The Laryngoscope

Case Report

More Than Just Tissue Diagnosis in a Patient With Maxillofacial Bony Lesions and Hypercalcemia

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Brown tumors are a definitive feature of hyperparathyroidism. They are well-demarcated osteolytic lesions commonly in the appendicular skeleton. Primary hyperparathyroidism is typically suggested by hypercalcemia and hypophosphatemia on routine labs. Much more rarely do these cases present with a craniofacial mass. Here we investigate a unique presentation of terminal stage primary hyperparathyroidism with a growing maxillary mass emphasizing the importance of a broad differential diagnosis and key diagnostic studies. Hyperparathyroidism can present in very unique ways. As otolaryngologists in the frontline, we must think beyond just tissue diagnoses so that appropriate and expedited care may be implemented.

Key Words: Brown tumor, osteitis fibrosa cystica, hyperparathyroidism.

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INTRODUCTION

Primary hyperparathyroidism (PHPT) is a common endocrine disease, occurring in one out of 1,000 men and with slight greater frequency in women. PHPT has evolved over the years from a disease presenting with profound symptomatology to a disease that is detected incidentally on routine laboratory testing. Osteitis fibrosa cystica, which includes brown tumors, are now seen in less than 5% of PHPT patients at initial presentation. Brown tumors commonly develop in the ribs, clavicle, tibia, femur, and pelvic bones. They are more rarely seen in the maxillofacial skeleton and even more rarely seen affecting the maxilla. Facial brown tumors typically are slow growing and asymptomatic. They are typically first noticed because of facial aesthetic changes. However, they can be painful and demonstrate ulcers and friability on examination, not unlike what we see with malignant lesions. Aside from the clinical exam, radiology may also demonstrate features easily mistaken for a malignancy.[1,2] Furthermore, these patients are typically referred because of suspicion for a malignant neoplasm, and otolaryngologists are already hard-wired to never miss a cancer diagnosis. As such, it is always important to maintain an open mind even when the clinical picture may appear so clear.

CASE REPORT

A 45-year-old Hispanic female with arthritis presents with an enlarging mass of her maxillary alveolar ridge. The mass had been growing for several months and was now associated with loose dentition. She now experiences pain in the region as well as intermittent bleeding. Further, she has paresthesia along her gingiva. Upon further questioning she notes diffuse bone pains over the last 2 years, mostly in the knees. She also has problems with constipation, headaches, and mood swings. She denies nephrolithiasis or overt psychosis or delusions. She takes an opiate pain killer for her knees and denies any tobacco or alcohol use. Her family history is unremarkable. On physical examination there is a firm mass on the buccal surface of the maxillary alveolar ridge adjacent to tooth 16, which is erythematous and bleeds easily. She also has loose dentition of the right mandibular canine. Her neck is without lymphadenopathy. A biopsy of the left maxillary lesion was performed and she was then sent for a computed tomography (CT) scan of the face with contrast, which revealed multiple mandibular and maxillary expansive, lucent, enhancing lesions with extraosseous extension (Fig. 1).

Her blood chemistries revealed a calcium of 14.4 mg/dL (8.9–10.3 mg/dL), phosphorus of 2.0 mg/dL (2.4–4.7 mg/dL), magnesium of 1.6 mg/dL (1.8–2.5 mg/dL),

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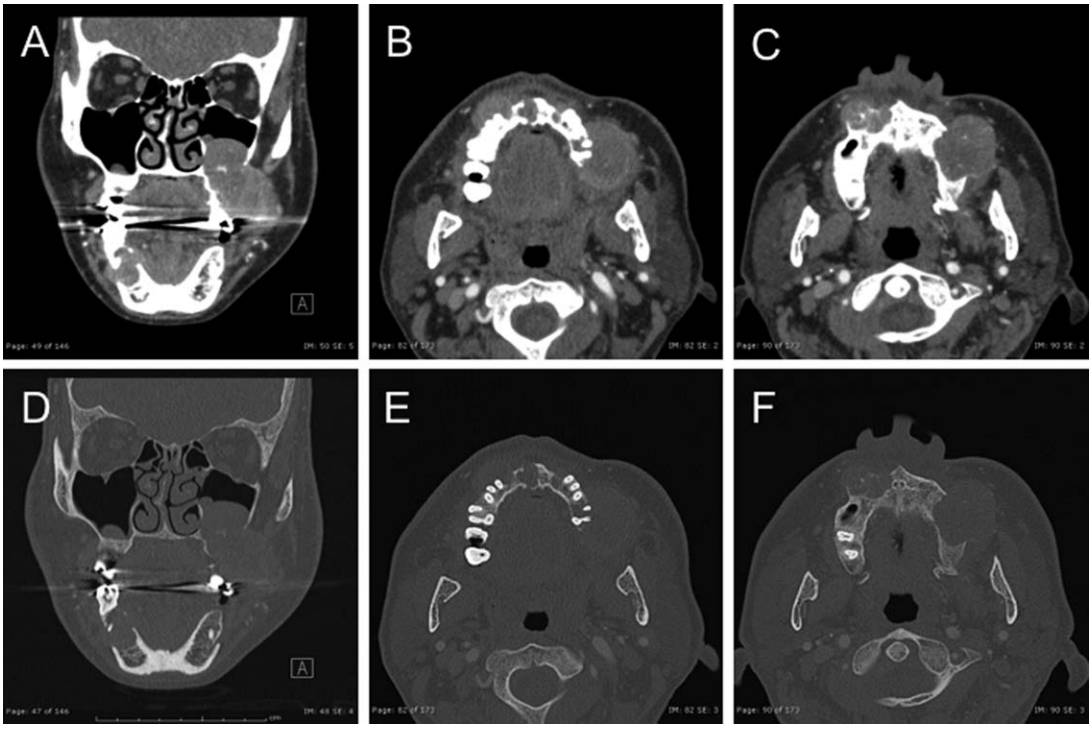

