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CASE REPORT
Other

Double trouble – thyro-pericarditis: rare presentation of Graves' disease as pericarditis—a case report

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Background Acute pericarditis is frequently encountered in clinical practice; however, pericarditis as the first presentation of Graves' disease is rare and mainly limited to case reports in the literature. We hereby report a case in which a young patient presented with pericarditis as the first manifestation of Graves' disease.

Case summary A 24-year-old male was admitted to hospital with presenting complaint of left-sided chest pain, gradual in onset, 6/10 in intensity, sharp in character, increased by deep breathing and improved by leaning forward. Patient also gave a history of insomnia, unintentional weight loss despite a good appetite, heat intolerance, and anxiety. On clinical examination, the patient had features of thyrotoxicosis, i.e., tachycardia, high volume pulse, and sweaty palms with fine tremors. There was no associated pericardial rub. Neck examination shows diffuse, non-tender goitre. Electrocardiogram findings were consistent with acute pericarditis. His thyroid function tests demonstrated hyperthyroidism and anti-thyroglobulin antibodies were also significantly elevated. Echocardiogram showed preserved left ventricular systolic function and a small global pericardial effusion without any signs of tamponade. He was diagnosed with Graves' disease revealing itself as pericarditis and was started on ibuprofen, beta-blockers, and carbimazole. Patient had marked clinical and biochemical improvement on 3 monthly follow-ups.

Discussion Thyro-pericarditis is a rare entity, and limited literature is available regarding this combination. The exact aetiology of Graves associated pericarditis is unknown. There is a possibility of interaction of autoantibodies with receptors on pericardium. Diagnosis is based on a detailed history, clinical examination, supplemented by relevant investigations (elevated free T4 and thyroid receptor antibodies, suppressed thyroid stimulating hormone (TSH) and Imaging via ultrasound). Mainstay of treatment includes non-steroidal anti-inflammatory drugs, beta-blockers, and anti-thyroidal medications.

Keywords Acute pericarditis • Pericardial chest pain • Graves' disease • Thyroid inferno • Autoimmune disorder • Case report

Learning points

- In patients with pericarditis, autoimmunity should always be kept in list of differentials.
- Graves can present as acute pericarditis, hence active search for signs and symptoms of Graves' could be rewarding and early commencement of treatment proves to be vital in symptoms control.

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Introduction

Acute pericarditis is defined as inflammation of the pericardium and is frequently encountered in clinical practice. Common causes of acute pericarditis include infections (both viral and bacterial), myocardial infarction, malignancy, and autoimmune disorders[1]. Autoimmunity is a common occurrence but its association with pericarditis is not fully understood. The relationship between Graves' disease and pericarditis is rare and mainly limited to case reports[3]. Herein, we present a case of a patient with pericarditis as the first manifestation of Graves' disease.

Timeline

Before admission: Tremors, anxiety, and unintentional weight loss.
Day 1: Typical pericardial chest pain with electrocardiogram (ECG) changes, thyroid functions showed thyrotoxicosis, and symptomatic management of pericarditis started.
Day 2: Echocardiographic conformation of small pericardial effusion and thyroid ultrasound showed features consistent with Graves' disease. In addition, thyroid receptor antibodies were positive and anti-thyroidals/beta-blockers were started.
Day 3: Clinical improvement in chest pain and systemic features of Graves' disease.
Day4: Patient discharged from hospital with further follow-up arranged under endocrinology.
Week 6: Normalization of thyroid functions and marked clinical improvement. Echocardiography and ECG were also normal.
Week 12: No recurrence of pericarditis and patient remained symptomatically and biochemically well.

