ESC HEART FAILURE
ESC Heart Failure 2021; **8**: 4313–4317
Published online 26 June 2021 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.13470

CASE REPORT

A rare cause of effusive–constrictive pericarditis

Andrea S. Giordani[1], Monica De Gaspari[2], Anna Baritussio[1]*, Stefania Rizzo[2], Elisa Carturan[2], Cristina Basso[2], Massimo Napodano[1], Luca Testolin[3], Renzo Marcolongo[4†] and Alida L.P. Caforio[1†]

[1]*Cardiology, Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padova, Via Giustiniani 2, Padova, 35128, Italy;* [2]*Cardiac Pathology, Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padova, Padova, Italy;* [3]*Cardiac Surgery, Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padova, Padova, Italy; and* [4]*Haematology and Clinical Immunology, Department of Medicine, University of Padova, Padova, Italy*

Abstract

Effusive–constrictive pericarditis (ECP) is an uncommon diagnosis, frequently missed due to its heterogeneous presentation, but a potentially reversible cause of heart failure. A 62-year-old Caucasian male presented with remittent right heart failure and mild–moderate pericardial effusion. Following an initial diagnosis of idiopathic pericarditis, indomethacin was started, but the patient shortly relapsed, presenting with severe pericardial effusion and signs of cardiac tamponade, requiring pericardiocentesis. ECP was diagnosed on cardiac catheterization. Cardiac computed tomography showed non-calcified, mildly thickened and inflamed parietal pericardium. Pericardiectomy was performed with symptoms remission. On histological examination of pericardium, chronic non-necrotizing granulomatous inflammation was noted. Polymerase chain reaction assay was positive for non-tuberculous mycobacteria. This case represents a rare finding of ECP with unusual presentation due to atypical mycobacteriosis in a non-immunocompromised patient and in a non-endemic area. Pericardiectomy can be an effective option in cases unresponsive to anti-inflammatory treatment, even in the absence of significant pericardial thickening or calcification.

Keywords Effusive–constrictive pericarditis; Pericardiocentesis; Pericardiectomy; Cardiac tamponade; Non-tuberculous mycobacteria

Received: 8 April 2021; Revised: 27 May 2021; Accepted: 31 May 2021
**Correspondence to: Dr Anna Baritussio, Cardiology, Department of Cardiac, Thoracic and Vascular Sciences and Public Health, University of Padova, Via Giustiniani 2, 35128 Padova, Italy. Email: anna.baritussio@aopd.veneto.it*
† These authors shared last authorship.

Introduction

We present the case of a 62-year-old Caucasian immunocompetent man who was diagnosed with effusive–constrictive pericarditis (ECP) at his third hospital admission, without any imaging finding of pericardial calcifications. The patient was successfully treated with pericardiectomy after failure of anti-inflammatory drugs. Of note, despite negative microbiological cultures on both pericardial and pleural effusion, a molecular diagnosis of non-tuberculous mycobacteriosis was made on pericardial biopsy. This case is intriguing because it shows the heterogeneous clinical spectrum of ECP in the same patient, who presented twice with subacute right-sided heart failure and afterwards with pending pericardial tamponade requiring pericardiocentesis. Moreover, our case demonstrates the complexity of ECP diagnosis that requires invasive haemodynamic assessment and cannot be excluded only by absence of pericardial calcification at cardiac imaging. Lastly, mycobacterium infection diagnosis was achieved only by histological examination followed by molecular analysis of the pericardium; otherwise, it would have almost certainly been missed, especially because the majority of patients with mycobacterial infections are immunocompromised, as opposed to our patient.

Case report

A 62-year-old Caucasian man presented to the Emergency Room (ER) because of 4 months lasting worsening dyspnoea. He was an active smoker and had no relevant co-morbidities. Six months before, he had suffered a motorbike accident with head and thoracic trauma, not requiring surgical intervention; after that, he did not suffer any physical limitation and returned to active life. At admission, physical examination

