Venous thromboembolism and thyric hyperplasia in the setting of silent Graves’ disease

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INTRODUCTION

Venous thromboembolism (VTE) is a multifactorial disease, with an incidence of 1 to 2 cases per 1000 annually(1). Several controlled and uncontrolled risk factors such as smoking, obesity, immobility, malignancy, and a family history of thrombotic disorders can contribute to a hypercoagulable state, leading to VTE. In current literature, associations have been made between hyperthyroidism and a hypercoagulable state presenting in the form of thrombosis in the cerebral venous system(2), however, no clear relationship between hyperthyroidism and venous thromboembolism has been established.

In this case, we discuss the presentation of deep vein thrombosis (DVT) and pulmonary embolism (PE) in a young and healthy patient with underlying asymptomatic Graves’ disease.

CASE PRESENTATION

Our patient is a 36 year-old-female with no significant past medical history who presented with worsening pain in her left leg. At an Emergency Department(ED) visit a week prior, she was diagnosed with a DVT of the left external iliac vein extending to the femoral vein.(iii) Anterior mediastinal mass (iv) Gross image of venous clot obtained from thrombectomy

In the ED, she complained of severe burning pain 8/10 in the left thigh, aggravated by ambulation and relieved by elevation and warm packs. Review of systems was obtained to determine if her DVT was provoked. She denied any recent travel, trauma, or known hypercoagulable state. She was not on oral contraception pills. Social history was positive for a 15 pack-year smoking history, with no significant family history of hypercoagulable events. She denied any medication use, including anticoagulants. She was diagnosed with a DVT of the left external iliac vein extending to the distal femoral vein and was sent home on Apixaban. A week later, failure to obtain relief of pain and swelling brought her back to the hospital.

On day 2, a repeat US was performed which showed a persistent DVT, along with thrombosis within the stents. The patient was promptly transferred to the Intensive Care Unit(ICU) for close observation. Over the next 24 hours, a combination of ultrasound-guided catheter-directed pharmacologic thrombolysis and mechanical thrombectomies were performed. No residual flow-limiting stenosis or thrombus was seen following this procedure.

On day 5, the patient began to experience pleuritic chest pain accompanied by shortness of breath. Computed tomography angiography(CTA) demonstrated a large pulmonary embolus in a branch of the right lower lobe, along with an incidental soft tissue density measuring 2.4 x 4.4 cm concerning for a thymoma/thymic mass. After discussion with the patient, it would be safe to hold her blood thinners to obtain a biopsy.

A Thyroid panel was performed, which showed a hyperthyroid picture with unmeasurable TSH, elevated thyroxine (T4) (18.3 mcg/dL), and free T4 (2.50 ng/dL) along with an elevated total tri-iodothyronine(T3) (217 mcg/dL) and free T3 (9.27 ng/dL) level. Physical exam and thyroid ultrasound showed a normal-sized thyroid gland. Immunologic testing was positive for thyroid peroxidase antibodies (TPO) and thyroid-stimulating antibodies (TSI) (13.5 IU/L) diagnosing Graves’ disease.

The patient was discharged on Methimazole, Atenolol, and LMWH, with instructions to follow up for pending studies, including evaluation for malignancy.

DISCUSSION

Based upon a thorough literature review, we found that the association between hyperthyroidism and a hypercoagulable state is multi-factorial. Hyperthyroidism favors a more pro-coagulable and hypofibrinolytic state through its effects on Von Willebrand factor, Factor VIII, fibrinogen, and plasminogen activator inhibitor-1(3).

A correlation between hypercoagulability and hyperthyroidism can be appreciated by a review of a meta-analysis that suggests that high levels of thyroid hormone can have a potentiating effect on the coagulation system(4), which is further elevated due to the increased burden of hyperthyroidism. It is derived that increased Factor VIII activity is attributed to the increased sensitivity to circulating catecholamines, a common phenomenon in hyperthyroidism(5). Although much research is warranted on this subject, it is our recommendation that underlying hyperthyroidism is suspected in unprovoked venous thromboembolism in patients with an otherwise negative hypercoagulability index.

The association between thyric hyperplasia and Grave’s Disease was first reported in the early 1900s. As with our patient, it is often discovered as an incidental mediastinal mass on imaging. The exact mechanism of the hyperplastic changes is unclear but seems to involve a complex interaction of immunological and hormonal mechanisms(6). Treatment of Graves’ disease has been shown to halt the growth of the thymus, often leading to resolution of the hyperplasia(7). Hence medical treatment and routine imaging without surgical intervention has been recommended(8).

REFERENCES


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