

CASE REPORT

Acute autoimmune myocarditis as a manifestation of Graves' disease: A case report and review of the literature

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Abstract

Acute myocarditis and hyperthyroidism are common diseases that often present in young, otherwise healthy patients. Autoimmunity is central to the pathogenesis of both. Patients presenting with acute myocarditis should be screened for symptoms of hyperthyroidism, and physicians should consider screening for myocarditis in patients with hyperthyroidism and persistent cardiac symptoms.

KEYWORDS

autoimmune, cardiac magnetic resonance imaging, Graves' disease, hyperthyroid, myocarditis

1 | INTRODUCTION

We report a case of acute myocarditis in the setting of new-onset Graves' disease. A previously healthy 29-year-old man presented with acute onset chest pain, palpitations, and elevated troponin. We discuss autoimmunity as an underlying cause of rare development of both acute myocarditis and Graves' disease.

Acute myocarditis is an acute inflammatory myocardial disease with a wide spectrum of clinical manifestations, ranging from asymptomatic to life-threatening presentations depending on the degree of myocardial involvement. There is strong evidence of an autoimmune pathological process in acute myocarditis, in many cases triggered by a viral infection.¹ Presentation of acute myocarditis often mimics acute coronary syndrome in young patients with otherwise minimal cardiovascular risk factors.^{1,2}

Graves' disease is an acute hyperthyroid state that often occurs in this same population of otherwise young, healthy patients and has a well-defined autoimmune etiology.³ Long-standing hyperthyroidism may result in cardiomyopathy, mediated via persistent hyperdynamic circulation and cardiac arrhythmia.⁴⁻⁶ Herein, we describe a rare case of acute hyperthyroidism (Graves' disease) that was complicated by acute myocarditis.

2 | CASE PRESENTATION

A previously healthy 29-year-old male presented to the emergency department (ED) with crushing chest pain. He reported one week of severe, episodic pain occurring at rest, associated with radiation to the scapula, diaphoresis, and nausea. He also reported palpitations beginning two weeks prior, which prompted an outside hospital ED visit. He was diagnosed with hyperthyroidism at that time based on low thyroid-stimulating hormone (TSH) and high free T4. He denied other symptoms of hyperthyroidism including diarrhea, anxiety, or weight loss. He was started on propranolol for symptomatic treatment and referred to endocrinology. After one week of therapy, the palpitations resolved but his chest pain ensued, prompting presentation to our ED.

Upon arrival, troponin was elevated at 6 ng/mL (reference level < 0.02 ng/mL). He was admitted and received aspirin, clopidogrel, and enoxaparin for suspected acute coronary syndrome. Over the next 4 hours, the patient's chest pain subsided. His troponin peaked at 10.57 ng/mL. Electrocardiography demonstrated sinus tachycardia with abnormal ST-segment convexity in V3-V6 and marginal ST-segment depression in III and aVF (Figure 1). Repeat thyroid studies demonstrated