Case presentation

A 24-year-old male was admitted to the acute medical assessment unit through emergency department with presenting complaint of left sided chest pain. Chest pain was gradual in onset, started overnight with 6/10 in intensity, sharp in character, increased by deep breathing and lying down, and improved by leaning forward. Chest pain was associated with nausea and single episode of non-bloody vomiting. Patient also reported fever, generalized tiredness, lethargy, and insomnia. Patient also had pounding of heart but thought that it was result of his anxiety. There was no history of sore throat, rigours, chills, cough, or sputum. Patient also denied history of shortness of breath, paroxysmal nocturnal dyspnoea, and orthopnoea or ankle oedema. There was no history of chest trauma or skin rash. There was no prior history of chest pains. Patient had history of insomnia, had significant unintentional weight loss of 6–8 kg over last 3 weeks despite good appetite, heat intolerance, shakiness of hands, and nervousness. He adamantly denied any visual disturbance or change in appearance of his eyes. His vitals on arrival were temperature 38°C, blood pressure 130/80 mmHg, heart rate 125 b.p.m., and respiratory rate 18.

On clinical examination patient looked anxious and in agony, there were fine tremors on outstretched hands with sweaty palms. His pulse was fast, regular, and high in volume. There was no exophthalmos clinically. Neck examination shows diffuse enlargement of thyroid gland which was non-tender, there was no associated lymphadenopathy. No bruit was heard over thyroid gland. On cardiac examination, heart tones were normal and no rub was appreciated. Respiratory and rest of systemic examination was normal. His medical history was only significant for anxiety disorder. He was a non-smoker and teetotaller. He denied use of herbal medicines or recreational drugs. Family history was unremarkable for pericarditis or thyroidal problems.

His electrocardiogram (ECG) (*Figure 1*) showed sinus tachycardia, diffuse ST-elevation in both chest and limb leads, PR depression in most of limb leads. In addition, there was PR elevation and reciprocal ST-depression in lead aVR. All of these features were suggestive of acute pericarditis. Chest X-ray was normal. Ultrasound thyroid with Doppler was done which showed enlarged thyroid with heterogeneous echotexture (*Figure 2A*) and increased vascularity also known as thyroid inferno (*Figure 2B*) suggestive of Graves' disease. In addition, there was neither focal nodule nor abnormality in thyroid, nor cervical lymphadenopathy. His thyroid function test demonstrated thyroid stimulating hormone (TSH) <0.02 mU/L (normal range 0.27–4.20) and freeT4 was >100 pmol/L (normal range 11–26). Antithyroglobulin antibodies were also significantly elevated 58.2 U/L (normal range 0–0.99). His first troponin was normal 14 ng/L (normal range 0–14), and repeat one was 19 ng/L (only minimally elevated). His C-reactive protein (CRP) was <5 mg/L (normal range 0–9) and erythrocyte sedimentation rate (ESR) was 5 (normal range 1–13). Antinuclear antibodies profile was negative (Supplementary material online), and rest of his blood investigations was unremarkable. Echocardiogram (*Figure 3*) was performed which showed preserved left ventricular systolic function without any regional wall motion abnormalities. There was a small global pericardial effusion noted (1 cm around right atrial free wall, 0.6 cm around lateral wall, and 0.3 cm posteriorly) which was not causing any haemodynamic compromise or tamponade. Right ventricular systolic function was preserved with no evidence of right heart strain.

His overall clinical picture, based on history and investigations, was consistent with a diagnosis of pericarditis associated with Graves' disease. Given his clinical context, he was started on ibuprofen 400 mg thrice daily (TDS) to control pain and inflammation with Pericarditis along with Omeprazole 40 mg once daily (OD). Carbimazole 40 mg OD was commenced to control Graves's systemic symptoms and Propranolol 40 mg TDS was prescribed to control anxiety, tremors, and tachycardia. Patient had remarkable improvement of his symptoms and was discharged a couple of days later with follow-up arranged in endocrine outpatients. He became clinically and biochemically euthyroid with subsequent thyroid functions after 12 weeks as: TSH 1.1 mU/L (normal range -0.27 to 4.20), free T4 20 pmol/L (normal range 11–26). Both his CRP and ESR on subsequent testing after 3 months remained normal. Both repeat ECG and echocardiography after 4 months revealed complete resolution of pericarditis.

