

Myopericarditis and thyroiditis: a case report

Ross J. Thomson ^{1,2*,†}, Nora Rossberg ^{1†}, Joseph Davar¹, and Carol Whelan^{1,3}

¹Department of Cardiology, Royal Free Hospital, Royal Free London NHS Foundation Trust, Pond Street, London NW3 2QG, UK; ²William Harvey Research Institute, Queen Mary University of London, 1 St Martin's le Grand, London EC1A 4AS, UK; and ³National Amyloidosis Centre, Royal Free Hospital, Royal Free London NHS Foundation Trust, Pond Street, London NW3 2QG, UK

Received 26 January 2021; first decision 2 March 2021; accepted 20 April 2021

Background

Hyperthyroidism is commonly associated with adverse cardiovascular effects, including tachydysrhythmia, heart failure, and hypertension, although the association between hyperthyroidism and myopericarditis is restricted to a small number of case reports.

Case summary

A 45-year-old Caucasian male with no past medical history was admitted with chest pain. The electrocardiogram demonstrated diffuse ST-segment elevation, the troponin T rose, and he was diagnosed with myopericarditis. He was noted to have markedly deranged thyroid function tests and a diagnosis of hyperthyroidism secondary to Graves' disease was made. He was treated with Bisoprolol, Carbimazole, Prednisolone, Ibuprofen, and Colchicine, his symptoms resolved rapidly and he was discharged. Five weeks later he re-presented with similar symptoms and recurrent pericarditis was diagnosed. His symptoms settled with a repeat course of steroids.

Discussion

We hypothesize that there may be an underappreciated link between hyperthyroidism and myopericarditis. Potential pathophysiological mechanisms include viral infection, autoimmunity, or changes in myocardial fat metabolism. Suggested management consists of a combination of current guidelines for the treatment of hyperthyroidism and pericardial disease, with attention to certain disease–drug interactions. Further research is required to evaluate the true incidence of hyperthyroidism-associated myopericarditis, elucidate its pathophysiology and instruct management.

Keywords

Pericarditis • Myocarditis • Hyperthyroidism • Thyroiditis • Case report

Learning points

- There may be an association between myopericarditis and thyroiditis, and it is conceivable that they share a common underlying pathophysiology in select cases.
- It would be reasonable to check the thyroid status of all patients presenting with myopericarditis, in the absence of another clearly identifiable aetiology.
- Steroids, although an effective treatment for thyroiditis, may increase the risk of recurrence of myopericarditis.

* Corresponding author. Tel: +44 7936767906, Email: r.thomson@qmul.ac.uk

† Joint first authors.

Handling Editor: Konstantinos Stathogiannis

Peer-reviewers: Domenico Filomena and Nidhi Madan

Compliance Editor: Christian Fielder Camm

Supplementary Material Editor: Christian Fielder Camm

© The Author(s) 2021. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Introduction

Hyperthyroidism causes a variety of cardiovascular effects, including tachycardia, arrhythmias, high output cardiac failure, and hypertension.¹ However, the association between pericarditis or myocarditis and thyrotoxicosis is rare, with only a handful of case reports described.^{1–6} The cardiovascular effects of hyperthyroidism are thought to be mediated by the actions of triiodothyronine on nuclear receptors in cardiomyocytes, leading to altered expression of genes involved in intracellular calcium homeostasis and in turn to increased chronotropy and inotropy. The mechanisms by which hyperthyroidism may lead to pericarditis and myocarditis are less well characterized. We present the case of a 45-year-old male admitted with acute chest pain and diagnosed with myopericarditis and Graves' disease.

Timeline

Day 0	Sudden onset central chest pain
October 2020	Brought to the heart attack centre by ambulance Electrocardiogram (ECG) demonstrated diffuse saddle-shaped ST-segment elevation Pericarditis diagnosed Admitted to the coronary care unit Commenced on Colchicine 500 µg BD and Ibuprofen 600 mg TDS
Day 1	Thyroid function tests showed severe hyperthyroidism Troponin T started to rise Diagnosis revised to myopericarditis Commenced on Prednisolone 30 mg OD, Carbimazole 40 mg OD, and Bisoprolol 2.5 mg OD
Day 3	Cardiac magnetic resonance imaging showed normal biventricular function, no imaging evidence of myocarditis, and an enlarged thyroid Discharged home after symptoms markedly improved
Day 38	Re-presented to the Emergency Department with recurrent chest pain
November 2020	ECG unremarkable Echocardiogram showed small pericardial effusion and echo-bright pericardium Commenced on Prednisolone 30 mg OD
Day 40	Discharged home after symptoms markedly improved
Day 110	Asymptomatic at latest follow-up

Case presentation

A 45-year-old Caucasian male was brought to the heart attack centre of our hospital by ambulance with a 24-h history of severe, sharp central chest pain exacerbated by inspiration and relieved by sitting

forward. He had no past medical history, took no regular medications, was an ex-smoker, and exercised regularly. Physical examination was unremarkable.

