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CASE REPORT

Insights Into a Hypercoagulable Case of Thyrocardiac Disease and Literature Overview

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Abstract

Hyperthyroidism is associated with a hypercoagulable state and has been described previously in case studies in the context of cerebral vein thrombosis and pulmonary emboli. In this case report, we present a middle-aged man with a rare combination of rheumatic mitral valve disease and thyroid storm complicated by enormous intracardiac thrombus burden. We aim to highlight the hypercoagulable state associated with thyrocardiac disease and to alert the physician to remain vigilant for not only this clinical entity but also for multiple disease states occurring in 1 patient.

Background

Thyrocardiac disease is a well-described medical entity. Its association with coagulation and fibrinolysis has been described increasingly in the last 2 decades; however, it is still currently underappreciated (1). Several studies including case reports have focused on hyperthyroidism causing thromboembolic disease both with and without atrial arrhythmias (2–8).

Objective

This case highlights the prothrombotic state associated with hyperthyroidism and cardiac disease.

Case Presentation

A 45-year-old African man with no pertinent medical history presented to a tertiary hospital in a thyroid storm secondary to Graves disease. He reported palpitations, fatiguability, bipedal edema, weight loss, and diarrhea in the preceding weeks. Of note, he was a smoker with a 10 pack-year history.

On clinical examination, he was found to be afebrile with a blood pressure of 136/87 mm Hg (MAP 103 mm Hg) and fast atrial fibrillation (AF) with ventricular rates of 170 beats/min confirmed on electrocardiogram (Figure 1). He had bipedal edema and no obviously noted

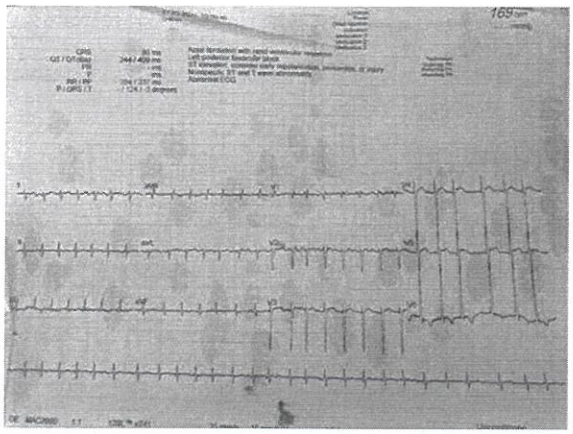

Figure 1. **Twelve-lead electrocardiogram shows rapid atrial fibrillation, biventricular hypertrophy, and right axis deviation.**

