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Case Report

15 Year Old Male with Primary Hyperparathyroidism due to Likely Ectopic Adenoma in the Parapharyngeal Space

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Abstract

Introduction: Primary Hyperparathyroidism (PHPT) is rare in pediatric patients. Ectopic parathyroid glands represent diagnostic challenges. Extensive testing may be required for localization. We report a pediatric patient with PHPT with an ectopic parathyroid lesion.

Case: 15 year old male presented with weight loss, hypercalcemia, and elevated PTH. Sestamibi scan was negative, and a 2.5 gland parathyroidectomy was not effective. Medical management with prednisone, cinacalcet, and calcitonin was unsuccessful. Calcium decreased with IV zolendronic acid. Further imaging and venous sampling were required to localize a lesion in the left parapharyngeal space. This was surgically removed. The question of parathyroid adenoma versus carcinoma remains unclear. He has been stable >1 year post-operatively.

Conclusion: For pediatric patients with PHPT and equivocal imaging, ectopic parathyroid adenoma must be considered. Advanced imaging studies and venous sampling may aid in localization.

Keywords: Primary hyperparathyroidism; Pediatrics; Ectopic adenoma; Parathyroid carcinoma; Venous sampling; Sestamibi scan

Abbreviations

PHPT: Primary Hyper Para Thyroidism; MEN: Multiple Endocrine Neoplasia; FNA: Fine Needle Aspiration; PET: Positron Emission Tomography scan; MRI: Magnetic Resonance Imaging; SPECT: Single Photon Emission Computed Tomography

Introduction

PHPT is more common in adults than pediatric patients [1]. Management is primarily surgical in children. Surgical complications include vocal cord paralysis and permanent hypoparathyroidism [1].

Symptoms of hyperparathyroidism include bone pain, abdominal pain, nephrolithiasis, and fatigue. Hypercalcemia can lead to arrhythmias and hypertension [2]. Diagnosis is confirmed by elevated or normal PTH levels with hypercalcemia. Ultrasound and sestamibi scan may localize the lesion. Sestamibi scanning localizes >80% of adenomas with a sensitivity of >75%, but reliability decreases with multiglandular disease [2]. Intraoperative PTH levels can confirm removal of the lesion; one sees decrease of PTH levels within minutes. If the lesion is not identified, one can remove 3.5 glands and consider thyroid lobectomy (due to 5% incidence of intrathyroidal parathyroid gland) [3].

Bone findings (osteitis fibrosa cystica) include demineralization, a coarsened trabecular pattern, subperiosteal reabsorption, brown tumors, and fractures [2].

Case Presentation

A 15 year old male presented with decreased appetite and weight loss. Calcium was 14.7mg/dl.

Additional history included musculoskeletal pain and headaches. No supplements. His grandmother had nephrocalcinosis, and grandfather had renal failure. Vital signs included blood pressure 127/67, weight 81.6kg, and height 183cm. He was well appearing. No thyromegaly or goiter. No muscle or abdominal tenderness or subcutaneous calcifications noted. Laboratory tests are summarized below (Table 1).

Liver functions, electrolytes, thyroid levels, and echocardiogram were normal. Hypercalcemia in the presence of an elevated PTH was consistent with PHPT. MEN evaluation revealed calcitonin <2 and negative RET testing.

He was placed on intravenous fluids for hypercalcemia, but remained hypercalcemic. Thyroid ultrasound showed a 14mm thyroid nodule in the right upper pole, which was mixed cystic and solid with vascularity. Fine Needle Aspiration (FNA) showed follicular cells. Sestamibi scan showed uniform uptake without evidence of hyperfunctioning parathyroid tissue. Neck CT was negative.

Because four-gland hyperplasia was a possibility as well as concern for intrathyroidal adenoma he underwent neck exploration, 3.5 gland parathyroidectomy and right hemithyroidectomy.

Intraoperatively, frozen section confirmed three glands as parathyroid tissue, thus 2.5 glands were excised. Pathology revealed normocellular parathyroid tissue. The left superior parathyroid gland was not located despite central neck dissection and exploration of the retroesophageal and superior mediastinal regions. The thyroid nodule was a benign cystic lesion. Intraoperative PTH increased peaking at 1200pg/mL.

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Table 1: Initial labs obtain upon presentation to the emergency department.

Test	Value
Calcium	16.5 mg/dL
Ionized Calcium	2.15 mmol/L
Phosphorous	2.7 mg/dL
Magnesium	1.8 mg/dL
Alkaline Phosphatase	599 U/L
Creatinine	1.3 mg/dL
Bicarbonate	28 mEq/L
BUN	14 mg/dL
25 Vitamin D	23.7 ng/mL
PTH	466.6 pg/mL
Urine Calcium/Creatinine ratio	0.4
TSH	1.66 uU/mL
FT4	0.96 ng/dL

BUN: Blood Urea Nitrogen, PTH: Para Thyroid Hormone, TSH – Thyroid Stimulating Hormone, FT4: Free T4

Medical management was undertaken to decrease the calcium levels. Cincalcet was increased to 120mg bid and 5 doses of prednisone 40mg administered with no effect. Calcitonin 300 IU bid was started, briefly decreasing levels to 12.5mg/dL, with subsequent return to baseline values. He required magnesium and phosphorous supplementation. He received 4mg of IV zolendronic acid, which reduced calcium to the normal range. PTH remained unchanged.