A 12-lead electrocardiogram (ECG) showed diffuse concave ST-segment elevation (*Figure 1*). The patient was admitted to the coronary care unit for observation with a presumptive diagnosis of pericarditis. Treatment with Colchicine 500 µg twice daily and Ibuprofen 600 mg three times daily was commenced.

Bloods (*Table 1*) revealed a normal troponin T (11 ng/L, normal < 14 ng/L), slightly elevated NT proBNP (875 ng/L, normal < 400 ng/L), raised C-reactive protein (32 mg/L, normal < 5 mg/L), and raised white cell count ($12.35 \times 10^9/L$, normal $3.5–11.0 \times 10^9/L$). Thyroid function tests showed marked hyperthyroidism: thyroid stimulating hormone <0.01 mU/L (normal 0.3–4.2 mU/L), free T4 62.2 pmol/L (normal 12–22 pmol/L), and free T3 32.8 pmol/L (normal 3.1–6.8 pmol/L). Polymerase chain reaction (PCR) for SARS-CoV-2 RNA and ELISA for SARS-CoV-2 antibody were negative. Blood cultures yielded no growth.

The endocrinology team were consulted. Antibodies against the TSH receptor were strongly positive (12.82 U/L, normal range 0–0.4 U/L) and antibodies against thyroperoxidase were negative. On specific questioning the patient denied the presence of neck pain and no tenderness was present on palpation of the thyroid. A diagnosis of Graves' disease was made. He was commenced on 5 days of Prednisolone 30 mg daily, Carbimazole 40 mg daily, and Bisoprolol 2.5 mg daily.

Over the next 2 days the troponin T rose, peaking at 181 ng/L. The diagnosis was revised to myopericarditis given the evidence of myocardial injury. The C-reactive protein also rose, peaking at 126 mg/L. A transthoracic echocardiogram showed normal biventricular function and no pericardial effusion. A cardiac magnetic resonance (CMR) imaging study (*Figure 2 and Video 1*) confirmed the presence of normal biventricular function and demonstrated no evidence of myocardial oedema on STIR imaging or parametric mapping (T1 964 ms, normal range 950–1100 ms by MOLLI; T2 45 ms, normal range 45–55 ms by TruFISP) and no evidence of myocardial enhancement on late gadolinium imaging. The patient's symptoms improved rapidly, and he was discharged after 3 days to finish the 5-day course of Prednisolone and Ibuprofen, and to continue treatment with Colchicine, Carbimazole, and Bisoprolol.

The patient remained well for the next month until he once again developed severe central chest pain. He presented to the Emergency Department, where he reported compliance with medication. The ECG was relatively unremarkable (*Figure 3*), with resolution of the ST-segment changes seen previously. The C-reactive protein (159 mg/L) and white cell count ($13.56 \times 10^9/L$) were elevated. The free T4 had normalized (9.1 pmol/L), although the TSH remained suppressed (<0.01 mU/L). The troponin T was normal (9 ng/L). PCR for SARS-CoV-2 RNA was negative. He was admitted to the cardiology ward for evaluation.

