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CASE REPORT
Other

A case report of acute myopericarditis associated with Graves' thyrotoxicosis

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Background The effects of hyperthyroidism on the heart are well documented, primarily consisting of supraventricular tachycardias, congestive heart failure, and dilated cardiomyopathy. Acute myopericarditis resulting from a hyperthyroid state is an uncommon but recognized association.

Case summary A 29-year-old man with a history of Graves' disease presented with chest pain and electrocardiogram changes suggestive of an infero-lateral ST-elevation myocardial infarction. However, emergent coronary angiography and bedside echocardiography were normal. Troponin-I was found to be >25 000 ng/L (normal value <57). Thyroid function tests showed a significantly raised free T4 and undetectable thyroid-stimulating hormone. Cardiovascular magnetic resonance (CMR) showed extensive myocardial oedema and late gadolinium enhancement (LGE) in keeping with acute myopericarditis, alongside an enlarged thyroid gland consistent with goitre. Propylthiouracil in combination with an angiotensin-converting enzyme inhibitor and beta-blocker were commenced and eventually definitive treatment with thyroidectomy was performed. Follow-up CMR at 6 months showed complete resolution of the prior noted oedema and a reduction in the location and extent of LGE with significant residual fibrosis.

Discussion Acute myopericarditis is a common diagnosis in young patients presenting with symptoms of chest pain with elevated troponin and is frequently related to a viral illness. Hyperthyroid states are also associated with acute myopericarditis and should be particularly considered in patients with a pre-existing thyroid condition or in those with symptoms suggestive of hyperthyroidism. Given the specific treatments required in a case of myopericarditis associated with hyperthyroidism, it is important to be aware of this association and consider screening where appropriate.

Keywords Case report • Graves' • disease • MINOCA • Myopericarditis • Thyrotoxicosis

Learning points

- An awareness of thyrotoxicosis as a possible cause for acute myopericarditis is important given this can be definitively treated.
- Thyroid function testing may be warranted in acute myopericarditis with no clear cause, in patients with symptoms consistent with hyperthyroidism or in those with pre-existing thyroid disease.
- Cardiovascular magnetic resonance provides a valuable diagnostic and prognostic role in inflammatory myocardial disease and may provide additional diagnostic information such as a large goitre requiring further evaluation.

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Introduction

Acute myopericarditis is an inflammatory condition with varied aetiologies. Whilst it is often self-limiting, some patients have more fulminant disease and chronic inflammation can lead to cardiomyopathy.[1] The gold-standard for diagnosis is endomyocardial biopsy (EMB), however, this carries a small risk of serious complications and is not always performed in practice. Cardiovascular magnetic resonance (CMR) has shown accurate correlation with areas of acute inflammation and can be an important adjuvant test.[1,2]

Graves' disease is an autoimmune condition characterized by hyperthyroidism and specific clinical findings. Cardiac manifestations include supraventricular tachycardias, dilated cardiomyopathy, and congestive cardiac failure.[3,4] Acute myopericarditis is less commonly reported but is nonetheless a recognized association.[1,5] The incidence of myocarditis in patients with Graves' disease is unknown, although one study of 443 patients with myocarditis reported only 0.5% of these cases to be associated with autoimmune hyperthyroidism.[6]

Timeline

Day 0	A 29-year-old male presents with chest pain and acute infero-lateral ST-elevation on electrocardiogram. Normal coronary angiography and echocardiogram. Raised troponin-I (>25 000 ng/L) Biochemically hyperthyroid.
Day 2	Cardiovascular magnetic resonance (CMR): widespread mid-wall and epicardial oedema suggestive of acute myopericarditis and enlarged thyroid.
Day 7	Presumed diagnosis of thyrotoxicosis-induced myopericarditis. Commenced on propylthiouracil, angiotensin-converting enzyme inhibitor, beta-blocker, and non-steroidal anti-inflammatory drugs and discharged.
8 months after admission	Outpatient thyroidectomy. Repeat CMR: resolution of oedema, significant residual non-ischaemic fibrosis.
9 months after admission	Asymptomatic at clinic review. Echocardiography: mildly dilated left ventricle with normal biventricular function.

Case presentation

A 29-year-old man presented to emergency services with 2 h of chest pain, preceded by 2 weeks of intermittent palpitations. His past medical history included Graves' disease for which he was prescribed carbimazole. He was a smoker but reported no other risk factors for ischaemic heart disease alongside no significant family history. On initial assessment, he had normal vital signs with a normal physical examination. Initial electrocardiogram showed persistent infero-lateral ST-elevation (*Figure 1*). Emergency coronary angiography revealed normal coronary arteries.

