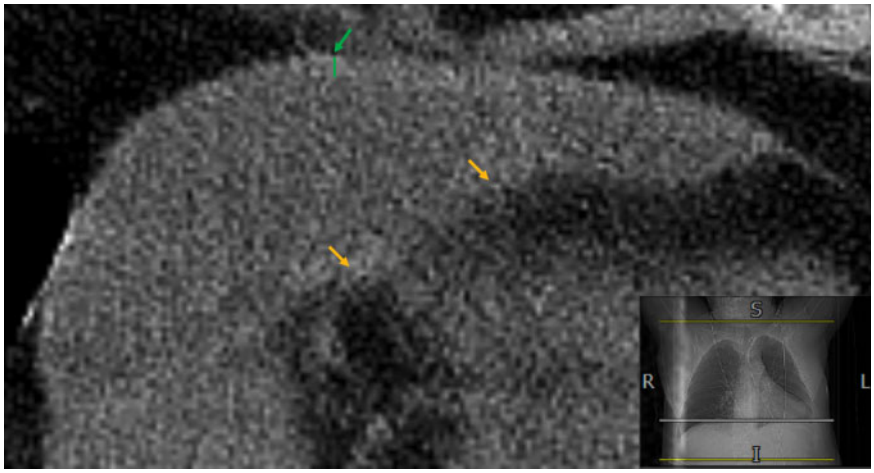

Figure 4 Interval unenhanced computed tomography thorax with soft tissue windowing in axial plane demonstrating the thickened parietal pericardium of 4.8 mm (arrowed green) and distorted cardiac border against the visceral pericardium (arrowed orange).

seldom the definitive management with effusions often reaccumulating.[4,8]

Rarely, effusive-constrictive CP can develop; hallmarked by tense effusions causing ventricular compression and adherence of the visceral pericardium to the heart.[3] Diagnosis requires persistently elevated right atrial pressures following decompression of the associated effusion.[9] Echocardiographic evidence of constriction with associated tamponade and the operative findings of a thickened, fibrotic pericardium with adhesion formation strengthens our diagnosis of effusive-constrictive CP.

The management of any underlying disease process is important to firstly address in cases of CP; a case of massive effusion and tamponade secondary to subclinical hypothyroidism was treated successfully with thyroxine supplementation.[10] However, the long-term management often warrants surgical intervention in cases of chronic and relapsing CP. The most effective means of surgical management remains a pericardiectomy.[11] In our case, the patient was receiving high intensity anti-TNFα therapy and with recurrent effusions, ventricular compression and pericardial constriction, surgical intervention was necessary.

The European Society of Cardiology Task Force recommend pericardiectomy as a safe and effective first-line treatment in cases of chronic effusive-constrictive pericarditis for symptomatic relief and reduction of relapses in cases of failed medial therapy.[12] Historically, pericardiectomy for constrictive pericarditis carried a high morbidity and mortality,[13] however advances in surgical techniques now quote an operative mortality of 6–12%.[14] Complete pericardiectomy is often a challenging procedure; requiring extensive sharp dissections of the visceral pericardium to allow adequate ventricular motion; however, it remains an effective means of definitive treatment.[15]

As a physician, careful patient selection is key; cases of chronic and symptomatic CP with class III-IV heart failure should be considered for pericardiectomy.[12] In our case, the patient was symptom free and haemodynamically stable; therefore, a pericardial window was opted for until significant symptoms develop to warrant a more complete, yet extensive surgical procedure.

Conclusion

CP is a chronic relapsing condition that should be considered as part of the differential in patients presenting with recurrent episodes of pericarditis with associated large effusions. Pericardiocentesis provides short-term relief with surgical intervention often warranted for definitive management to allow freedom from the sequelae of pericardial constriction and heart failure alongside control of any underlying disease process.

Lead author biography

Dr Simran Shergill graduated from the University of Birmingham in 2015. He completed his MRCP in 2018 and is currently working as a Cardiology Specialty Doctor at South Warwickshire NHS Foundation Trust.

Supplementary material

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

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

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

Funding: none declared.

References

1. Brawley RK, Vasko JS, Morrow AG. Cholesterol pericarditis. Considerations of its pathogenesis and treatment. *Am J Med* 1966;**41**:235–248.
2. Alexander JS. A pericardial effusion of "gold-paint" appearance due to the presence of cholesterin. *BMJ* 1919;**2**:463–463.
3. Fernandes F, Vieira GS, Arteaga E, Ianni BM, Pêgo-Fernandes P, Mady C. Cholesterol pericarditis. A specific but rare cause of pericardial disease. *Arq Bras Cardiol* 2001;**76**:393–394.
4. Adamson VW, Slim JN, Leclerc KM, Slim AM. A rare case of effusive constrictive cholesterol pericarditis: a case report and review. *Case Rep Med* 2013;**2013**:1–2.
5. Camprubí M, Mercé J, Raventós A. Pericardial constriction secondary to cholesterol pericarditis. *Rev Esp Cardiol* 2006;**59**:289–290.
6. Noiri E, Itoh T. Disorder of pericardial fluid cholesterol metabolism in cholesterol pericarditis. *Jpn J Med* 1991;**30**:393–393.
7. Barcin C, Yalcinkaya E, Kabul HK. Cholesterol pericarditis associated with rheumatoid arthritis: a rare cause of pericardial effusion. *Int J Cardiol* 2013;**166**:e56–e58.
8. González Raya A, Avivar Oyonarte C, Benayas Bellido P. Massive pericardial effusion with cardiac tamponade secundary to cholesterol pericarditis. *Clin Lab* 2012;**7**:817–820.
9. Sagristà-Sauleda J, Angel J, Sánchez A, Permanyer-Miralda G, Soler-Soler J. Effusive–constrictive pericarditis. *N Engl J Med* 2004;**350**:469–475.
10. Setty NS, Sadananda KS, Nanjappa MC, Patra S, Basappa H, Krishnappa S. Massive pericardial effusion and cardiac tamponade due to cholesterol pericarditis in a case of subclinical hypothyroidism: a rare event. *JACC* 2014;**63**:1451.
11. Pino RB, Santiago MO, Álvarez EI. Cholesterol crystals in pericardial effusion. *Clin Chim Acta* 2019;**493**:S221.
12. Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J*et al.*; ESC Scientific Document Group. ESC Guidelines for the diagnosis and management of pericardial diseases: the Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2015;**36**:2921–2964.
13. Creech JO, Hicks JW, Snyder HB, Erickson EE. Cholesterol pericarditis; successful treatment by pericardiectomy. *Circulation* 1955;**12**:193–198.
14. Chowdhury UK, Subramaniam GK, Kumar AS, Airan B, Singh R, Talwar S *et al.* Pericardiectomy for constrictive pericarditis: a clinical, echocardiographic, and hemodynamic evaluation of two surgical techniques. *Ann Thorac Surg* 2006;**81**:522–529.
15. Khandaker MH, Schaff HV, Greason KL, Anavekar NS, Espinosa RE, Hayes SN *et al.* Pericardiectomy vs. medical management in patients with relapsing pericarditis. *Mayo Clin Proc* 2012;**87**:1062–1070.