Troponin T remained normal. The patient was diagnosed with recurrent pericarditis, without myocardial involvement. He was commenced on 5 days of Prednisolone 30 mg daily and Colchicine was increased to 500 µg three times daily. A transthoracic echocardiogram (*Figure 4 and Video 2*) showed normal biventricular function,

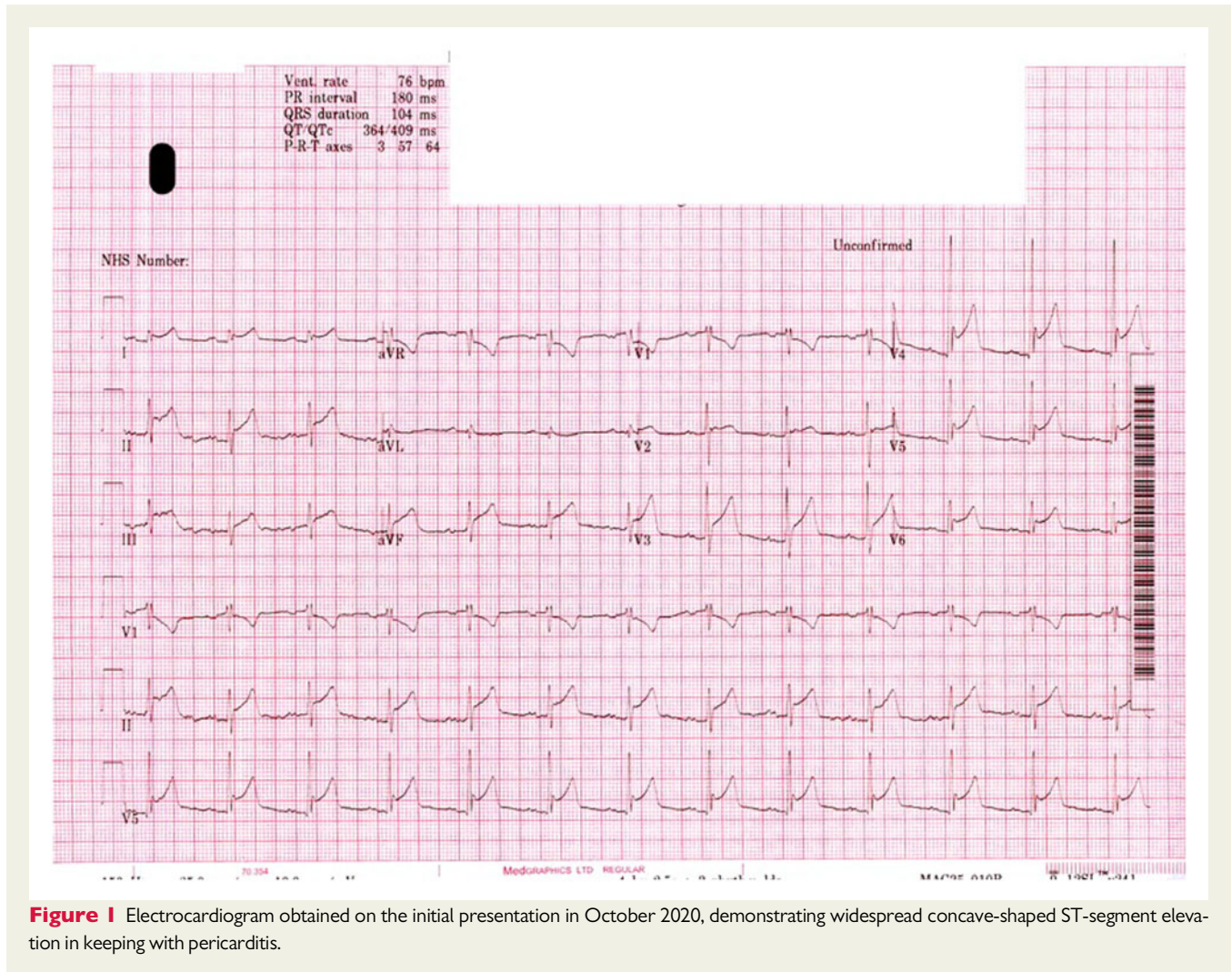


Figure 1 Electrocardiogram obtained on the initial presentation in October 2020, demonstrating widespread concave-shaped ST-segment elevation in keeping with pericarditis.

echo-bright pericardium, and a 1 cm pericardial effusion around the right ventricular free wall.

The patient's symptoms improved rapidly, and he was discharged to finish the course of Prednisolone and continue treatment with Colchicine, Ibuprofen, Bisoprolol, and Carbimazole. At the latest follow-up, 3 months after his second discharge, he remained asymptomatic.

Discussion

We describe the case of a previously healthy 45-year-old male who presented with a typical history of pericarditis who went on to develop concomitant myocardial inflammation and was diagnosed with Graves' disease. In this case of myopericarditis there was no preceding viral prodrome, history of drug use, or other apparent precipitant apart from thyroid disease.