A subsequent echocardiogram demonstrated normal biventricular size and function with no regional wall motion abnormalities. Laboratory studies showed a raised high sensitivity troponin-I at >25 000 ng/L (normal <57 ng/L) and deranged thyroid function tests with a thyroid-stimulating hormone (TSH) of <0.05 mIU/L (normal 0.20–4.00) and a free T4 of 122.5 pmol/L (normal 10–20). At this stage, a diagnosis of myopericarditis was made and non-steroidal anti-inflammatory drugs were commenced. After consultation with the endocrinology team, carbimazole was switched to propylthiouracil.

Cardiovascular magnetic resonance was performed to elucidate an underlying cause. Late gadolinium enhancement (LGE) imaging demonstrated significant mid-wall and epicardial hyper-enhancement in the basal-mid inferior/infero-lateral segments, together with further mid-wall enhancement in the mid-apical septal segments. Pericardial LGE was demonstrated within the mid to apical-inferior and infero-lateral segments. Myocardial oedema, as indicated by increased signal intensity on T2-weighted imaging, was noted in the mid antero-septum (*Figure 2*). Left ventricular (LV) size and function were normal on cine imaging. Black blood imaging demonstrated a markedly enlarged, symmetric thyroid gland (*Figure 3*).

The patient was commenced on an angiotensin-converting enzyme inhibitor (ACEi) and beta-blocker due to the potential risk of adverse LV remodelling and arrhythmia. Troponin-I (450 ng/L) and free T4 (73.7 pmol/L) were repeated prior to discharge. The patient's symptoms settled and he was discharged for outpatient follow-up.

The patient was seen in endocrinology clinic and subsequently underwent elective thyroidectomy with oral thyroxine replacement.

Repeat CMR at 8 months showed complete resolution of myocardial oedema. There was a significant reduction in the intensity and anatomical extent of LGE although significant residual fibrosis was noted. Indexed LV cavity size was at the upper limits of normal with normal systolic function (*Figure 4*).

A multi-disciplinary team decision was made to continue low-dose ACEi and beta-blocker therapy and for ongoing monitoring of the patient's LV function. Repeat echocardiography at 9 months showed normal biventricular volumes and systolic function. On subsequent clinic review, there were no cardiovascular symptoms.

Discussion

This patient, with known Graves' disease, presented with concurrent thyrotoxicosis and myopericarditis. The impression of the treating team was of a possible causal link between the two, with an association between these conditions described in a number of case reports.[5,7,8] In this case, causation was not definitively demonstrated but was considered likely due to the improvement in cardiac biomarkers alongside thyroid function and by a lack of early recurrence following thyroidectomy.