was remarkable for bilateral jugular distension, pulmonary base percussion dullness, symmetric leg oedema, and hydrocele. Electrocardiogram showed sinus rhythm with flattened T waves in inferior and lateral leads. Chest X-ray demonstrated bilateral pleural effusion. An abdominal ultrasound revealed ascites (15 mm perihepatic fluid). Transthoracic echocardiography (TTE) showed mild left ventricular (LV) dysfunction (ejection fraction 47%), moderate circumferential pericardial effusion (maximum thickness 15 mm) with no signs of tamponade, and dilated inferior vena cava. Cardiac magnetic resonance (CMR) confirmed mild LV impairment and pericardial effusion without evidence of pericardial thickening. A thoracoabdominal computed tomography (CT) showed reactive lymph nodes in the mediastinum; mild enhancement of the pericardial layers was reported. Blood chemistry showed slightly elevated C-reactive protein, normal brain natriuretic peptide, and negative Quantiferon test. Because influenza A swab resulted positive, the patient was diagnosed with viral polyserositis and treated with Oseltamivir. At discharge, pericardial effusion was mild (maximum thickness 8 mm at TTE). After 1 month, the patient presented again to the ER with signs and symptoms of right ventricular (RV) failure. A repeat TTE showed severe pericardial effusion (maximum thickness 23 mm) with initial signs of tamponade, so a pericardiocentesis was performed (350 cc, bloody effusion) (*Figure 1*, Supporting Information, *Video S1*). Microbiological analysis on pericardial fluid was negative. A repeat CMR showed mild pericardial effusion with no evidence of myocardial or pericardial late gadolinium enhancement (*Figure 2*); a total-body positron emission tomography-CT scan only showed mild hypermetabolic activity at left pulmonary base together with pleural effusion, with no cardiac involvement. At cardiac catheterization, the 'dip-and-plateau' pattern (*Figure 3A*) and increased right atrial pressure (17 mmHg, *Figure 3B*) after pericardiocentesis were consistent with ECP. A thoracentesis was performed to

Figure 1 Transthoracic echocardiogram: diastolic (A) and systolic (B) parasternal long-axis views showing moderate pericardial effusion with initial proto-diastolic collapse of the right ventricle (red star).

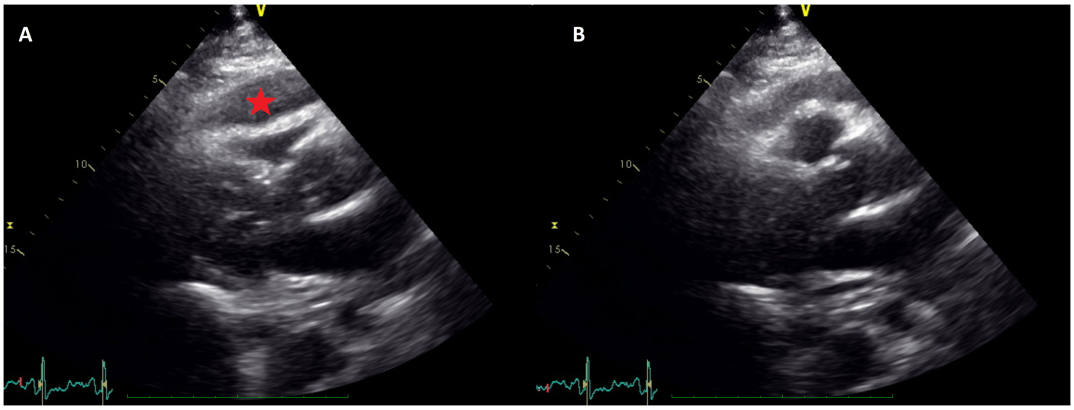
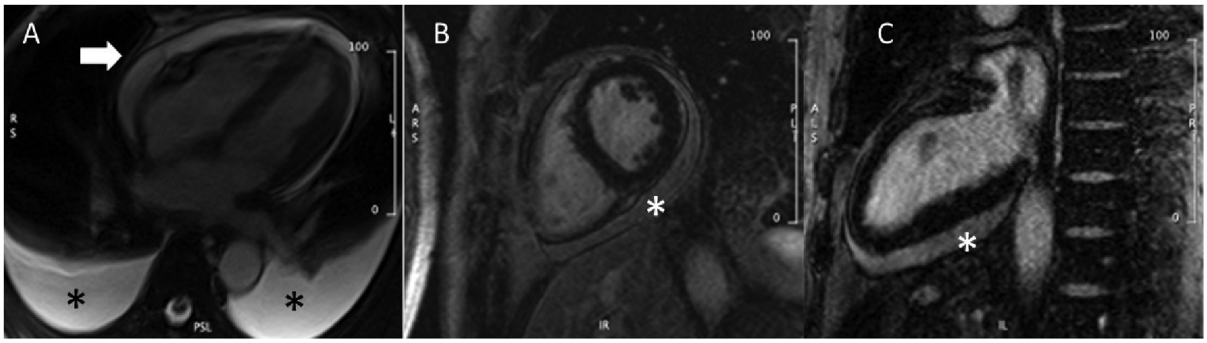
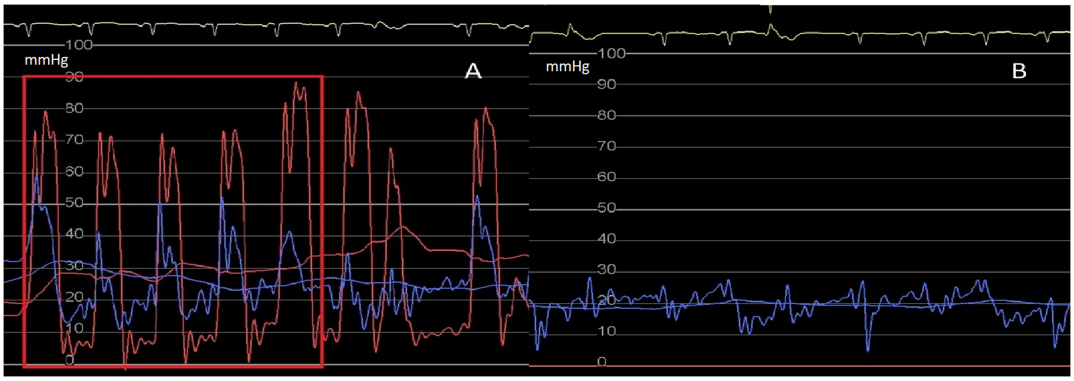


