CLINICAL VIGNETTE

A Case of Primary Hyperparathyroidism

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Case

A 64-year-old man with a past medical history of depression, and family history of primary hyperparathyroidism presented with fatigue and was found to have hypercalcemia. On initial evaluation, he reported several months of fatigue and denied polyuria, weakness, and constipation. He had no history of nephrolithiasis. Calcium was elevated at 10.9 mg per deciliter with an ionized calcium of 1.48, PTH was 117.9 pg per milliliter and the vitamin D level was 27 ng per milliliter. An ultrasound of his parathyroid did not show a nodule. DXA scan showed osteoporosis with a T score of -2.6 in the femoral neck and lumbar spine. 24-hour urinary calcium collection was not consistent with familial hypocalciuric hypercalcemia (FHH). Parathyroid scan showed a right inferior parathyroid adenoma and was referred for parathyroidectomy.

The patient was evaluated for MEN1 that can cause primary hyperparathyroidism, antierior pituary adenomas and pancreatic neuroendocrine tumors. Additional labs, included prolactin and gastrin testing that was normal. Brain MRI was negative for a pituitary adenoma. MEN1 genetic testing was also negative. Familial etiologies of primary hyperparathyroidism such as the CDC73 gene mutation where felt to be unlikely. The patient was referred for surgery and had a parathryroidectomy. After surgery his PTH dropped from 270 pg per milliliter to 15pg oer milliliter. His ionized calcium decreased to 1.24 after surgery. His surgical pathology showed a right inferior parathyroid adenoma. Bone density testing one year after surgery showed no improvement and bisphosphonate therapy was recommended. His depression did not recur after surgery.

Discussion

Primary hyperparathyroidism is the third most common endocrinologic disorder.[1] The prevalence of primary hyperparathyroidism is 23 cases per 10,000 women and 8.5 cases per 10,000 men.[2] Primary hyperparathyroidism occurs when one or more parathyroid glands makes excessive parathyroid hormone that causes hypercalcemia. 80% of cases are caused by a single gland adenoma while 10% involve more than one parathyroid gland. Parathyroid carcinoma is extremely rare representing <1% of all cases.[2]

Primary hyperparathyroidism is frequently diagnosed when it is asymptomatic based upon lab findings of hypercalcemia. Classic symptoms of hyperparathyroidism include polyuria, fatigue, constipation and abdominal pain.[3] Other findings include osteoporosis and nephrolithiasis. Bone density is frequently decreased with hyperparathyroidism which causes marked loss of bone density in the radius.[4] There is less impact on lumbar spine bone density.[2] In one study, radiographic kidney stones were seen in 7-20% of patients with primary hyperaparathyroidism.[2]

Primary hyperparathyroidism is diagnosed by labs showing an elevated PTH or an inappropriately normal PTH in the setting of an elevated calcium. Phosphorus is usually low. As Vitamin D levels influence PTH levels, the Endocine Society recommends a goal vitamin D of >30ng/ml. Lithium and thiazide diuretics can also cause hypercalcemia. Thiazide diuretics can cause hypercalcemia by increasing reabsorption of calcium in the kidney. Lithium causes hypercalcemia though increased parathyroid hormone secretion. To diagnose primary hyperparathyroidism, it is important to rule out FHH. This can be done by obtaining a 24-hour urinary calcium showing calcium<100 mg/24 hour.[4] After diagnosing primary hyperparathyroidism, imaging should evaluate bone density. A renal ultrasound should be performed to screen for nephrolithiasis. Prior to surgery, imaging should be done to localize the adenoma with ultrasound or sestamibi imaging. The sensitivity of neck ultrasound is 42-82%, while sestamibi imaging is 90% sensitive in detecting single adenomas.[4] Bilateral neck exploration performed by an experienced surgeon is highly successful in treating hyperparathyroidism.

Treatment of primary hyperparathyroidism is surgical parathyroidectomy. The decision for surgery is based upon guidelines from the 4th International Workshop recommending surgery for patients with calcium levels> 1 mg per deciliter above the upper limit of normal, patients<50 years old, and T score<-2.5. Other indications for surgery include nephrolithiasis and Crcl<60.[5] For patients who decline surgery or are not surgical candidates, calcium and bone density should be monitored annually. Bone density should be monitored every 1-2 years. These patients are recommended to use vitamin D supplements to maintain normal levels, and consider treatment of osteoporosis.[2] These patients should not limit dietary calcium, as this can increase parathyroid hormone levels.

Symptoms attributed to primary hyperparathyroidism including fatigue, depression, anxiety as well as cognitive changes such as concentration issues and memory complaints. Several studies have attempted to quantify the impact of hyperparathyroidism

on these symptoms, and any changes, that occur with parathyroidectomy. Some studies indicate that parathyroidectomy can improve neurocognitive function in patient with primary hyperparathyroidism.[6] A case control study of 39 postmenopausal women used standardized tests (i.e. Beck Depression Inventory and others) to elucidate this question. This study found worse depression in patients with primary hyperparathyroidism. Cognition function was also impaired. After surgery, depression scored showed improvement.[7] A prospective study examined depression (as measured by the Patient Health Questionnaire-9), suicidal ideation and health related quality of life (HRQOL) in 194 patients undergoing parathyroidectomy. At 12 months, depression had improved. Suicial ideation had decreased as well. HRQOL improved over the first post-operative year.[8] While more studies are needed to study the impact of hyperparathyroidism on neurocognitive function, the studied to date suggest that neurocognitive function is impacted by primary hyperparathyroidism, and may be improved with surgical parathyroidectomy.

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