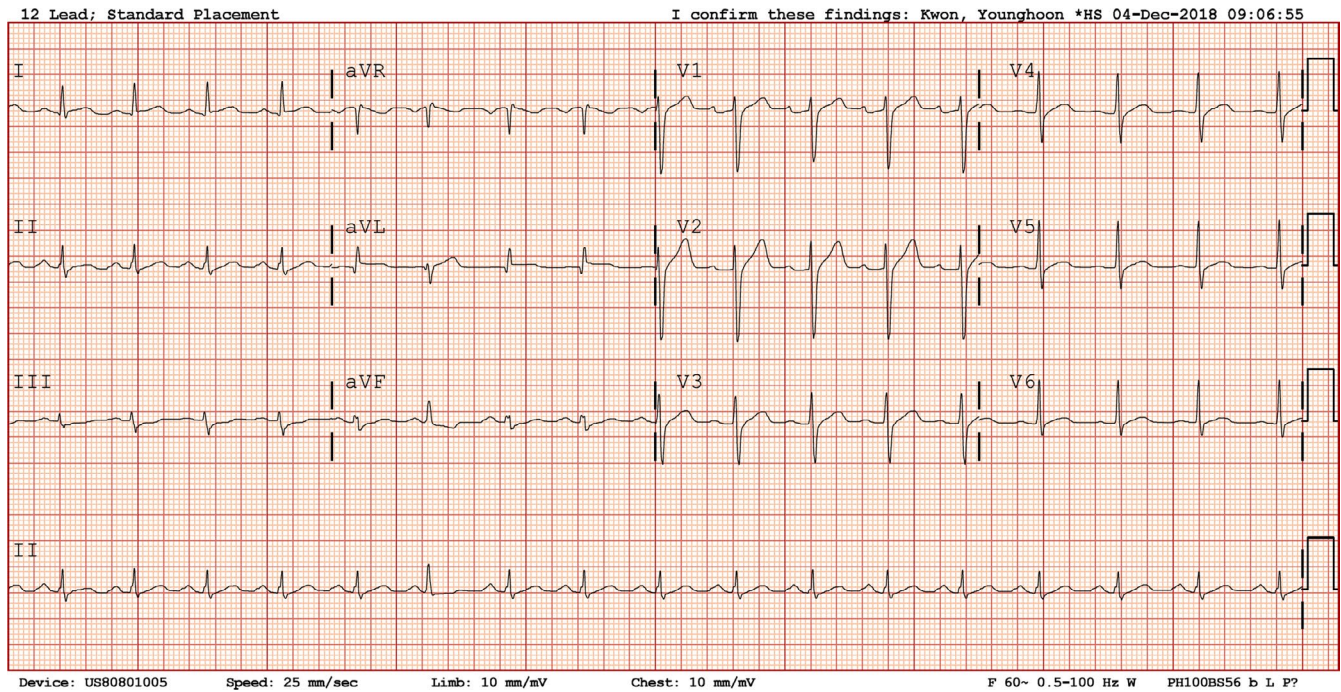


FIGURE 1 Initial electrocardiograph demonstrating sinus tachycardia with abnormal ST-segment convexity in V3-V6 and marginal ST-segment depression in III and aVF



FIGURE 2 A, Native T2 mapping 4 chamber view demonstrates diffuse myocardial edema with a range of 50-60. B and C, Phase sensitive inversion recovery images in four chamber and mid-short axis view show subepicardial late gadolinium enhancement in the mid lateral wall, as noted with red arrows. Additionally, elevated extracellular volume (ECV) over 30% in the corresponding segments noted

undetectable TSH (reference level 0.45-4.5 mIU/L) and elevated thyroid hormones including free T4 of 3.5 ng/dL, total T4 of 17.5 μ g/dL, and free T3 of 12.1 pg/dL, consistent with hyperthyroidism (reference levels 0.7-1.5 ng/dL, 4.9-11.0 μ g/dL, and 2.3-4.2 pg/mL, respectively).

Given the patient's young age and lack of significant cardiovascular risk factors, cardiac magnetic resonance imaging (CMR) was performed, demonstrating diffuse left ventricular edema and subepicardial late gadolinium enhancement in the mid-to-distal anterior and anterolateral walls (Figure 2). There was mild hypokinesis of the corresponding areas with a global left ventricular ejection fraction of 54%. Similar mild

regional wall motion defect was noted on limited echocardiogram. These findings were consistent with a clinical picture of acute myocarditis. Because these findings did not support a diagnosis of acute coronary syndrome, cardiac catheterization was not pursued.

The concurrent presentation of acute myocarditis and acute hyperthyroidism raised our suspicion for a viral etiology. While the patient did not recall a preceding illness, his occupation as a dialysis nurse was considered a risk factor for exposure. Given that viral infection is the most commonly identified cause of myocarditis, subclinical hyperthyroidism secondary to a virus was the suspected underlying etiology.