Figure 2 Cardiovascular magnetic resonance: four-chamber cine sequence showing circumferential pericardial effusion (A, white arrow) and bilateral pleural effusion (A, black asterisk). Mid-cavity short-axis (B) and two-chamber long-axis T1-weighted post-contrast sequences (C) showing circumferential pericardial effusion with proteinaceous characteristics (white asterisks) and absence of myocardial and pericardial late gadolinium enhancement.



DOI: 10.1002/ehf2.13470

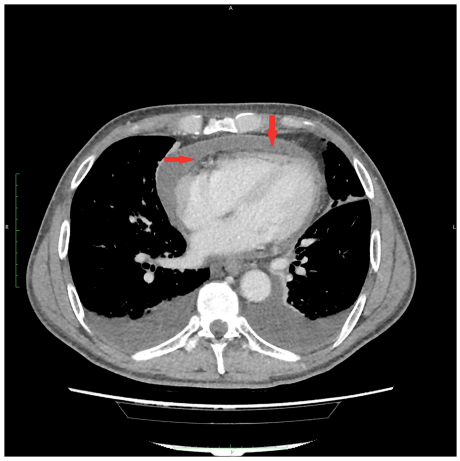
Figure 3 Cardiac catheterization after pericardiocentesis shows combined left ventricular (A, red line) and right ventricular (A, blue line) catheterization. The red box highlights the 'dip-and-plateau' pressure pattern (otherwise known as the 'square root sign'). Right atrium catheterization (B) shows persistently elevated right atrial pressure after pericardiocentesis (medium pressure: 17 mmHg).



drain right pleural effusion, and microbiological analysis on pleural fluid resulted negative. The patient was successfully treated with indomethacin and discharged.

Five months later, he presented again to the ER because of RV failure. A TTE showed moderate pericardial effusion; a cardiac CT showed mild thickening and inflammation of parietal pericardium, without calcification (*Figure 4*). After Heart Team evaluation, the patient underwent pericardiectomy with complete symptoms remission. At histological examination, pericardial thickening with non-necrotizing granulomas including rare giant cells was noted (*Figure 5*). A polymerase chain reaction (PCR) assay was positive for non-tuberculous mycobacteria. Microbiological cultures on pericardial effusion were negative. The patient is nowadays totally asymptomatic and is regularly followed up at our outpatient clinic.

Figure 4 Cardiac computed tomography: thickening of parietal pericardium (arrows), with no evidence of pericardial calcification. Bilateral pleural effusion is also present.