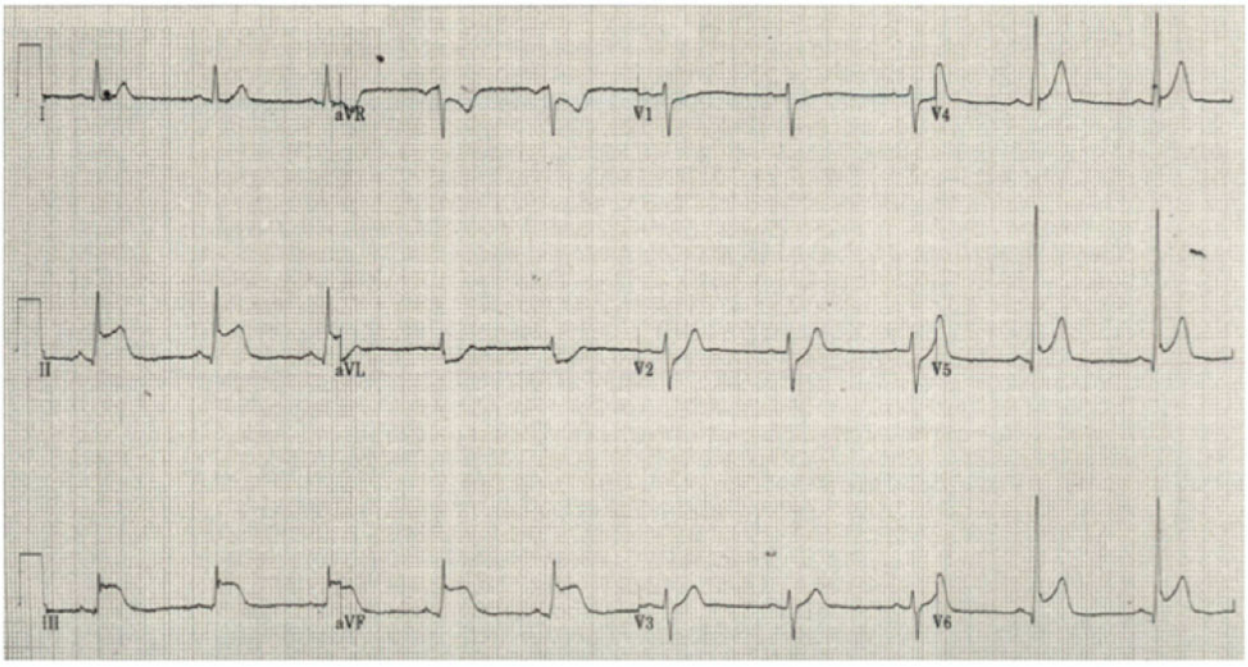

Figure 1 Admission electrocardiogram showing infero-lateral ST-segment elevation.

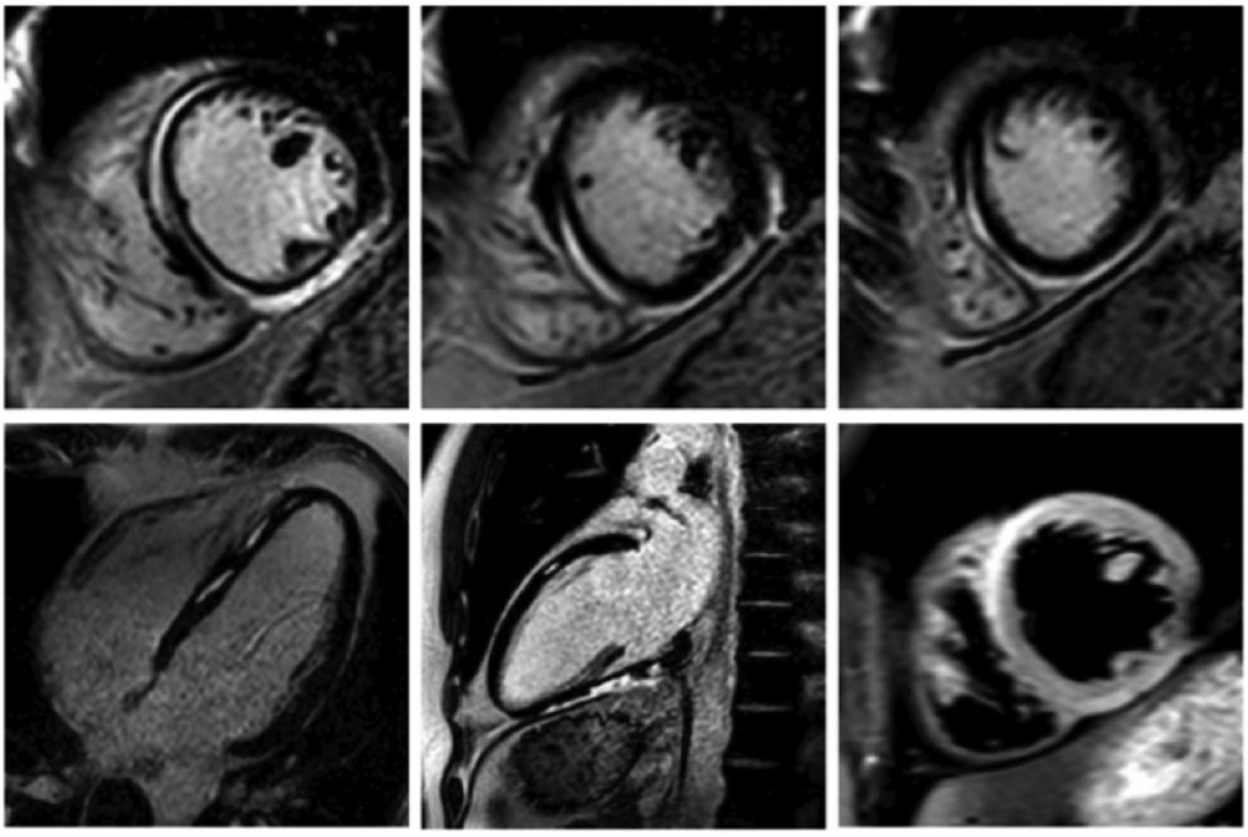

Figure 2 Cardiovascular magnetic resonance images at initial presentation showing marked mid- and epicardial hyper-enhancement in multiple segments on late gadolinium enhancement images and an area of myocardial oedema, in the anteroseptum on T2-weighted imaging. Top row (left to right): Basal short axis (SA), Mid-ventricular SA, Apical SA. Bottom row (left to right): four-chamber, two-chamber, T2-short tau inversion recovery (STIR) at mid-ventricular level.