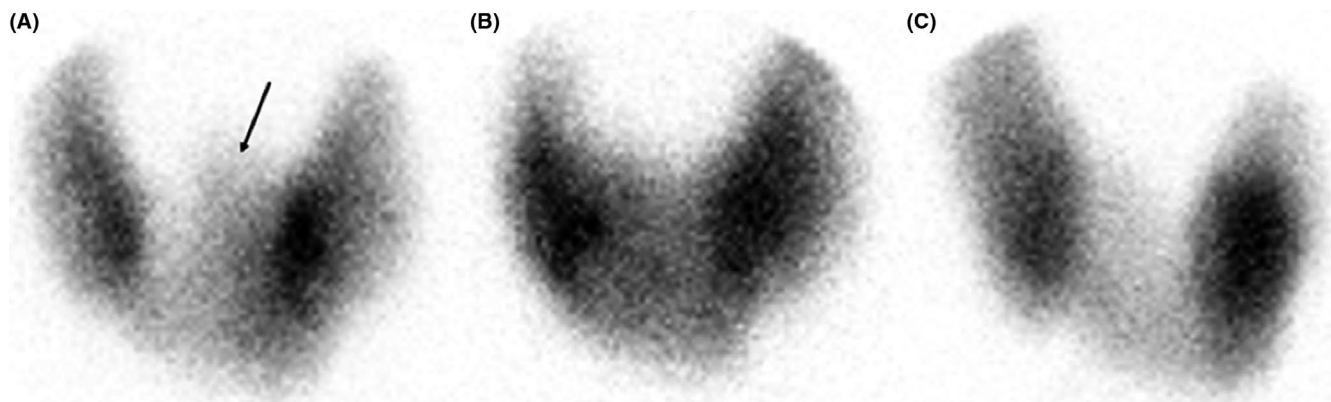


FIGURE 3 Anterior (A) and bilateral oblique (B,C) pinhole collimator images of an iodine-123 uptake scan obtained 4 h after injection show diffusely increased thyroid gland uptake. Pyramidal lobe is also visualized (arrow). The calculated I-123 uptake values were 43% at 4 h (normal: 6%-18%) and 45% (normal: 10%-30%) at 24 h consistent with Grave's disease

In consultation with endocrinology, the patient was started on a beta-blocker to control tachycardia and a nonsteroidal anti-inflammatory medication, as is standard of care for viral thyroiditis.⁷ The decision was made to switch from propranolol to metoprolol as the two medications have equivalent efficacy in the treatment of thyroid disease,^{8,9} while metoprolol additionally has well-established efficacy in the treatment of heart failure.¹⁰ Given his stability, he was discharged with an arrangement for a follow-up visit.

3 | OUTCOME AND FOLLOW-UP

Upon follow-up in endocrinology clinic, the patient endorsed persistent symptoms of hyperthyroidism including heat intolerance and muscle weakness. New tremor was noted on examination. TSH remained undetectable with elevated free T3 and free T4. Additionally, the patient's thyroid-stimulating immunoglobulin index was elevated to 4.5 (reference level ≤ 1.3) and thyrotropin-binding inhibitory immunoglobulin was elevated to 9.15 IU/L (reference level 0-1.75 IU/L). Thyroid scan demonstrated diffusely increased radiotracer uptake consistent with Graves' disease (Figure 3). These findings favored Graves' disease over viral thyroiditis as the etiology of the patient's hyperthyroidism. Based on this, the patient was started on methimazole 10 mg twice daily.

Three months following hospitalization, the patient experienced resolution of all cardiac symptoms including any recurrent chest pain, palpitations, shortness of breath, or excessive fatigue. He was continued on metoprolol. A repeat echocardiogram six months following hospitalization demonstrated left ventricular ejection fraction 60%-65% with a resolution of regional wall abnormality previously noted. Left ventricular diastolic function was normal as evidenced by the following indices: mitral valve E/A ratio 1.3, deceleration time 177 ms, septal e' 10 cm/s, lateral e' 13 cm/s, and E/E' ratio 6.6.

4 | DISCUSSION

Long-standing hyperthyroidism has a well-defined association with cardiac arrhythmias, congestive heart failure, and dilated cardiomyopathy.^{3,4,11} There are numerous reports of acute dilated cardiomyopathy in the setting of Graves' disease, especially in the context of severe hyperthyroidism.^{12,13} Less common cardiac complications of Graves' disease include coronary vasospasm, in some cases causing myocardial infarction, and myxoid valve degeneration.^{3,14,15} This case of acute myocarditis in a young patient represents a rare presentation of autoimmune myocarditis associated with Graves' disease.

Acute myocarditis is well characterized in a large cohort study by Ammirati et al² The vast majority of patients presented with chest pain, electrocardiographic changes, and elevated troponin, often preceded or accompanied by fever or other infectious symptoms. An autoimmune disorder was observed in 7.2% of all patients and up to 15% of severe cases, with eosinophilic granulomatosis with polyangiitis and mixed connective tissue disease being the most common.² This provides evidence that acute myocarditis often occurs in the context of systemic autoimmune disease.