Discussion

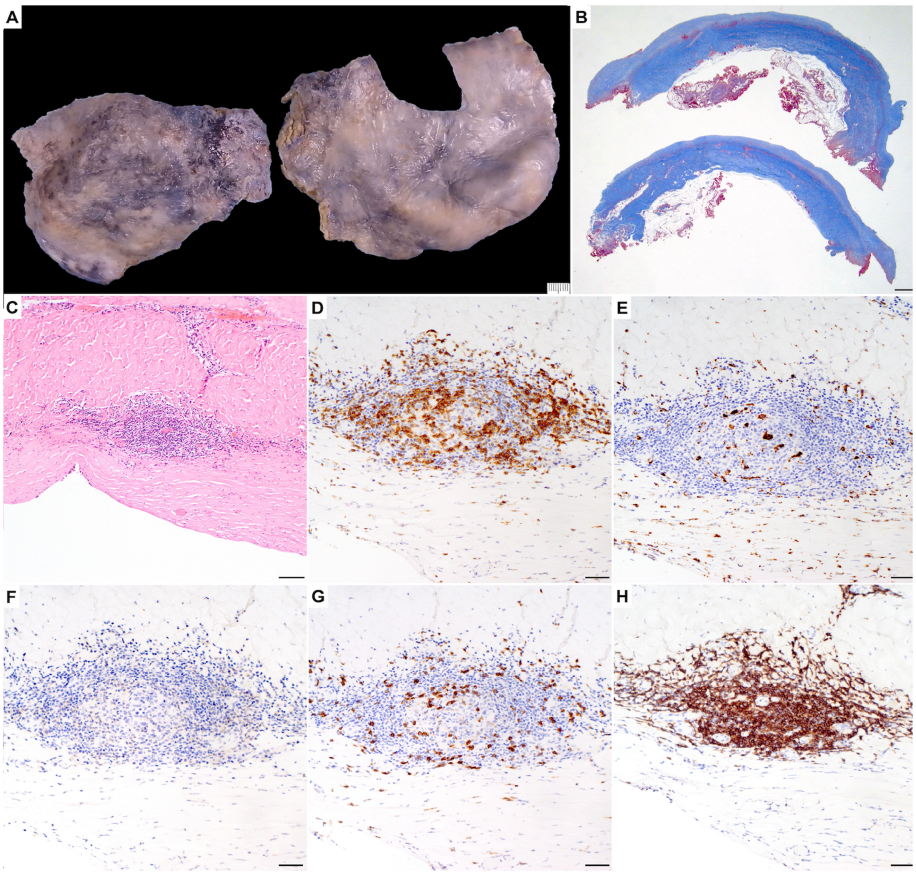
Effusive–constrictive pericarditis is a clinical entity characterized by decreased pericardial compliance associated with pericardial effusion.[1] Underlying pathophysiology is determined by inflammation of the pericardial sac with reduction of pericardial compliance, together with formation of pericardial fluid under pressure.[2] Clinical onset is heterogeneous: symptoms range from cardiac tamponade requiring urgent pericardiocentesis to, more frequently, subacute presentation. In the latter situation, RV failure symptoms are patients' most common complaint.

Effusive–constrictive pericarditis diagnosis may be challenging because its clinical presentation has considerable overlap with other pericardial syndromes and, more importantly, nowadays only invasive haemodynamic assessment can accurately describe this condition. In fact, the hallmark of ECP is the persistence of elevated right atrial pressure after drainage of pericardial fluid.[3] To date, biomarkers or non-invasive imaging tools are not suitable to achieve the diagnosis. The correct identification of patients affected by ECP requires a high index of clinical suspicion, and, notably, diagnosis is often achieved after cardiac catheterization showing consistent haemodynamic findings. In addition, because this disease has a long and silent course before overt clinical onset, its features may be heterogeneous and it may be difficult to relate it to its true aetiology.[4]

We highlight the importance of considering ECP diagnosis even if there is no imaging evidence of pericardial calcification or severe thickening, as large evidence exists of non-thickened pericardium determining constriction. An explanation for this has been proposed by Talreja *et al*.[5]: apart from reduced pericardial compliance due to calcifying processes, shrinkage in pericardial volume, caused by excessive pericardial collagen degradation and reduced production,

DOI: 10.1002/ehf2.13470

Figure 5 Surgical pathological analysis of the pericardiectomy specimen. Macroscopic view (A) and histological panoramic view (B) confirming diffuse severe fibrous thickening (B, Heidenhain trichrome stain). At histology, multiple foci of chronic inflammation are evident (C, haematoxylin–eosin, 50×; D, CD3+ T-lymphocytes; E, CD68+ macrophages; F, CD4+ T-helper lymphocytes; G, CD8+ cytotoxic T-lymphocytes; H, CD20+ B-lymphocytes; all D–H 100×). Scale bars represent 500 μm (B), 100 μm (C), and 50 μm (D–H).



may determine constriction. As a consequence, constriction can result even with a normal thickness pericardium.