The exact mechanism of acute myopericarditis in patients with Graves' disease is unclear. Endomyocardial biopsy is a tool that may allow the aetiology of myopericarditis to be more accurately defined[9]; for example, the finding of lymphocytic infiltrates without viral genome might raise the possibility of an autoimmune process.[1,10] These infiltrates have been previously noted in patients with autoimmune myopericarditis related to hyperthyroidism, supporting autoimmunity as the underlying process.[5,8] Indeed Koshiyama *et al.*[11] isolated TSH receptors on cardiac myocytes when investigating myocarditis associated with Graves' disease, leading them to suggest direct autoimmunity to this receptor as a possible mechanism.

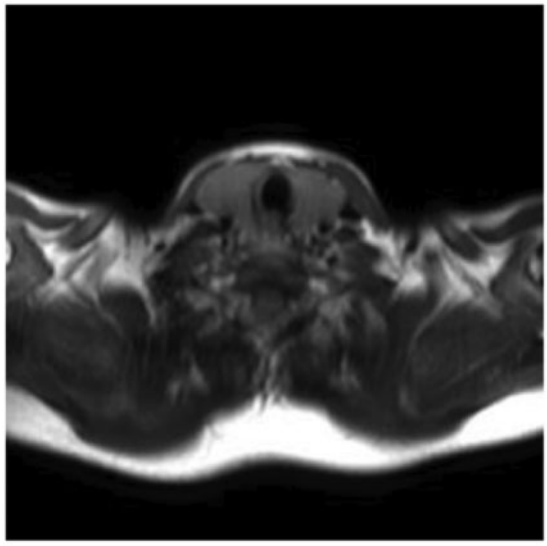

Figure 3 Cardiovascular magnetic resonance images on initial presentation showing enlarged thyroid gland (goitre) on black blood imaging.

In this case, EMB was not performed as CMR offered a very likely diagnosis of acute myopericarditis[1,2,8] without exposing the patient to further procedural risks; furthermore, a significant clinical and biochemical improvement was seen with propylthiouracil. The use of CMR here also allowed for early detection of the patient's goitre, something that had not been previously reported but is clearly of potential diagnostic relevance.

Alongside diagnostic information, CMR can aid in risk stratification in myopericarditis. Grani *et al.*[12] compared CMR findings to outcomes in patients with myopericarditis, finding a hazard ratio of 2.2 for major adverse cardiovascular events (MACE) in patients with LGE compared with those without. The highest probability of MACE-free survival was observed in those with LV ejection fraction >40% and no LGE present on CMR. The significance of the location of LGE was also reviewed, with septal involvement related to an increased risk of MACE in this study. In a similar retrospective study, LGE outside the infero-lateral segments was associated with increased risk of MACE.[13] In this gentleman, the

