Parathyroid cysts rarely cause hyperparathyroidism. In addition, they rarely occur in the thymus. We report a 56-year-old woman with hypertension on telmisartan and hydrochlorothiazide, who developed symptomatic hypercalcemia for a month. Initial serum calcium was 15.6 mg/dL, together with inappropriately elevated intact PTH at 437 pg/mL. Coincidentally, an anterior mediastinal mass on chest imaging was found. Biopsy of the mass revealed parathyroid tissue. She was treated sequentially with saline rehydration and frusemide calciuresis, intravenous pamidronate and calcitonin, which lowered her calcium to 11.1 mg/dL. Normocalcemia was finally achieved following surgical extirpation of the mass. Histology confirmed an intrathymic parathyroid cyst. Definitive treatment by resection of the mass is potentially curative.

Keywords: mediastinal, intrathymic, parathyroid cyst, hyperparathyroidism, hypercalcemia

Introduction

Hypercalcemia due to an ectopic intrathymic parathyroid cyst over-expressing parathyroid hormone (PTH) eutopically can pose diagnostic challenges and may contribute to failed parathyroid exploration. Parathyroid cysts, many being non-functional, account for approximately 0.5%–1% of all parathyroid pathologies.1) Functional parathyroid cysts presenting as hypercalcemia are distinctly esoteric, constituting only about 1% of all cases of hyperparathyroidism.2) Although the inferior parathyroid glands are notorious for descending with the thymus into the anterior mediastinum during their embryologic development, ectopic functioning intrathymic parathyroid cyst as a category is extremely rare and serves as a potential pitfall for the unwary thoracic surgeon. Very few case reports have been described showing functioning parathyroid tissue within anterior mediastinal masses.

Case Report

The patient was a 56-year-old Chinese woman with hypertension, controlled with telmisartan and hydrochlorothiazide, who presented with a month’s duration of constipation, increased thirst, and anorexia. She also reported a weight loss of 5 kg and non-productive cough over a few months but denied other systemic symptoms such as chest pain, night sweats, or dyspnea. Her two brothers had lung and nasopharyngeal carcinoma respectively, but she has no family history of any endocrinopathies. On physical examination, she was alert and rational. Her
blood pressure was 150/70 mmHg, and she was dehydrated. She had no ptosis, clubbing, pallor, dysphonia or neurological deficits. There was no goitre or any neck masses. Her serum calcium (adjusted for albumin) was high at 15.6 mg/dL/L (normal: 8.6–10.3), serum phosphate low at 1.25 mg/dL (normal: 2.48–4.95) associated with inappropriately high intact PTH at 437 pg/mL (normal: 10–60). Serum creatinine was normal at 0.9 mg/dL (normal: 0.5–1.1).

A plain chest roentgenogram (Fig. 1) showed a prominent right cardiac border consistent with a right para-cardiac mass. Computed tomography (CT) scan of the neck, thorax, and abdomen revealed a lobulated soft tissue mass in the anterior mediastinum (Fig. 2). No enlarged parathyroid gland was visible. A dual-phase Tc-99m sestamibi parathyroid scan was negative for any culprit hyperfunctioning parathyroid tissue in the neck or mediastinum. CT-guided needle biopsy of the mediastinal mass revealed fibroadipose tissue with a few clusters of bland epithelial cells containing ovoid, smooth contoured nuclei, evenly dispersed chromatin, indistinct nucleoli and moderate amounts of pale eosinophilic cytoplasm. These cells showed strong, diffuse immunoperoxidase staining for chromogranin and PTH (Fig. 3).

Together with slow intravenous infusions of two consecutive doses of synthetic salmon calcitonin 300 International Units (IU) each and pamidronate 90 mg, her serum calcium was lowered to 11.1 mg/dL. The cardiothoracic surgeon was consulted, who then performed a video-assisted thoracoscopic surgery (VATS) to excise the mass. A 10-cm smooth, glistening cyst containing hemorrhagic fluid was excised. Histology uncovered features of mediastinal/thymic parathyroid cyst with rims of hyperplastic parathyroid tissue along the wall of the cyst. Postoperatively, her recovery was prompt as her total serum calcium declined rapidly to 8.44 mg/dL and plasma intact PTH levels decreased sharply to 81.6 pg/mL. Postoperative bone mineral densitometry was normal.
Discussion

Primary hyperparathyroidism is generally due to single parathyroid adenoma, followed by multiple adenomas, hyperplasia and rarely, parathyroid carcinomas. Parathyromatosis and ectopic hyperparathyroidism pose distinct diagnostic challenges and frequently confuse physicians and parathyroid surgeons alike. In this patient, the clue for an ectopic source was the initial serendipitous presence of a mediastinal mass and negative tracer uptake in the parathyroid glands in the neck. Arguably, the suspicion of false negative parathyroid imaging coupled with the application of traditional localization algorithms could have led to unnecessary conventional neck exploration had the chest radiography been inadvertently omitted. As such, unusual etiologies such as ectopic thymic PTH secretion or intrathymic ectopic parathyroid tissue hypersecreting PTH in an eutopic fashion became candidate differential diagnoses.

True ectopic production of PTH occurs when non-parathyroid tissue ‘illegitimately’ secrete PTH, whereas eutopic production of PTH strictly refers to the hormone being secreted by ectopically sited parathyroid glands/tissues such as within the mediastinum or thymus gland. Since both parathyroid glands and the thymus originate from the same pharyngeal pouch, it is postulated that cysts bud off from the parathyroid glands during embryogenesis and migrate aberrantly with the thymus gland into the mediastinum. Sometimes these migrated parathyroid tissue/adenomas degenerate to form cysts in the mediastinum. Shields et al. found 39 out of 94 patients with functional mediastinal cysts causing hyperparathyroidism and 7 of these patients developed severe parathyroid crises. Parathyroid cysts may cause compressive symptoms as they enlarge onto neighboring structures, resulting in dysphonia, stridor, dysphagia or chest pain. They are rarely malignant except for the atypical cystic parathyroid adenoma which occasionally exhibits features of carcinoma, though angio-invasion and/or metastases are not associated. Thymomas, being the commonest anterior mediastinal tumor in adults, have been described to cause systemic, autoimmune-mediated endocrine manifestations including hyperparathyroidism. IntrathyMIC PTH-secreting adenomas had been found to express the parathyroid-specific GCMB gene, suggesting that these tumors were derived from parathyroid cells that had migrated aberrantly during embryogenesis. Thymomas as an ectopic PTH source are exceedingly rare. In the last case report, an excised epithelial thymoma with no parathyroid tissue was found to express PTH mRNA. Ectopic PTH secretion has been reported in lung, thyroid, ovarian and pancreatic cancers.

It is useful to measure PTH in the cystic fluid as cell yield may be low for parathyroid tissue on biopsy. PTH levels can range from several hundred to >400000 pg/mL in non-functioning cyst and several million pg/mL in functioning ones. The treatment of choice for an intrathyMIC parathyroid cyst is surgical, and video-assisted thoracoscopic surgery (VATS) has arisen as a minimally invasive method for resecting mediastinal parathyroid glands and avoiding the complications and higher morbidity of a sternotomy. Her serum calcium and PTH normalized after surgery, consistent with existing literature about good curative rates post excision. This case illustrates the importance of pre-operative localization (including a plain chest radiograph) and the need to consider rare entities when preliminary neck scans are negative in those with primary hyperparathyroidism.

References