The true incidence of pericarditis and myocarditis associated with hyperthyroidism is unknown, although we believe there may be an underappreciated link between the two disease entities. Mavrogeni *et al.*⁷ assessed 50 patients with hyperthyroidism and persistent cardiac

symptoms despite 1–3 months of treatment-induced euthyroidism. Using CMR, findings were compatible with myocarditis in 15 of these patients.

Several different mechanisms have been proposed to explain the link between hyperthyroidism and myopericarditis, including a viral aetiology. For example, Epstein–Barr virus has been described as a trigger for both pericarditis and Graves' disease.² It is plausible that our patient had an undiagnosed viral infection that initiated inflammation of the thyroid gland, pericardium, and myocardium.

There is also evidence to suggest an autoimmune aetiology of both thyroiditis and myopericarditis, in particular Graves' disease.⁸ Fatourechki and Edwards⁹ evaluated endomyocardial biopsy samples from 11 patients with Graves' disease and unexplained low-output cardiac failure and found that two had lymphocytic infiltrates suggestive of an autoimmune myocarditis. A further theory is that thyroid hormones may lead to a change in myocardial fat metabolism,¹⁰ although this is more commonly described in hypothyroidism.

There is currently a lack of data to guide the management of myopericarditis specifically in the setting of hyperthyroidism. Management of hyperthyroidism secondary to Graves' disease, summarized in the guidelines from the European Thyroid Association,¹¹

Table 1 Myopericarditis and thyroiditis: a case report

Laboratory parameter	Day 0 First admission	Day 2	Day 38 Second admission	Reference range
Haemoglobin (g/L)	129	123	132	135–170
White blood cell count ($\times 10^9/L$)	12.35	7.71	13.58	3.5–11
Platelets ($\times 10^9/L$)	201	165	235	140–400
Sodium (mmol/L)	142	142	138	135–145
Potassium (mmol/L)	4.2	4.3	4.1	3.5–5.1
Urea (mmol/L)	5.7	6.9	5.4	2.1–7.1
Creatinine (mmol/L)	68	76	78	66–112
C-reactive protein (mg/L)	32	126	159	<5
Procalcitonin ($\mu\text{g/L}$)			0.13	<0.5
Troponin T (ng/L)	11	181	9	<14
NT pro B-type natriuretic peptide (ng/L)	875		410	<400
Free T4 (pmol/L)	62.2		9.1	12–22
Thyroid stimulating hormone (mU/L)	<0.01		<0.01	0.3–4.2
Anti-nuclear antibodies		Negative		
Anti-neutrophil cytoplasmic antibodies		Negative		
Thyroperoxidase antibodies		Negative		
TSH receptor antibodies		Positive		
SARS-CoV-2 RNA	Negative		Negative	
SARS-CoV-2 total antibody	Negative			
HIV-1 and -2 total antibody	Negative			
Hepatitis A IgM antibody	Negative			
Hepatitis B s antigen	Negative			
Hepatitis C IgG antibody	Negative			
Epstein–Barr virus IgM antibody	Negative			
Epstein–Barr virus IgG antibody	Positive			
Cytomegalovirus IgM antibody	Negative			
Cytomegalovirus IgG antibody	Negative			

HIV, human immunodeficiency virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TSH, thyroid stimulating hormone.

centres around the administration of antithyroid drugs such as Propylthiouracil or Carbimazole. Betablockers are used to diminish the adrenergic symptoms of the hyperthyroid state. The addition of corticosteroids is recommended in thyrotoxic storm to inhibit peripheral conversion of T4 to T3.

European Society of Cardiology guidelines¹² on the management of pericarditis advise restriction of physical activity, Aspirin or non-steroidal anti-inflammatory drugs (NSAIDs), and the addition of Colchicine to improve treatment response and reduce the risk of recurrence. Low- to moderate-dose corticosteroids are suggested as second-line agents in patients who have contraindications or non-response to first-line treatments. The risk of recurrence of pericarditis is higher in patients treated with corticosteroids, especially if given in higher doses.¹³ Myopericarditis is defined by the classical features of pericarditis and elevated biomarkers (e.g. high sensitivity troponin) suggestive of myocardial inflammation. Management is similar to pericarditis, except that hospitalization is recommended for monitoring and the duration of abstinence from physical activity should be at least 6 months.¹² A 2013 Cochrane systematic review¹⁴ examining the impact of steroids on viral myocarditis found no benefit in terms of mortality benefit but a potential improvement in left ventricular

function and reduction in peak biomarker level, although the trials included in this review were small and of poor methodological quality. A recent expert review advises against the use of steroids in myocarditis, except in the case of rare aetiologies such as eosinophilic or giant cell myocarditis.¹⁵ In our patient, steroids were initiated primarily to treat thyrotoxicosis and a second course was given to treat refractory pericarditis that had recurred despite treatment with NSAIDs and Colchicine.

