CLINICAL VIGNETTE

Hyperthyroidism and the Liver, It's Complicated

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Case Presentation

A 27-year-old female with scoliosis presented with intermittent bilateral lower extremity (BLE) weakness. Four months prior to admission she noted bilateral lower extremity weakness a few hours after receiving the Pfizer COVID booster. The weakness spontaneously resolved the next day without any residual deficits and the patient did not pursue medical evaluation. However, her symptoms recurred a few weeks later causing her to fall while walking. She reported her legs "giving out" without loss of consciousness, head trauma or major injury. The weakness again resolved and she deferred medical evaluation. When her symptoms recurred a third time and persisted for several hours she presented for evaluation.

She reported mild heat intolerance, bilateral upper extremity tremors, and feeling tired and stressed due to her school and work schedule. She denied recent trauma, diplopia, dysphagia, dysarthria, aphasia, ataxia, numbness, paresthesia, bowel or bladder incontinence or retention, weight loss, infectious signs or symptoms associated with any of these episodes. She reported taking OTC vitamins and supplements, but no alcohol or illicit drug use. Physical exam was remarkable for sinus tachycardia, an enlarged thyroid, and BLE weakness. Her neurological exam was otherwise intact. Vital signs noted sinus tachycardia to 120-130, without other abnormalities. Laboratory findings noted mildly elevated aspartate aminotransferase AST) 65 U/L, alanine aminotransferase (ALT) 77 U/L, erythrocyte sedimentation rate (ESR) 40 mm/hr, and c-reactive protein (CRP) 2.2 mg/dL. Thyroid function returned positive, with elevated FT4 of 5.6 and TSH < 0.02. Neurology was consulted and recommended MRI brain and cervical/thoracic/lumbar spine which were unremarkable. No further neurological testing was performed. Endocrinology advised further testing and imaging which revealed uncontrolled hyperthyroidism due to Grave's disease. She was prescribed methimazole and propranolol with improvement in her symptoms. The liver function enzymes continued to slowly rise, peaking on hospital day 3 with AST 90 U/L and ALT 158 U/L, ALK Phos 152 U/L. They were normal on follow up outpatient testing.

Discussion

Thyroid hormones are involved in many intracellular metabolic pathways of the heart, nervous system, and gastrointestinal tract.[1] Variations in thyroid hormones above or below normal range can lead to derangements in such pathways resulting in organ dysfunction.[1-3] Liver dysfunction is reported in 15-79% of patients with untreated or uncontrolled hyperthyroidism.[1] Excessive thyroid hormones can lead to liver dysfunction through several mechanisms. They include direct liver toxicity due to increased metabolism from hyperthyroidism leading to increased liver oxygen demand with free radical formation causing hepatoxicity.[1,4] This may result in elevated AST and ALT.[1-4] High metabolic rates can also lead to accelerated glycogen and protein decomposition causing liver degeneration.[1] Elevated thyroid hormones may also lead to apoptosis causing a cholestatic pattern of injury with increased bilirubin and jaundice.[4] Elevated ALP and GGT can also result from increased osteoblastic activity in hyperthyroidism.[4] Hyperthyroidism can indirectly worsen liver dysfunction through thyrotoxic heart failure. Auto-immune related disease such as Grave's disease can occur with other liver diseases such as primary biliary cirrhosis or autoimmune hepatitis.[4] Double hits to the liver can result in more profound dysfunction with fulminant hepatitis in 1-2% of cases.[1,4] The severity of dysfunction appears to depend in part on the severity and longevity of the hyperthyroidism. Severity can be measured as the level of free hormones.[2] Treatment with normalization of liver function, is common once antithyroid therapies are started and help to prevent disease progression.[1-4]

Conclusion

Hepatic dysfunction due to hyperthyroidism is not rare.[1-4] Patients who present with abnormal liver function tests of unclear etiology should be evaluated for hyperthyroidism.

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