To further complicate this picture, underlying causes of ECP are highly heterogeneous, ranging from iatrogenic interventions (previous cardiac surgery, thoracic irradiation) to chest trauma and infectious agents. Among the latter ones, mycobacteria are often related to pericarditis, especially in immunocompromised patients; the association of mycobacteria and pericarditis in immunocompetent subjects is anecdotal.[6]

Effusive–constrictive pericarditis is *per se* an uncommon diagnosis: in Europe, 1.3% of patients undergoing pericardiocentesis,[1] and 6.9% of patients with clinical diagnosis of cardiac tamponade,[3] according to the literature. This case confirms the utility of histological examination of pericardium in supposed idiopathic ECP and highlights the importance of using PCR for aetiological diagnosis of chronic pericarditis cases even in the absence of infectious signs at routine microbiological tests.[7]

It is recognized that pericardiectomy is the gold standard treatment for ECP if first-line drug therapy is not successful, effectively relieving patients' symptoms and having a favourable long-term outcome.[8] However, due to its intrinsic mortality and morbidity risk, this option should be offered only to selected patients. As in this patient's case, male sex, post-inflammatory aetiology, including infectious disease, and New York Hear Association I or II functional class before intervention are associated with better outcome.[8]

The association of 'mycobacteria other than tuberculosis' and pericarditis is a rare finding; in a large cohort of 282 patients with atypical mycobacteria-related diseases, only one patient presented with pericarditis, notably with constrictive pattern.[9] To our knowledge, this is the fourth reported case of acute presentation of non-tuberculous mycobacteria-related pericarditis in an immunocompetent host.[6,10,11] In one of the previously reported cases, similarly to ours, atypical mycobacteria were only found in the pericardium.[10]

DOI: 10.1002/ehf2.13470

Conflict of interest

None declared.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Video S1. Supporting information.

References

1. Miranda WR, Oh JK. Constrictive pericarditis: a practical clinical approach. *Prog Cardiovasc Dis* 2017; **59**: 369–379.
2. Syed FF, Ntsekhe M, Mayosi BM, Oh JK. Effusive-constrictive pericarditis. *Heart Fail Rev* 2013; **18**: 277–287.
3. Sagristà-Sauleda J, Angel J, Sánchez A, Permanyer-Miralda G, Soler-Soler J. Effusive–constrictive pericarditis. *N Engl J Med* 2004; **350**: 469–475.
4. Aursulesei V, Cozma A, Bulughiana S, Costache II. Constrictive pericarditis—still an overlooked entity. *Arch Clin Cases* 2016; **03**: 31–36.
5. Talreja DR, Edwards WD, Danielson GK, Schaff HV, Tajik AJ, Tazelaar HD, Breen JF, Oh JK. Constrictive pericarditis in 26 patients with histologically normal pericardial thickness. *Circulation* 2003; **108**: 1852–1857.
6. Marvisi M, Bassi E, Zanlari L, Civardi G. A case of *Mycobacterium avium* complex infection in an immunocompetent man presenting with pericarditis and an HRCT pattern of lymphangitis. *Eur J Intern Med* 2008; **19**: 300–302.
7. Zamirian M, Mokhtarian M, Hosein Motazedian M, Monabati A, Reza RG. Constrictive pericarditis: detection of mycobacterium tuberculosis in paraffin-embedded pericardial tissues by polymerase chain reaction. *Clin Biochem* 2007; **40**: 355–358.
8. Szabó G, Schmack B, Bulut C, Soós P, Weymann A, Stadtfeld S, Karck M. Constrictive pericarditis: Risks, aetiologies and outcomes after total pericardiectomy: 24 years of experience. *Eur J Cardio-thoracic Surg* 2013; **44**: 1023–1028.
9. Ellis ME, Qadri SMH. Mycobacteria other than tuberculosis producing disease in a tertiary referral hospital. *Ann Saudi Med* 1993; **13**: 508–515.
10. Moskowitz RS, Brickman R, Moeller C. A case study of *Mycobacterium avium* complex infection presenting with acute pericarditis. *Am J Med* 2014; **127**: e9–e10.
11. Corey GR, Campbell PT, Van Trigt P, Kenney RT, O'Connor CM, Sheikh KH, Kisslo JA, Wall TC. Etiology of large pericardial effusions. *Am J Med* 1993; **95**: 209–213.