In the absence of specific guidance, a combination of the above treatment strategies is a sensible approach for patients presenting with hyperthyroidism-associated pericarditis or myocarditis. However, individual patient factors must be taken into consideration and management tailored accordingly. Furthermore, satisfactory treatment of the underlying hyperthyroidism seems crucial in the effective resolution of pericarditis.⁸ Continuation of Colchicine to cover the period until thyroid hormones have normalized should be considered.⁸

Cardiac magnetic resonance has emerged as the diagnostic modality of choice in patients with suspected myocarditis.¹⁶ Although endomyocardial biopsy is still considered the 'gold standard' investigation,¹⁷ this technique is not widely available and is associated with

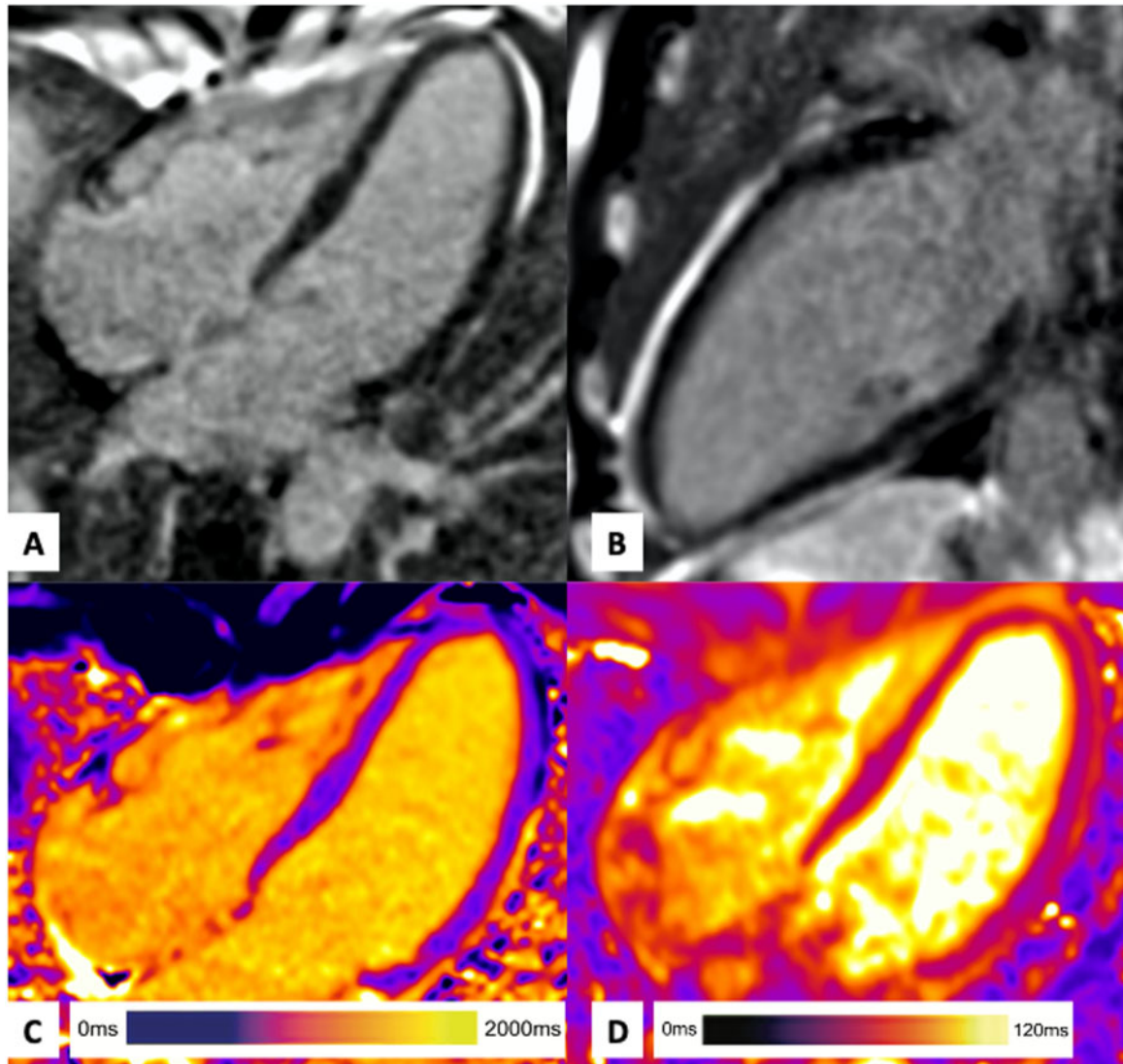
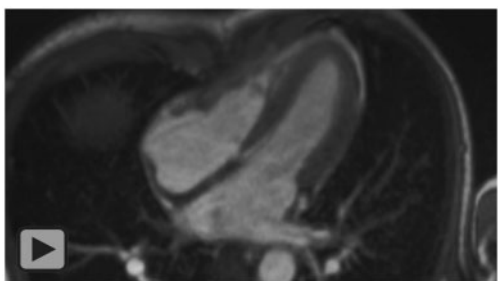