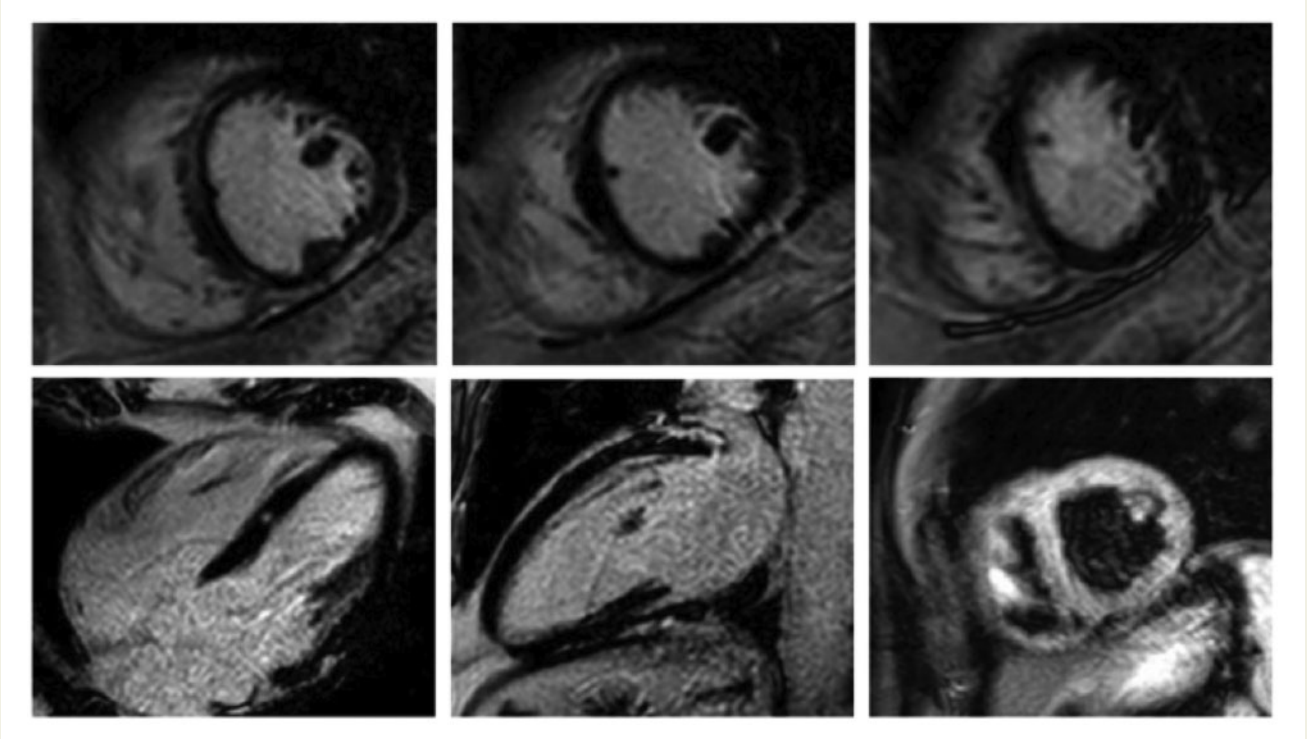

Figure 4 Cardiovascular magnetic resonance images from scan at follow-up, 8 months after acute event. Significant improvement seen in the extent of prior noted late gadolinium enhancement with resolution of myocardial oedema, though with residual fibrosis present. Top row (left to right): Basal SA, Mid-ventricular SA, Apical SA. Bottom row (left to right): four-chamber, two-chamber, T2 STIR.

findings of borderline ventricular dilatation and marked septal LGE were felt to be of sufficient concern to recommend continuation of low-dose ACEi and beta-blocker, particularly given that he had tolerated these without adverse effects.

Cases of acute myopericarditis have recently been linked to arrhythmogenic cardiomyopathy[14] (AC), with the pattern and extent of the LGE seen on CMR here raising this as a possibility. Desmoplakin genetic variants in particular have been noted in these patients and their relatives. Piriou *et al.*[15] performed genetic analysis on families with a history of acute myocarditis for genetic variants known to be associated with AC. They reported several variants in this cohort relating to the desmoplakin gene. However, inclusion criteria required a family to have a history of both acute myocarditis and sudden cardiac death, whilst also excluding those with a confirmed autoimmune cause. The patient was evaluated in the regional inherited cardiac conditions clinic by a consultant cardiologist with relevant expertise; a detailed family history yielded no signal for cardiomyopathy or sudden-death so genetic testing and family screening were not recommended. The patient remains under active follow-up.

Whilst rates of long-term complications from acute myopericarditis are low, there is the possibility of significant morbidity or mortality. A retrospective analysis[6] of 443 cases of myocarditis found that 7% of patients had an associated autoimmune condition, rising to 15% in complicated presentations. This is significant given that cardiac mortality and heart transplant in this study were reported only in patients with complicated presentations.

Conclusion

In cases of acute myopericarditis, the recognition of an underlying autoimmune condition such as Graves' disease may enable clinicians to offer potentially curative treatment. This, alongside the possibility of an increased risk of complications, leads us to conclude that clinicians should be aware of the link between Graves' thyrotoxicosis and acute myopericarditis and consider thyroid function testing in patients with known thyroid disease, symptoms consistent with hyperthyroidism or an enlarged thyroid on CMR.

Lead author biography

Thomas S. Anderton is a Cardiology Registrar in West Yorkshire, UK. Having completed undergraduate medical training at the University of Bristol and Foundation training in Leeds; he is now in the early stages of general cardiology training.

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.

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