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A Young Man with Hypercalcemia

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Keywords

primary hyperparathyroidism; brown tumors; osteitis fibrosa cystica

A well-developed man in his 20s presented to our hospital with a clinically significant elevation in serum calcium level to (14.1 mg/dL [reference range, 8.6–10.2 mg/dL]) found on routine laboratory tests. He was highly functional and denied abdominal pain, dysuria, anxiety, lethargy, and constipation. Findings from his physical examination were within normal limits. He did not have any palpable thyroid nodules or cervical lymphadenopathy. Given his elevated calcium level, parathyroid hormone (PTH) was drawn, and results returned significantly elevated at 1377 pg/mL (reference range, 10–65 pg/mL). Because of the extremely elevated PTH level, a technetium Tc 99m sestamibi single-photon emission computed tomographic/computed tomographic (SPECT/CT) scan was obtained, which identified a lesion in the location of the right inferior parathyroid gland, measured at 2.2 cm (Figure, A). In addition, CT showed associated lytic bone lesions of the left mandibular ramus, left scapula, and C5 vertebra (Figure, B).

What is your diagnosis?

- A. Parathyroid carcinoma
- B. Multiple myeloma
- C. Primary bone tumor
- D. Osteitis fibrosa cystica

Diagnosis

- D. Osteitis fibrosa cystica

The patient underwent right inferior parathyroidectomy, with intraoperative return to normal PTH levels of 50 pg/mL after removal of the affected gland. He recovered without issues postoperatively. Final pathologic findings demonstrated a parathyroid adenoma weighing 5.9

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g. No malignant cells were identified. Follow-up imaging 8 months later revealed interval healing of his lytic bone lesions (Figure, C).

In the setting of prolonged hyperparathyroidism, chronic PTH activity results in osteopenia and, in long-standing and severe cases, osteitis fibrosa cystica, manifested by resorption of subperiosteal bone and brown tumors (collections of osteoclasts, fibrous tissue, and demineralized bone with the brown color characterized by hemosiderin deposition).¹. Clinically, osteitis fibrosa cystica symptoms include bone swelling, pathological fractures, and bone pain. Imaging studies show brown tumors of osteitis fibrosa cystica as lytic lesions (radiolucent regions of bone resorption on CT) generally located in the facial bones, pelvis, ribs, and femur.². These lesions may be mistaken for primary bone tumors radiologically; in particular, those in the head and neck may have radiologic features similar to those of sinonasal tumors, sarcomas, salivary gland tumors, and plasmacytomas.³ The incidence of osteitis fibrosa cystica has become less frequent over time, currently occurring in less than 1% of patients, likely due to earlier biochemical detection of hyperparathyroidism.⁴ Brown tumors are frequently treated pharmacologically, and generally improve by addressing the underlying hyperparathyroidism. However, in some cases surgery is needed, specifically in cases of pathologic fracture or increased pain.

Osteitis fibrosa cystica can resemble metastatic parathyroid carcinoma, primary bone tumors, or multiple myeloma, both clinically and radiographically, with extremely elevated PTH levels and lytic bone lesions.^{2, 5, 6}. Thus, clinicians should entertain a careful differential diagnosis and with consideration of both disease processes. Of note, both primary and secondary hyperparathyroidism can lead to osteitis fibrosa cystica. Key features to distinguish primary from secondary hyperparathyroidism include evidence of renal dysfunction, generally lower calcium levels with correspondingly elevated PTH level, lower vitamin D levels, and decreased urinary calcium excretion. Sestamibi imaging is increasingly being used to identify hyperfunctioning parathyroid glands in cases of secondary hyperparathyroidism, which frequently identifies multiple hyperfunctioning glands.⁷. While the differential diagnosis between hyperparathyroidism with osteitis fibrosa cystica and parathyroid carcinoma can be difficult, some key clinical clues exist. Notably, the average PTH level in patients diagnosed as having parathyroid adenoma is comparatively lower, often no more than 15% to 30% above the normal range or even within normal range,⁸ although in rare instances markedly elevated PTH and calcium levels may be noted.⁹. Patients with parathyroid carcinoma, however, often present with serum PTH levels up to 10 times the normal range¹⁰. In addition, about one-third of these individuals have lymph node, liver, and/or bone lesions; comparatively, patients with parathyroid adenomas should have no pathologic lymph nodes, liver lesions, and a much lower rate of osteitis fibrosa cystica and bone lesions.⁸.

Although the extremely elevated PTH level and suspicious [Tc-99m] sestamibi SPECT/CT scan findings in this case gave rise to concern about parathyroid carcinoma, the pathologic findings confirmed the final diagnosis of parathyroid adenoma. This case highlights the need for surgeons to be aware of the potential for primary hyperparathyroidism with brown tumors to present similar clinical features to parathyroid carcinoma.

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A Preoperative-SPECT/CT scan

Figure 1. Preoperative SPECT CT

Preoperative imaging reveals uptake in the right inferior neck, consistent with a right inferior parathyroid gland lesion.

B Preoperative CT scan

Figure 2. Preoperative CT Neck
Significant lytic and erosive lesion in the left neck at the level of C5.

C Postoperative CT scan **Figure 3. Postoperative CT Neck**

CT neck 8 months postoperatively reveals interval improvement and healing of the lesion at level C5.