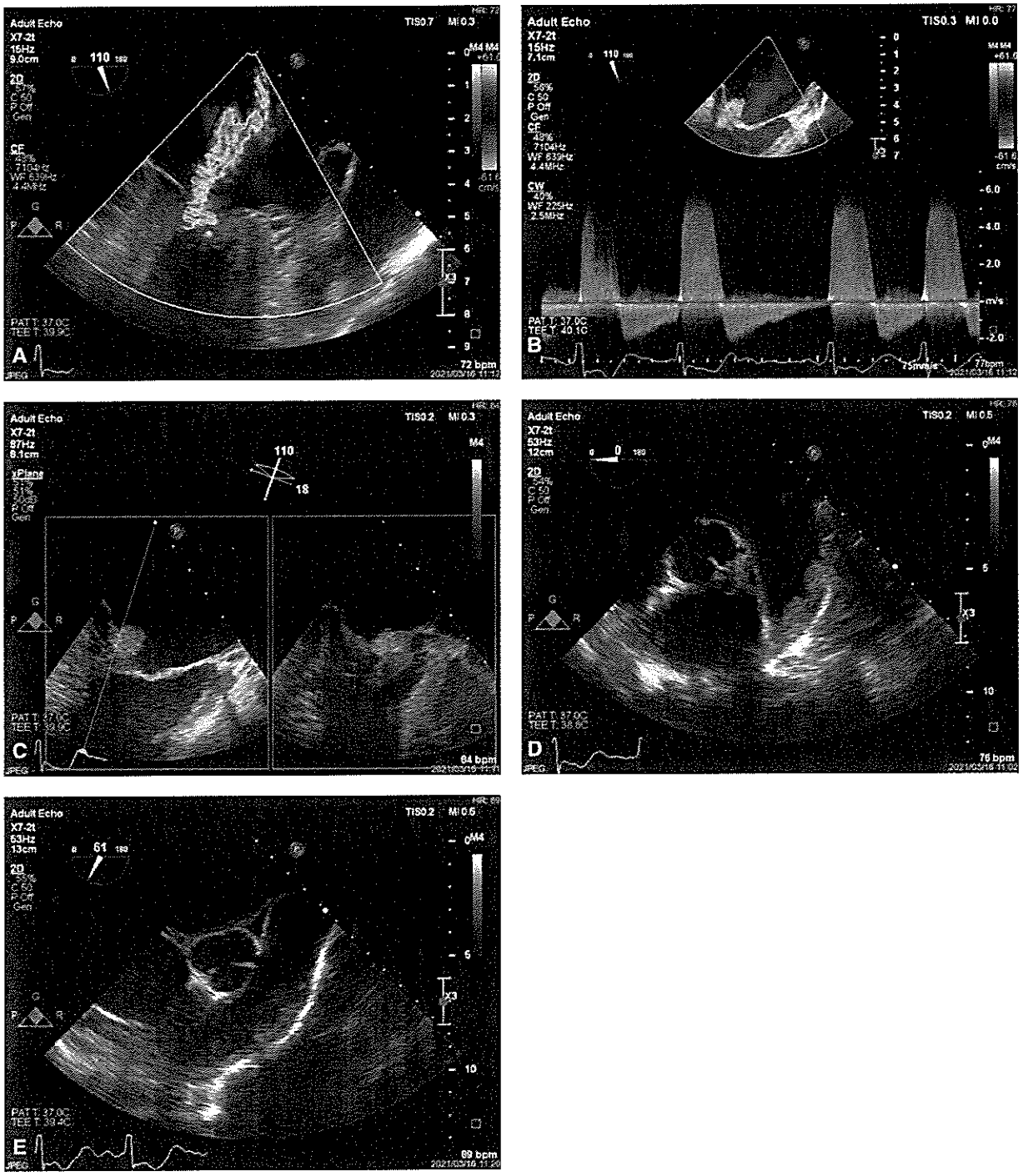

Figure 2. **(A and B) Dilated left atrium with rheumatic mitral regurgitation and mitral stenosis. (C) Rheumatic mitral stenosis with thrombus on the posterior mitral leaflet is noted. (D) Rheumatic mitral stenosis with thrombus in left atrial appendage. (E) Extensive thrombus along the right ventricular outflow tract and pulmonary artery.**

goiter. Cardiac auscultation revealed S1 with loud, palpable P2 with pansystolic murmurs in the tricuspid and mitral areas. Transthoracic echocardiography revealed biventricular enlargement, left atrial dilatation (59 mm) with rheumatic moderate mitral stenosis, severe mitral regurgitation, and severe tricuspid regurgitation. Left ventricular ejection fraction was reduced at 39% and pulmonary artery systolic pressure was elevated at 77 mm Hg. Multiple intracardiac thrombi were found on the left atrial appendage, posterior mitral leaflet, right ventricular outflow tract (RVOT), and the proximal pulmonary artery that were confirmed on transesophageal echocardiography (Figure 2A–E).

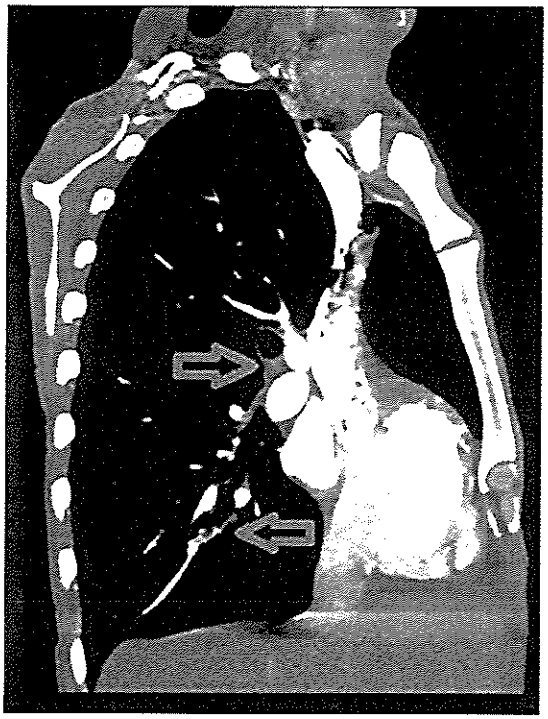

Figure 3. Sagittal view of the chest with filling defect in the segmental branch pulmonary artery suggestive of pulmonary embolism (*arrows*).