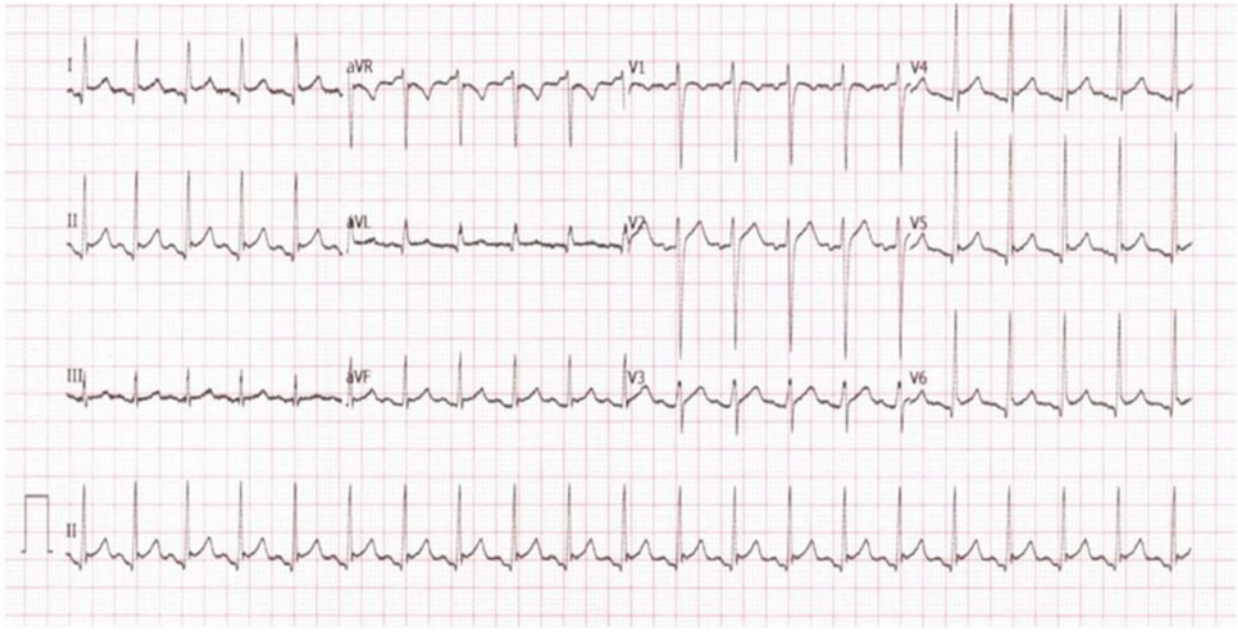

Figure 1 Diffuse saddle shaped ST-elevation, PR depression in most of the leads, PR elevation in aVR.