Figure 2 Cardiac magnetic resonance imaging performed during the initial admission demonstrated no evidence of enhancement on late gadolinium imaging nor any evidence of oedema on parametric mapping. (A) Late gadolinium imaging, four-chamber view; (B) late gadolinium imaging, two-chamber view; (C) native T1 map by MOLLI, four-chamber view, normal range 950–1100 ms; (D) native T2 map by TruFISP, four-chamber view, normal range 45–55 ms.



Video 1 Cardiac magnetic resonance imaging performed during the initial admission demonstrated normal biventricular function. Steady state free precession (SSFP) cines, four-chamber view then two-chamber view.

... sampling error and substantial procedural risk. CMR allows for the simultaneous assessment of ventricular function, hyperaemia, myocardial oedema, myocardial fibrosis following myocyte death, and features associated with myocarditis such as pericardial effusion. The Lake Louise criteria¹⁸ set out a constellation of CMR findings that are commonly used to diagnose myocarditis, although they prioritize specificity over sensitivity,¹⁶ and real-world studies have highlighted that patients may have biopsy-proven myocarditis despite not meeting the CMR criteria.¹⁹ Recognizing this limitation, the authors of the Lake Louise criteria recommend that CMR is repeated within 1–2 weeks in patients with a non-diagnostic scan in whom the pre-test probability of myocarditis is high. In this case, the normal CMR may reflect technical factors such as the dose of gadolinium administered, the timing of image acquisition relative to contrast administration, and pulse sequence characteristics such as the inversion time chosen