Further imaging was obtained. Full body sestamibi scan showed increased uptake in the left parapharyngeal space at C2, medial to the internal jugular and internal carotid vessels. PET scan revealed multiple hypermetabolic lytic bone lesions. MRI of these bone lesions appeared benign and was thought to be brown tumors.

Further evaluation of the left parapharyngeal lesion was needed before proceeding to surgery. The patient underwent catheterization for venous sampling along the internal jugular veins. Two PTH levels were obtained in locations in the area of the suspected lesion. Results are in Table 2.

Venous sampling confirmed increased PTH levels in the left superior neck region corresponding to the Sestamibi scan. The neck CT was re-reviewed and a mass was identified in the left parapharyngeal space. The initial Sestamibi also was reviewed, and the lesions had been read as salivary gland uptake. He returned to the operating room. A mass was identified in the left parapharyngeal space between the great vessels and appeared to involve the vagus nerve. It was not possible to safely remove this lesion completely as it was tightly adherent and appeared integrated with the nerve sheath. It was enucleated with only the capsule remaining. Intraoperative PTH dropped to 61pg/mL.

Calcium decreased on postoperative day one, and he had mildly elevated PTH levels in response to hypocalcemia. He required a calcium infusion for ten days and was discharged on calcitriol and oral calcium. Pathology demonstrated findings compatible with a low grade neuroendocrine tumor. He developed left true vocal fold immobility and Bell's palsy. The Bell's palsy resolved, but the hoarse voice persisted. He had persistent hypertension and elevated creatinine. Renal biopsy confirmed nephrocalcinosis. Imaging of the bone lesions showed improvement six months postoperatively. He remained normocalcemic with normal PTH on calcitriol and calcium supplements one year later.

Table 2: Venous sampling results (note, 2 PTH levels were obtained on the left side as this was the area of highest concern based on PET scanning) [10].

Location in IJ (nearest spinous process)	PTH Level
Baseline	813.9
C2 Right	459 pg/mL
C4 Right	643 pg/mL
C6 Right	689 pg/mL
C2 Left	674, 617 pg/mL
C4 Left	1274, 1585 pg/mL
C6 Left	1952, 1693 pg/mL
Right Adrenal	628 pg/mL
Right IVC	845 pg/mL
Left Adrenal	630 pg/mL
Left IVC	884 pg/mL

Discussion

This case represents an unusual occurrence of PHPT in a pediatric patient, resulting from an ectopic tumor location. Pediatric PHPT patients have more severe symptoms, signs of end-organ damage, and bone involvement tied to diagnosis delay [4]. They have more failed surgeries due to ectopic parathyroid adenomas. These characteristics were noted in our patient.

When PHPT is diagnosed but Sestamibi and ultrasound are negative, other imaging may be considered. Contrast 4D CT may be helpful, with the benefit of evaluating enhancement with time. This uses a larger dose of radiation which is a concern in pediatric patients. Sestamibi scanning can be performed with ^{123}I as an additional marker or with SPECT/CT. PET scanning can also be considered either as an FDG PET or with C-11 methionine. Studies have shown ^{123}I Sestamibi is as effective as C-11 methionine, though the latter is less available [5-7].

Another method for locating lesions is venous sampling. Studies assessing its effectiveness have yielded mixed results. It assesses PTH gradients, as areas surrounding the lesion demonstrate higher PTH levels. It is somewhat invasive. Complications include hematoma, contrast side effects, wound infections, pseudo aneurysm, and perforation of blood vessels [7,8].

In pediatric patients with PHPT and negative imaging, care should be taken to review the imaging for ectopic glands. The parapharyngeal space is a known but rare site for an ectopic adenoma [9].

Multiple medications are available to treat hypercalcemia. Calcitonin increases renal calcium excretion and decreases bone resorption by affecting osteoclasts. It works rapidly but, due to receptor down-regulation, the response is short-term. Bisphosphonates inhibit calcium release by interfering with osteoclast mediated bone resorption. Corticosteroids decrease calcitriol production, and cinacalet acts at the calcium sensor in the parathyroid gland to inhibit

PTH secretion. Our patient responded only to bisphosphonate therapy.

Parathyroid carcinoma is rare, and is difficult to distinguish from adenoma or hyperplasia. It is characterized by extreme elevations in PTH and calcium, hoarseness, neck mass, local tumor invasion, and recurrence of hyperparathyroidism after the lesion is removed. In this case, the parathyroid lesion was found to be adherent to the sheath of the vagus nerve – this could be the location where the gland developed, or may be a sign of invasion; more typical of an adenocarcinoma. Reassuringly, the parathyroid hormone levels have not increased >1 year after surgery.

In conclusion, this case was unique for several reasons. First, the degree calcium elevation necessitated a trial of multiple medications not generally utilized in pediatrics. Secondly, the adenoma discovered is presumed to be the left superior parathyroid in an aberrant location. This necessitated further imaging and venous sampling, which is not frequently used, especially in pediatric patients. Finally, given the level of PTH elevation and adherence of the lesion to the vagus nerve sheath, parathyroid carcinoma remains a concern. The patient has remained recurrence-free for >1 year.

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