Journal of Clinical Images and Case Reports

Commentary A SCITECHNOL JOURNAL

Symptomatic Hypercalcemic Patient: A Rare Case Presentation

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Received date: May 06, 2022, Manuscript No. CICR-22- 66881;

Editor assigned date: May 09, 2022, PreQC No. CICR -22-66881(PQ);

Reviewed date: May 23, 2022, QC No CICR -22-66881;

Revised date: June 09, 2022, Manuscript No. CICR -22- 66881 (R);

Published date: June 16, 2022, DOI: 10.4172/CICR.1000223.

Description

A common etiology of hypercalcemia is Primary Hyperparathyroidism. Eighty percent of the time a single adenoma is present. Labs usually show an elevated Parathyroid hormone. Head and neck US, Sestamibi and CT scanning are important for localization. In our case, diagnostic results suggested a right lower pole location for a parathyroid adenoma. Referral to General Surgery was made for focused neck dissection. Bilateral neck exploration was required as only three glands were identified. After exploration of possible ectopic inferior gland locations, a right thyroid lobectomy was performed. This ectopic location was confirmed via intraoperative serial PTH measurements. This case illustrates a rare ectopic location for a parathyroid adenoma. Primary Hyperparathyroidism (PHP) is a disease of abnormal calcium and phosphate homeostasis. The etiology being an elevated Parathyroid hormone (PTH) level with subsequent hypercalcemia and low phosphate levels. The increase in serum calcium levels are related to increased bone resorption and increased renal and gut uptake. It is the 3rd most common endocrine disorder. When hypercalcemia is present, a PHP etiology is usually considered with a twice normal or greater intact PTH level. Risk factors for PHP include hereditary causes such as multiple endocrine neoplasias, exposure to ionizing radiation, prolonged lithium therapy, reduced physical activity, and low calcium intake. At times, patients are mildly symptomatic with nonspecific symptoms such as fatigue, mild depression, or cognitive impairment.

Parathyroid Etiology

Symptomatic patients with PHP may present with multi-organ disorders such as nephrolithiasis, renal insufficiency, peptic ulcer disease, pancreatitis, bone pain, secondary fractures, osteoporosis, osteitis fibrosa cystica, lethargy, psychosis or even coma with severe hypercalcemia Also, with severe hypercalcemia with a parathyroid etiology, carcinoma should be considered. This case study describes a 46-year-old, mildly symptomatic, African American male patient who was found to have, through routine lab testing through his primary care physician, calcium of 10.8 mg/dL. Subsequent labs revealed a PTH level of 191.5 pg/mL and a vitamin D level of 29 ng/mL. Calcium that is bound to vitamin D is an inactive form. The patient's past medical history was significant for gout. However, the patient denied a history of head or neck radiation, kidney stones, peptic ulcer disease, or a previous malignancy. Review of systems was positive for fatigue, but negative for myalgias and malaise. Family history was negative for endocrine neoplasias.

The Endocrinologist rechecked lab work multiple times which showed a PTH level in the range of 400- 500 pg/mL and a Ca level in the range of 10.8-13.5 mg/dL. Ultrasound of the neck showed a lower right inferior mixed solid/cystic appearing dominant thyroid nodule with small punctate calcifications. FNA showed benign fibroadipose tissue containing heterotopic thymic tissue with cystic change admixed with two microscopic foci of benign thyroid tissue. Lymph node tissue fragments showed no evidence of metastatic disease. It should be noted that Pathology reexamined the FNA slides post-surgery and a single slide suggested parathyroid tissue. Finally, a Sestamibi scan showed evidence of a parathyroid adenoma at the level of the inferior right thyroid gland. The patient was referred to General Surgery for a focused right parathyroidectomy. Intraoperatively, bilateral neck exploration was required as only three of the four parathyroid glands were initially identified. After an extensive exploration of possible ectopic locations for an inferior gland, a right thyroid lobectomy was performed. The presence of an intrathyroid adenoma was confirmed through intraoperative serial PTH measurements. Pre-operative PTH level was 354 pg/mL; 10-min post gland removal PTH level was 10 pg/mL and 15-min post gland removal PTH level was 12 pg/mL. Post-op serial sections of the tissue specimen showed a thyroid lobe containing an intrathyroidal parathyroid adenoma (4 cm), along with an incidental benign colloid nodule. For cases of hypercalcemia due to primary hyperparathyroidism, a single adenoma is present 80% to 85% of the time. Neck ultrasound and Sestamibi scanning are used to visualize the location of the parathyroid adenoma. If ultrasound results are unclear as to location, CT scanning is often used.

Embryogenesis

Parathyroid adenomas are more common in those greater than 50 years of age and women more than men. Parathyroidectomy is usually recommended in cases of less than 50 years of age, history of kidney stones, serum calcium level greater than 1mg/dL above the upper limit of normal, and reduced bone density. However, surgery can also be offered to asymptomatic and minimally symptomatic elderly patients under certain circumstances. Normal parathyroid gland anatomy consists of four glands, two superior and two inferior. During embryogenesis the fourth branchial pouch gives rise to the superior glands and the third branchial pouch gives rise to the inferior glands and the thymus. Parathyroid adenomas can be found in several ectopic locations due to the defects caused during the embryological descent of the parathyroid glands. Ectopic superior parathyroid glands are commonly found in the tracheoesophageal groove and the retro esophageal region. Ectopic inferior parathyroid glands can be found in the anterior mediastinum, usually associated with the thymus, within the thyroid gland, and within the carotid sheath. The location of the inferior parathyroid gland is more variable as it takes the longer migratory route during embryogenesis. In one of the clinical studies, 202 patients were analyzed for ectopic locations of parathyroid glands 38% percent were found to be in the thymus, 31% in the retro esophageal region and 18% intrathyroidal. The intrathyroidal location being the rarest. Preoperative localization of the adenoma is very important. Imaging modalities such as dual phase 99mTc- Sestamibi scintigraphy is currently the gold standard in diagnosing and localizing parathyroid adenomas. FNA can not only assist in localizing

ectopic adenomas, but also suggest the presence of a concomitant thyroid carcinoma in a prominent thyroid nodule. In this case, Ultrasound imaging and Sestamibi scanning suggested a right lower lobe location.

FNA was used to possibly obtain a tissue diagnosis preoperatively. Initially however, an intrathyroid ectopic location was not confirmed by FNA. Serial PTH measurements were thereafter utilized perioperative which assisted in confirming that the adenoma had been excised. Parathyroid adenomas are primarily treated through surgical resection with a curative rate in 95- 97% of cases. Generally, 6-16% of parathyroid adenomas occur in ectopic locations. Where the inferior glands are concerned however, the mediastinum and intrathyroid locations are most likely. This is due to abnormal migration during embryogenesis. Occasionally, a fourth, usually ectopic gland cannot be found resulting in continued refractory hypercalcemia postoperatively. Therefore, thorough perioperative evaluation is necessary to avoid post-surgical failure. Finally, to avoid leaving an ectopic gland, it is important to have an experienced surgeon conduct a methodical intraoperative search. When only three glands are found and the missing gland is in the inferior position, the final step is a thyroid lobectomy on the side of the missing gland.