Thyroid function tests revealed thyroid-stimulating hormone level of <0.01 mIU/L, free T4 level 39.2 pmol/L, and thyroid-stimulating hormone receptor antibody of 39.33 IU/L, which was indicative of hyperthyroidism secondary to Grave's disease. A raised D-dimer of 5.48 mg/L also was noted.

Once the patient was successfully anticoagulated and a reasonable drop in FT4 was seen, a computed tomography pulmonary angiogram was done to confirm peripheral pulmonary emboli (Figure 3). Bilateral lower-lobe acute pulmonary emboli were noted. Due to low clinical suspicion for deep venous thrombosis (DVT) and a Wells score of zero, no further studies for lower-limb DVT testing were done.

It is important to emphasize that in this case, there were multiple possibilities to entertain the origin of the intracardiac clots. Rheumatic mitral valve disease (MVD) complicated by AF, thrombophilia, a possible patent foramen ovale, infective endocarditis, nonbacterial thrombotic endocarditis, and hypercoagulable state due to hyperthyroidism were considered. An intracardiac shunt was excluded by a negative bubble test finding on transesophageal echocardiography study, and thrombophilia and nonbacterial thrombotic endocarditis were excluded with negative antiphospholipid antibodies and negative autoimmune studies. The patient failed to fulfill the Duke's criteria for infective endocarditis. Rheumatic MVD complicated by AF explained the left-sided thrombi. However, in view of RVOT and pulmonary artery thrombi, hyperthyroidism was likely the main contributor to the hypercoagulable state.

The patient was followed up a month later. The AF had resolved, and repeat transthoracic echocardiography showed no thrombi in the RVOT or pulmonary artery; however, there was a hypermobile thrombus on the posterior mitral valve leaflet secondary to partial clot dissolution (Figure 4A and B). Due to the high risk for embolization, the patient was transferred urgently for mitral valve replacement. Rheumatic MVD and presence of left atrial appendage thrombus were confirmed intraoperatively (Figure 4C). Histologic specimens revealed valvular tissue with calcification. No vegetation was seen. He had a good postoperative outcome and was well at 1 month of follow-up. Written informed consent was obtained from the patient for publication of this article and the accompanying images.

Discussion

Since 1912, numerous case reports have been written up eluding to the link between hyperthyroidism and venous thrombosis—in the form of DVT, pulmonary emboli, as well as cerebral vein thrombosis (2–6). Hyperthyroidism affects the coagulation system and causes a hypercoagulable and decreased fibrinolytic state, with increased levels of von Willebrand factor, factor VIII, and fibrinogen, among others (1, 9–11). Histologic comparison of clots from euthyroid individuals and patients with hyperthyroidism showed denser fibrin network in the latter group and increased clot lysis time, which is consistent with decreased fibrinolysis (10). The proposed mechanisms by which the thyroid hormone affects the coagulation system have been divided into genomic and nongenomic groups (10, 11). Genomic influences involve thyroid hormone receptor subtype B (THRB)-mediated effects on the production of coagulation factors (11). Patients with defective THRB have elevated circulating thyroid hormones; however, they do not respond to the hormones at a tissue level (11). The hypothesis is structured around the fact that THRB is abundant in the liver, which is responsible for the synthesis of some coagulation factors (11).

Nongenomic pathways include mechanisms that do not rely on the interaction between thyroid hormone and the nuclear receptors (10). They include thyroid hormone–mediated increase in procoagulants including platelet activation as well as the release of specific cytokines (10).

Our patient had multiple factors that portended to the high thrombus burden. Aside from the hypercoagulability and endothelial dysfunction caused by the hyperthyroidism, AF combined with heart failure and valve disease exacerbated stasis of blood and contributed to the prothrombotic state. In the current case, the combination of multiple comorbidities contributing to an extreme state of hypercoagulability is an uncommon presentation and to our knowledge has not been described previously. It serves to draw attention of the clinician to maintain a state of vigilance and do a complete examination and investigations of comorbidities such as valvular heart disease, as in this case, and not merely attribute the heart failure and hypercoagulable state to hyperthyroidism and AF.

