CLINICAL VIGNETTE

Pulmonary Embolism in a Hyperthyroid Patient

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Case Report

A 47-year-old female with recently diagnosed hyperthyroidism presented to the ED with severe right-sided sharp and stabbing chest pain, which radiated from her mid-thoracic spine to anterior hemithorax. She had been diagnosed with hyperthyroidism a month prior with complaints of fatigue, weight loss, tachycardia, and dyspnea on exertion and had declined medication management at the time of diagnosis. On the night prior to her presentation to the emergency department, she began having right back pain, which then moved to her anterior chest and escalated overnight, prompting her to come for evaluation. The pain was worse with inspiration and she denied cough, phlegm production, fever or hemoptysis. She specifically noted that her tachycardia and dyspnea had been unchanged and no worse than the past month. Her pain had almost resolved before being evaluated by the emergency room physician and she was planning to leave without being seen. Initial laboratory studies were unremarkable except for an elevated D-Dimer of 1517ng/mLFEU. CT angiogram of the chest revealed large right-sided pulmonary emboli with posterior and basal right lower lobe infarction.

The patient had no common risk factors for hypercoagulability. She was not using oral contraceptives. She had no prior history of blood clots and no family history of bleeding disorders or blood clots. There was no recent trauma or surgery and no known history of malignancy. She had no history nor signs or symptoms of connective tissue disease and no prior miscarriages. She recently traveled from Southern California to Oregon by car, but she had stopped every hour or two to stretch her legs and relieve her chronic low back pain. She denied any leg edema. She was admitted to the hospital for anticoagulation therapy. Lower extremity Dopplers were negative for deep vein thrombosis. Her laboratory evaluation for inherited and acquired hypercoagulable states (including Factor V Leiden, Antithrombin III, protein C, protein S, prothrombin 20210 A mutation) was negative. Her Factor VIII activity level was elevated at 132%. Her TSH level was less than 0.02 mcIU/mL with a free T3 level of 1189 pg/dL.

Discussion

Pulmonary embolism is a leading cause of death in the United States with an incidence of 0.5 to 1 per 1000 in the general population. Common risk factors for thromboembolic disease are divided into two categories: inherited and acquired. Inherited risk factors include factor deficiencies (antithrombin III, protein C, protein S), factor hyperactivity (Factor VII and Factor VIII) in the coagulation cascade, and dysfibrinogenemia that results in a prothrombotic state. Factor V Leiden and prothrombin gene (20210 A variant) mutations may also cause variable hypercoagulability and are the most frequent causes of an inherited hypercoagulable state, accounting for 50-60% of cases. Acquired risk factors for thromboembolic diseases are quite varied with malignancy and surgery or trauma being the most common underlying pathologies. Other causes include: oral contraceptive use, hormone replacement therapy, pregnancy, immobilization, congestive heart failure, stroke, smoking, obesity, advanced age, and prior thromboembolic episode[1]. Autoimmune diseases can disturb the coagulation system with antiphospholipid syndrome being the most common. Acute hyperthyroidism is also a recognized but not well-remembered cause of acquired hypercoagulable state due to the rarity of the occurrence of the thromboembolic disease associated with hyper-thyroidism.

The association of hyperthyroidism with a thrombotic event was made by Kaliebe in 1913. He presented a patient with thyrotoxicosis who developed cerebral venous thrombosis[2]. Numerous studies of the relationship between coagulation and thyroid funct-ion, as well as, several review papers on the topic have since been published. In a recent article by Kim et al from New Zealand, the incidence of sympto-matic thromboembolic disease was 0.7% in a review

of 428 consecutive patients with acute hyperthyroidism presenting to endocrine clinic[3]. In another much larger study from Taiwan, the researchers used the country's National Health Insurance Database and calculated that the incidence of pulmonary embolism in the patients with acute hyperthyroidism was 0.16%, a 2.3 fold increase from a baseline of 0.06% in patients without thyroid disorder[4]. Despite a low overall occurrence, pulmonary emboli accounted for up to 18% of all deaths from thyrotoxicosis[5].

The coagulation cascade and fibrinolysis pathways are influenced by thyroid hormone effects on synthesis and breakdown of coagulation factors. Elevations in factor VIII, factor IX, fibrinogen, von WIllebrand factor and plasminogen activator inhibitor-1 are seen in hyperthyroidism. Elevated thyroxine stimulates the liver to produce acute phase reactants and thus, increases coagulability. Endothelial function of blood vessels are also disturbed with increased fibronectin and von Willebrand antigen levels detected in thyrotoxicosis. The overall effect of thyroxine is increased coagulation and decreased fibrinolysis, tipping the scale towards thrombosis of the vessels. With treatment of hyperthyroidism, elevated factor VIII, Factor IX, fibronectin, and tissue plasminogen activator Ag levels decrease[6-9].

Conclusion

Hyperthyroidism is an acquired prothrombotic state and it should be considered in the evaluation of patients admitted with thromboembolic complications. Hyperthyroid patients who are hospitalized for treatment of thyrotoxicosis or other medical conditions should receive prophylactic anticoagu-lation similar to patients with underlying malignancy to reduce risk of VTE. Initiation of oral contraceptive pills or addition of other potentially thrombogenic agents should be done with caution. Acute hyperthyroidism is a reversible prothrombotic state with normalization of coagulation and endothelial factors occurring after treatment; once a euthyroid state has been achieved, the patient's anticoagulation therapy for VTE may be stopped after 3-4 months.

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