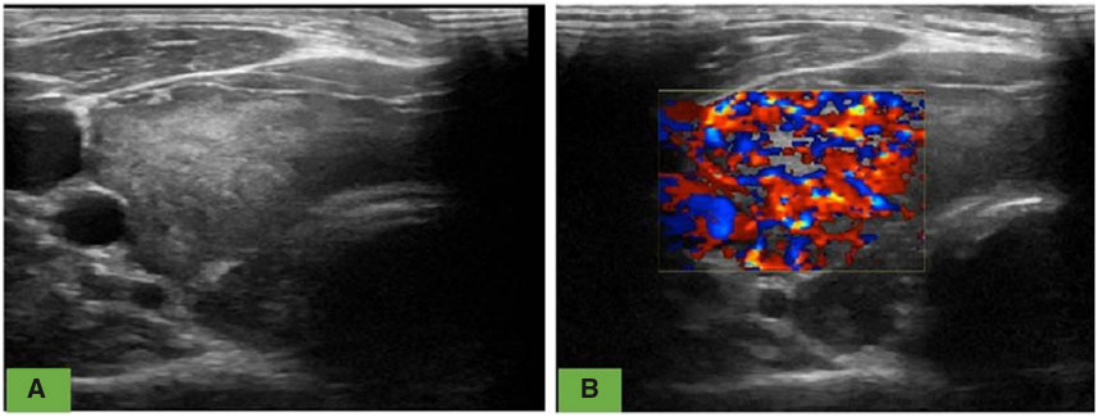

Figure 2 (*A*) demonstrates enlarged thyroid gland on ultrasound imaging and (*B*) shows increased vascularity of thyroid on colour Doppler.

Discussion

Graves' disease is an autoimmune thyroid disorder which results in overproduction of thyroid hormones resulting in thyrotoxicosis. Most common cardiac manifestations of Graves' disease are atrial fibrillation, tachycardia induced cardiomyopathy, and heart failure; however, thyrotoxicosis pericarditis is a rare and uncommon presentation.[1]

The exact pathophysiology and concurrent occurrence of Graves' disease and pericarditis is unknown.[2,3] There is an intricate relationship between autoantibodies and viral infection in pathogenesis of Grave disease and pericarditis. The most common pericardial manifestation in autoimmune disorders is pericarditis.[4] Similarly, viral infections like influenza, Coxsackie virus Epstein–Barr Virus, are commonly related to both Graves' disease and pericarditis.[5,6] Likely plausible explanation is that autoantibodies or viral infections interact directly or indirectly with some receptors on the pericardium in Graves' disease, resulting into pericarditis. Additionally, there are case reports of recurrent pericarditis; however, the likely mechanism is unknown but could be interaction of either autoantibodies and viral infections interaction with pericardial receptors or poor compliance with anti-thyroidal treatment.[7]

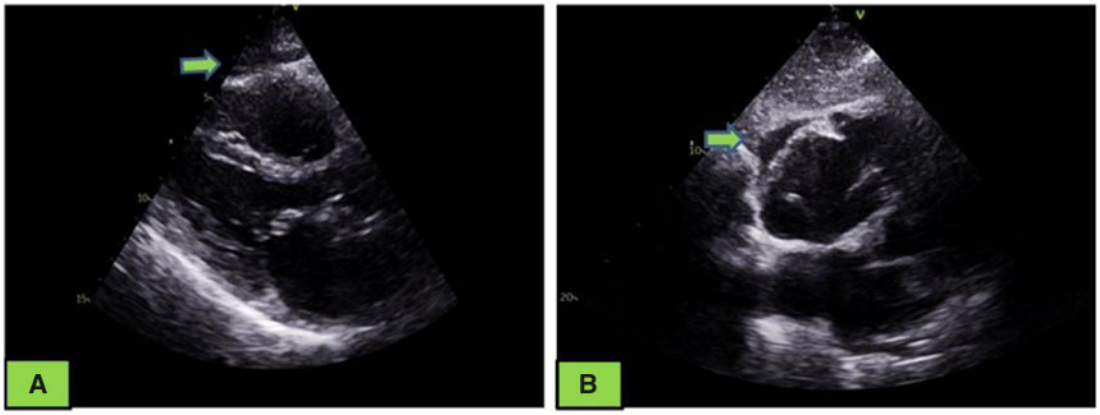

Figure 3 Parasternal long axis (*A*) and subcostal view (*B*) shows small global pericardial effusion without tamponade.