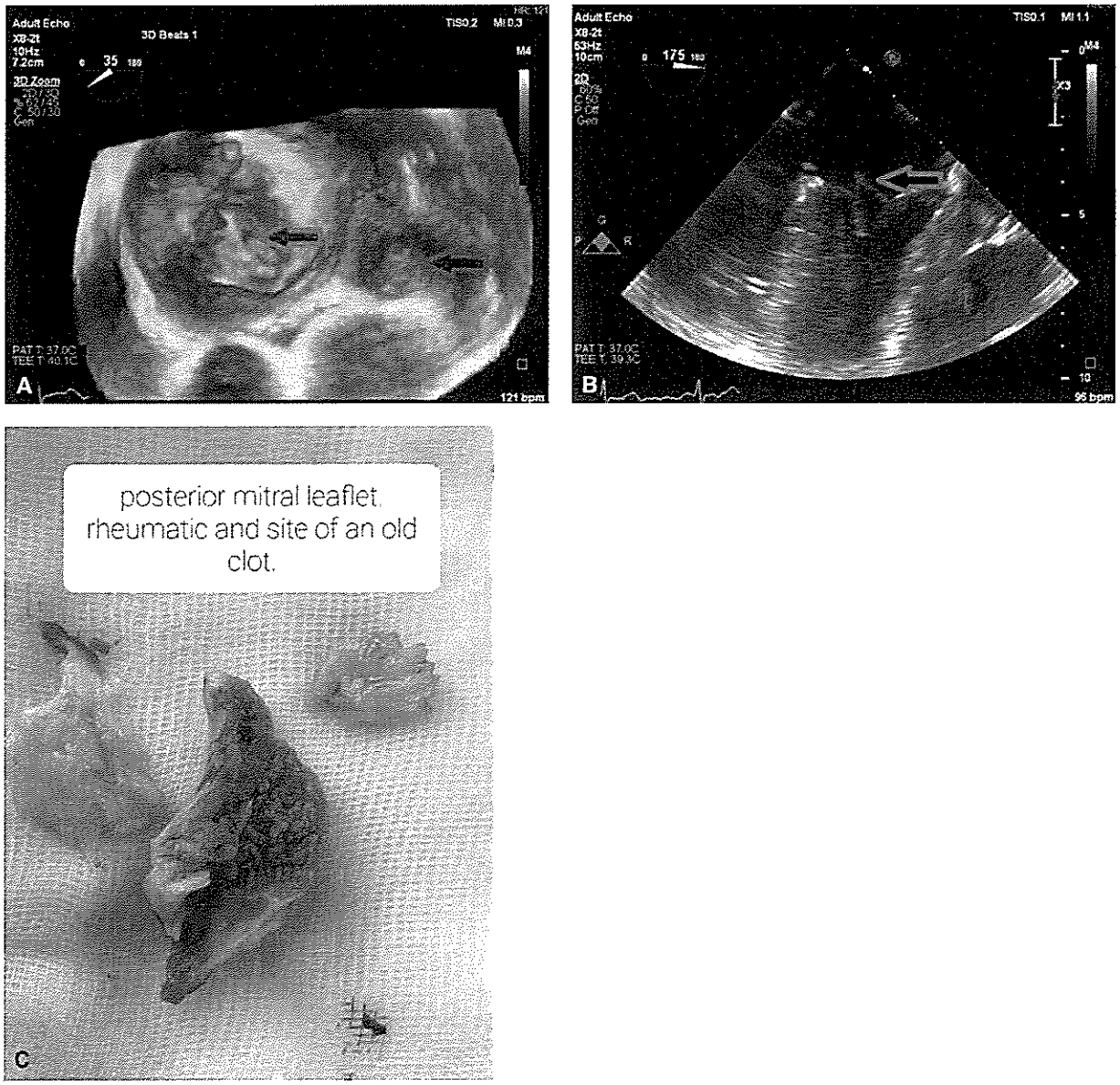

Figure 4. Transesophageal echocardiographic view with 3-dimensional reconstruction showing large mobile thrombus on the posterior mitral leaflet (A, *blue arrow*), left atrial appendage (A, *red arrow*). (B) Comparative 2-dimensional view showing thrombus (*blue arrow*) on the follow-up visit. (C) Intraoperative specimen showing rheumatic posterior mitral leaflet and the site of old thrombus.

In addition, there are currently no clear guidelines in terms of anticoagulation for high-risk patients with hyperthyroidism in the absence of AF. Of note, increased thyroid hormone levels enhance the anticoagulative effect and antithyroid agents (propylthiouracil and methimazole) decrease the anticoagulative effect of vitamin K antagonists (12). Thus, careful consideration for initiating anticoagulation as well as monitoring of international normalized ratio within recommended levels during treatment of this group of patients is necessary.

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