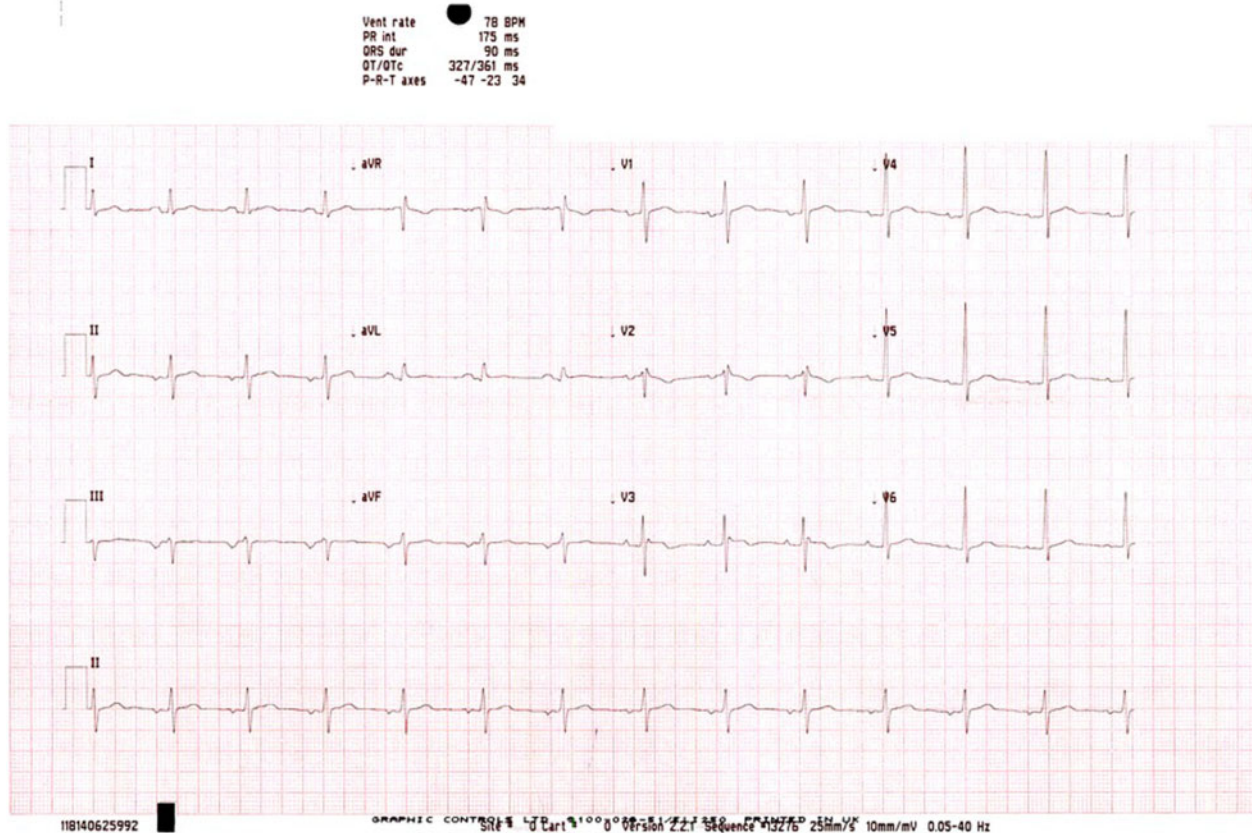


Figure 3 Electrocardiogram obtained on the initial presentation in November 2020, demonstrating normalization of the previously seen ST-segment changes.

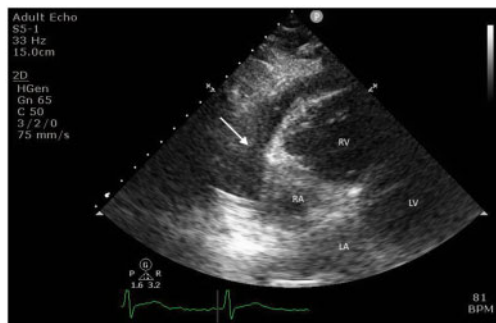
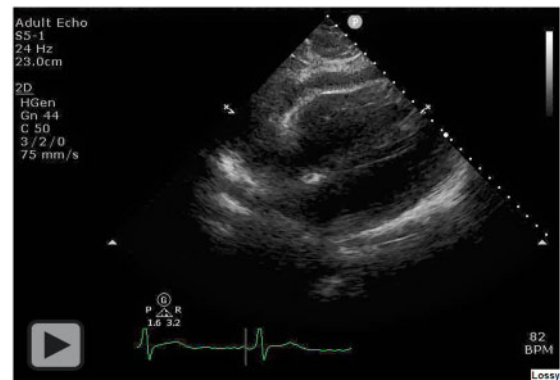


Figure 4 Still image from a transthoracic echocardiogram, subcostal view, demonstrating a small pericardial effusion (white arrow) around the right atrium and right ventricle. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.



Video 2 Video clip from a transthoracic echocardiogram, subcostal view, demonstrating a small pericardial effusion without collapse of the right atrium or ventricle in diastole.

to suppress the signal from the normal myocardium.²⁰ It may also have been a consequence of the timing of imaging relative to the onset of illness, or the nature of the myocardial damage. For example, it is conceivable that diffuse, mild myocardial damage may have led to a

troponin rise but no discrete area of oedema of sufficient severity to be detected on CMR.

Further research is required to elucidate the true prevalence and pathophysiology of hyperthyroidism-associated pericarditis

and myocarditis to inform management strategies for affected patients.

Lead author biography



Ross J. Thomson studied medicine at New College, University of Oxford and is now a Specialist Registrar in Cardiology and NIHR Academic Clinical Fellow in London. His research is centred on the use of big data and real-world evidence to improve the diagnosis and management of cardiovascular disease. He sits on the finance committee of the British Cardiovascular Society and is the Lead Junior Editor at *European Heart Journal - Case Reports*.