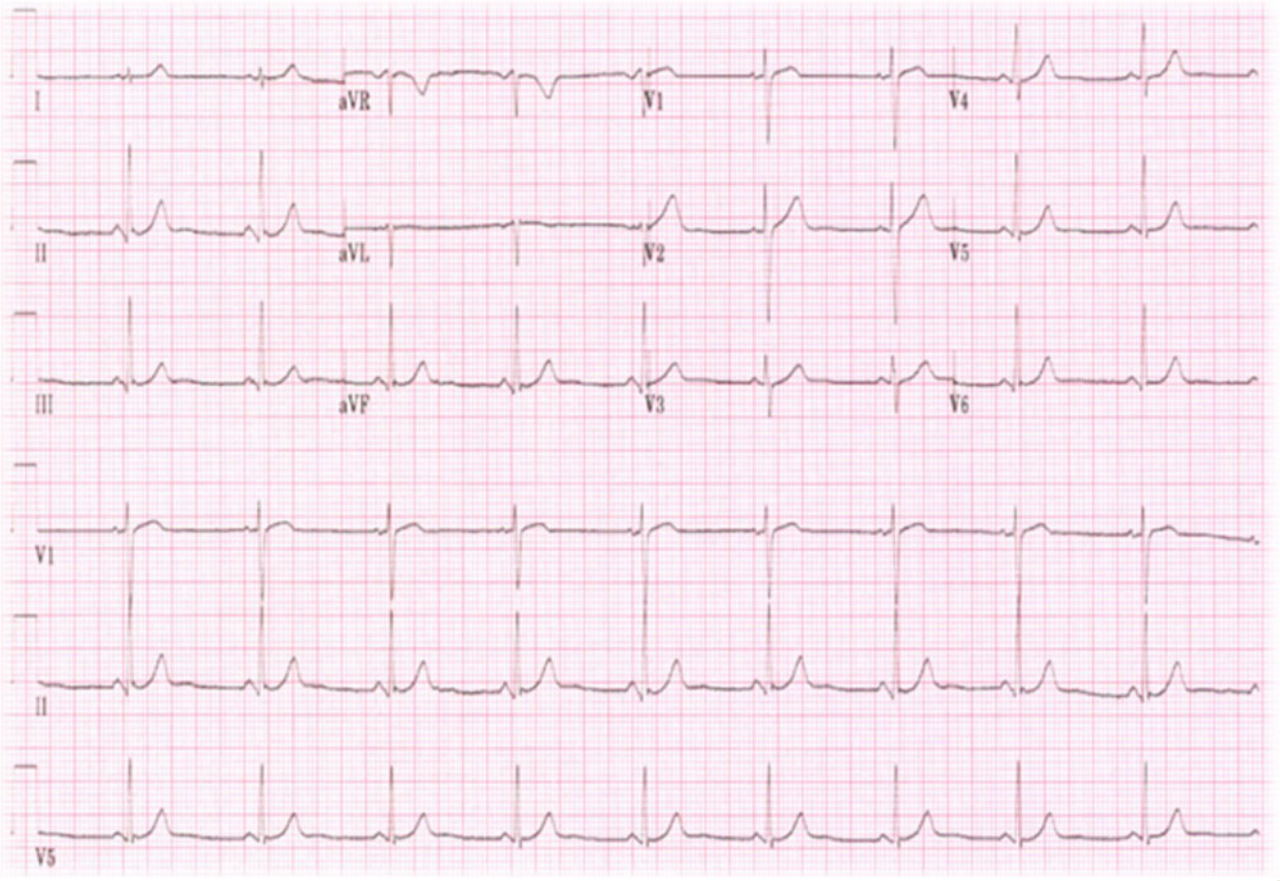

Figure 4 Repeat electrocardiogram showing normalization following treatment.

Graves' disease is typically diagnosed by constellation of clinical features suggestive of hyperthyroidism coupled with suppressed TSH, elevated thyroid hormone concentrations, and elevated levels of thyroid-stimulating immunoglobulins or TSH receptor antibodies.[7] Thyroid ultrasound scan typically shows heterogeneous enlarged gland with increased vascularity on Doppler which is the hallmark of Graves' disease.[8] Radioactive thyroid uptake scan is one of the definitive diagnostic test, which typically shows diffuse uptake of the gland

in Graves' disease. Due to its limited availability, high cost, and ionizing radiation exposure,[9] this could be reserved for cases in which there is doubt about the diagnosis.