Mavrogeni et al¹⁶ investigated the relationship between autoimmunity in thyroid disease and myocarditis in 250 patients with hyperthyroidism and persistently high anti-thyroglobulin and antimicrosomal antibodies despite being euthyroid on treatment. Fifty patients had persistent cardiac symptoms including chest pain, dyspnea, and palpitations. Many underwent CMR, which demonstrated myocarditis. Endomyocardial biopsy in selected patients revealed lymphocytic infiltration without viral infection, indicative of autoimmune etiology.¹⁶ This study demonstrated that (a) a large proportion of patients with hyperthyroidism suffer from cardiac symptoms; (b) myocarditis is often the underlying cause;

and (c) persistent autoimmunity may cause inflammation in both the thyroid and myocardium, even in the absence of active viral infection.

Our case report differs from the case series by Mavrogeni et al in multiple ways. Though participants in the Mavrogeni study manifested persistent cardiac symptoms, they were clinically euthyroid with normal thyroid hormone levels and had negative cardiac enzyme studies. Our case report concerns a patient with active symptoms of hyperthyroidism, elevated thyroxine, suppressed TSH, and acute onset of cardiac symptoms with elevated cardiac enzymes.

Another relevant case series reinforces the hypothesis that autoimmune myocarditis is a rare manifestation of Graves' disease. Eleven patients with Graves' disease and unexplained systolic dysfunction underwent endomyocardial biopsy, and two of these biopsies revealed lymphocytic infiltrates consistent with autoimmunity.¹⁷

There is still no consensus on the exact mechanism underlying the autoimmune myocarditis syndrome. For example, some authors have identified TSH receptor in cardiac myocytes, findings which have not been reproduced by others.¹⁸⁻²⁰ Other researchers have argued that cardiac antigens such as the beta-1 adrenergic receptor are the target of autoimmunity, a proposition that is yet to be confirmed.²¹ Existing studies show that up to 20% of patients with hyperthyroidism have cardiac symptoms.¹³ Screening all hyperthyroid patients with CMR to investigate for myocarditis is cost prohibitive, but echocardiography may be pursued as a more cost-effective study in selected patients. Appropriate patients would include those with severe, recurrent cardiac symptoms or cardiac symptoms that fail to resolve after appropriate management of hyperthyroid disease. On the other hand, all patients presenting with acute myocarditis should be screened for symptoms of hyperthyroidism, especially extracardiac manifestations such as tremor, weight loss, anxiety, or heat intolerance. Further testing, starting with a screening TSH, should be pursued if those symptoms are present. Physicians should have an especially high index of suspicion for atypical cases of acute myocarditis, such as patients who do not report any viral prodrome. While the prevalence of autoimmune hyperthyroidism disease in myocarditis is low (0.5%-1.0%),² early identification of these patients will aid in timely treatment of acute hyperthyroidism and prevention of other complications associated with the hyperthyroid state.

We recommend using beta-blockers for the treatment of acute myocarditis associated with hyperthyroidism. Not only is the use of beta-blockers for myocarditis a common, well-established practice,² this medication will also provide significant reduction in symptoms of hyperthyroidism.^{8,9} Additionally, diuretics may be used as needed for more severe cases of myocarditis leading to symptoms of heart failure.^{1,2} Although there is not yet consensus on the use of immunosuppressive agents for the treatment of myocarditis, recent

research suggests that immunosuppressive medications such as prednisone may provide short- and long-term benefits for cardiac function.²² Given the suspected autoimmune etiology of the myocarditis associated with hyperthyroidism, physicians should consider administering a short course of steroids in these cases.

Patients with clinical symptoms of hyperthyroidism and a suppressed TSH should have further testing performed to determine the etiology of hyperthyroidism. These tests may include a radioactive iodine uptake scan, thyrotropin-binding inhibitory immunoglobulin, thyroid-stimulating immunoglobulin index, antimicrosomal antibodies, and antithyroglobulin antibodies.^{7,23} As previously discussed, hyperthyroid symptoms may be managed with beta-blockers while awaiting definitive diagnosis and treatment of underlying thyroid pathology.

In conclusion, we report a rare presentation of concurrent Graves' disease and autoimmune myocarditis.

CONFLICTS OF INTEREST

No authors have any conflict of interest to declare.

AUTHOR CONTRIBUTIONS

SL: Drafted the manuscript; KK, YJL, SM, and YK: Revised the manuscript; YK, KK, and SL: Involved in patient care; YJL: Reviewed, formatted, and interpreted all radiologic imaging. All authors have read and approved the final version of the manuscript.

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