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

- Gupta P, Chhabra L, Hiendlmayr B, Spodick DH. Thyrotoxic pericarditis: an underappreciated phenomenon. *Int J Cardiol* 2015;**198**:32–33.
- Inami T, Seino Y, Goda H, Okazaki H, Shirakabe A, Yamamoto M et al. Acute pericarditis: unique comorbidity of thyrotoxic crisis with Graves' disease. *Int J Cardiol* 2014;**171**:e129–e130.
- Kwak T, Zoubi MA, Bhavith A, Rios CR, Kumar S. Acute myocarditis in body-builder from coxsackievirus and thyrotoxicosis. *J Cardiol Cases* 2016;**14**:123–126.
- Lancaster ST, Koons KL, Lee YJ, Mazimba S, Kwon Y. Acute autoimmune myocarditis as a manifestation of Graves' disease: a case report and review of the literature. *Clin Case Rep* 2019;**7**:1489–1493.
- Tsai M-S, Yang C-W, Chi C-L, Hsieh C-C, Chen W-J, Huang C-H. Acute pericarditis: a rare complication of Graves' thyrotoxicosis? *Am J Emerg Med* 2006;**24**:374–375.
- Koo EH, Kim SM, Park SM, Park JW, Kim EK, Lee GY et al. Acute recurrent pericarditis accompanied by Graves' disease. *Korean Circ J* 2012;**42**:419–422.
- Mavrogeni S, Markussis V, Bratis K, Mastorakos G, Sidiropoulou EJ, Papadopoulou E et al. Hyperthyroidism induced autoimmune myocarditis. Evaluation by cardiovascular magnetic resonance and endomyocardial biopsy. *Int J Cardiol* 2012;**158**:166–168.
- Schwier NC, O'Neal K. Pharmacotherapeutic management strategies for thyroid disease-induced pericarditis. *Ann Pharmacother* 2020;**54**:486–495.
- Fatourechi V, Edwards WD. Graves' disease and low-output cardiac dysfunction: implications for autoimmune disease in endomyocardial biopsy tissue from eleven patients. *Thyroid* 2000;**10**:601–605.
- Chhabra L, Spodick DH. A comment on thyrotoxic pericarditis. *Int J Cardiol* 2014;**173**:587.
- Kahaly GJ, Bartalena L, Hegedüs L, Leenhardt L, Poppe K, Pearce SH. 2018 European Thyroid Association guideline for the management of Graves' hyperthyroidism. *Eur Thyroid J* 2018;**7**:167–186.
- Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J et al.; ESC Scientific Document Group. 2015 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.
- Imazio M, Bobbio M, Cecchi E, Demarie D, Pomari F, Moratti M et al. Colchicine as first-choice therapy for recurrent pericarditis: results of the CORE (COlchicine for REcurrent pericarditis) trial. *Arch Intern Med* 2005;**165**:1987–1991.
- Chen HS, Wang W, Wu SN, Liu JP. Corticosteroids for viral myocarditis. *Cochrane Database Syst Rev* 2013;**10**:CD004471.
- Tschöpe C, Cooper LT, Torre-Amione G, Linthout SV. Management of myocarditis-related cardiomyopathy in adults. *Circ Res* 2019;**124**:1568–1583.
- Friedrich MG, Marcotte F. Cardiac magnetic resonance assessment of myocarditis. *Circ Cardiovasc Imaging* 2013;**6**:833–839.
- Caforio ALP, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB et al.; European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J* 2013;**34**:2636–2648.
- Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT et al.; International Consensus Group on Cardiovascular Magnetic Resonance in Myocarditis. Cardiovascular magnetic resonance in myocarditis: a JACC white paper. *J Am Coll Cardiol* 2009;**53**:1475–1487.
- Lurz P, Eitel I, Adam J, Steiner J, Grothoff M, Desch S et al. Diagnostic performance of CMR imaging compared with EMB in patients with suspected myocarditis. *JACC Cardiovasc Imaging* 2012;**5**:513–524.
- Bonekamp D, Zimmerman SL. Case 47 - Inappropriate inversion time selection for late gadolinium enhancement imaging section 6 - Cardiovascular MRI artifacts. Pearls and pitfalls in cardiovascular imaging. Cambridge University Press 2015;146–149.