The treatment options in thyro-pericarditis include:

(1) Non-steroidal anti-inflammatory drugs (NSAIDS): To reduce inflammation of pericardium and chest pain.
(2) Colchicine: can be used if NSAIDS are contraindicated, failed to improve symptoms or recurrent pericarditis.
(3) Beta-blockers to control heart rate, tremors, heat intolerance, anxiety, and nervousness.
(4) Anti-thyroid agents should be commenced at time of diagnosis to help achieve euthyroid status. Poor adherence with anti-thyroidal treatment is considered to be one of risk factors for recurrent pericarditis.
(5) Recurrent pericarditis may occur in up to 30% of patients after an initial episode of acute pericarditis. Treatment should comprise of an NSAID, typically with a 2- to 4-week tapering after the resolution of symptoms, along with at least 6 months of colchicine. Low dose corticosteroids should be reserved for those who have failed to respond despite treatment combination of NSAID plus colchicine. Anti-interleukin 1 therapy (e.g. Anakinra and Rilonacept), Methotrexate, Mycophenolate mofetil, intravenous immunoglobulins could potentially be a treatment option for patients with refractory, corticosteroid-dependent disease.[10]

Conclusion

Graves' disease, presenting as pericarditis, is a rare entity and current literature is restricted mainly to case reports. Autoimmunity is a known association with pericarditis and should be suspected in patients with relevant history and clinical examination. In pericarditis, active search for signs and symptoms of Graves could be rewarding and early commencement of treatment proves to be beneficial in symptoms control.

Lead author biography

Mohsin has been training as a Cardiology trainee in South Yorkshire deanery NHS England and has special interest in Interventional Cardiology.

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 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.

References

1. 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.
2. Sugar SJ. Pericarditis as a complication of thyrotoxicosis. *Arch Intern Med* 1981; **141**:1242.
3. Tsai MS, Yang CW, Chi CL, Hsieh CC, Chen WJ, Huang CH. Acute pericarditis: a rare complication of Graves' thyrotoxicosis? *Am J Emerg Med* 2006;**24**: 374–375.
4. Permanyer-Miralda G, Sagristá-Sauleda J, Soler-Soler J. Primary acute pericardial disease: a prospective series of 231 consecutive patients. *Am J Cardiol* 1985;**56**: 623–630.
5. Nagata K, Fukata S, Kanai K, Satoh Y, Segawa T, Kuwamoto S, *et al.* The influence of Epstein–Barr virus reactivation in patients with Graves' disease. *Viral Immunol* 2011;**24**:143–149.
6. Zafrir B, Aviv A, Reichman N, Flatau E. Epstein–Barr virus-associated pericarditis and pericardial effusion: case report and diagnostic aspects. *Eur J Intern Med* 2005;**16**:528–530.
7. Cullen D, Munjal N, Chalal H, Ramgopal S, Tas E, Witchel S. Pericarditis as the presenting feature of Graves disease in a pediatric patient. *Pediatr Emerg Care* 2017;**33**:268–270.
8. Hari Kumar K, Pasupuleti V, Jayaraman M, Abhyuday V, Rayudu BR, Modi K. Role of thyroid Doppler in differential diagnosis of thyrotoxicosis. *Endocr Pract* 2009; **15**:6–9.
9. Donkol RH, Nada AM, Boughattas S. Role of color Doppler in differentiation of Graves' disease and thyroiditis in thyrotoxicosis. *World J Radiol* 2013;**5**: 178–183.
10. Chiabrando JG, Bonaventura A, Vecchié A, Wohlford GF, Mauro AG, Jordan JH, *et al.* Management of acute and recurrent pericarditis. *J Am Coll Cardiol* 2020;**75**: 76–92.