Fig. 1. Facial computed tomography with contrast. Coronal (A, D) and axial (B, C, E, F) sections demonstrate multiple mandibular and maxillary expansive, lucent enhancing lesions with extraosseous extension, and some with internal matrix calcification (A, D). (A–C) Soft tissue windowed. (D–F) Windowed for bone. With a multifocal presentation, the differential diagnosis may include metastases, myeloma with plasmacytomas, multiple odontogenic tumors, or brown tumors (osteitis fibrosa cystica).

albumin 3.3 g/dL (3.5–4.8 g/dL), and parathyroid hormone (PTH) level of 1,202 pg/mL (15–65 pg/mL). The pathology of the maxillary lesion showed numerous multinucleated giant cells, stroma with fibroblastic proliferation, and interstitial hemorrhage (Fig. 2A). Acid-fast bacilli were not detected. CD68 stained positive in the multinucleated giant cells (Fig. 2B).

Given these osteitic bony changes and her remarkably elevated calcium and PTH, she was then sent for a four-dimensional (4D) parathyroid CT scan. This revealed a 1.5-cm nodule deep to the right inferior pole of the thyroid gland (Fig. 3). She was taken to the operating room soon after where a 1.8 cm, 1.5 gram parathyroid adenoma was removed (Fig. 4). Six months after her parathyroidectomy, her symptoms and lesions were nearly resolved (Fig. 5). Her maxillary lesion was no longer detectable, her teeth were no longer loose, and her mouth and bone pain had resolved.

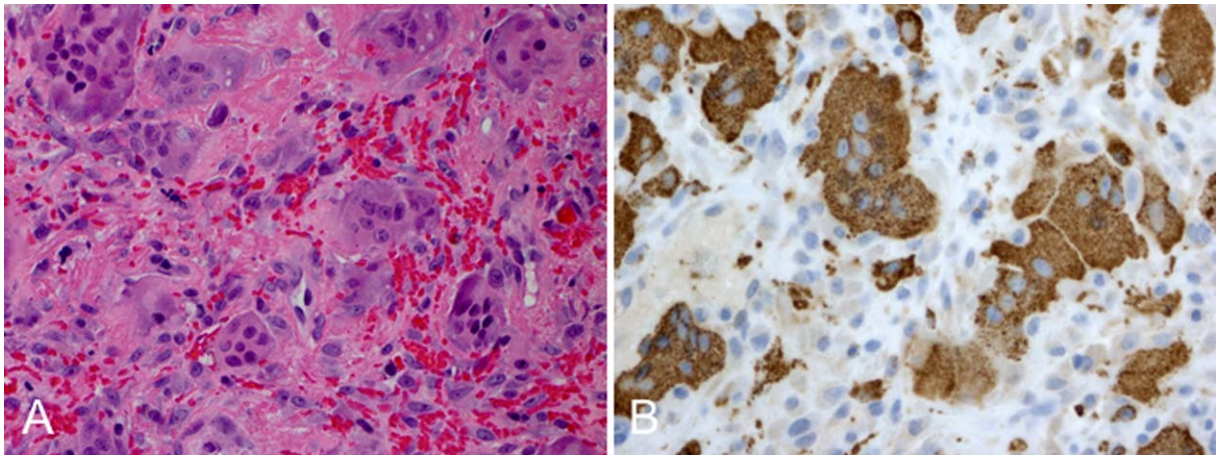

Fig. 2. Left maxillary lesion incisional biopsy. (A) Hematoxylin and eosin–stained slide shows numerous multinucleated giant cells. Stroma shows fibroblastic proliferation and interstitial hemorrhage. Negative for acid-fast bacilli or fungi. (B) CD68 immunostaining is positive in multinucleated giant cells. Diagnosis is compatible with brown cell tumor. Magnification: 40×. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

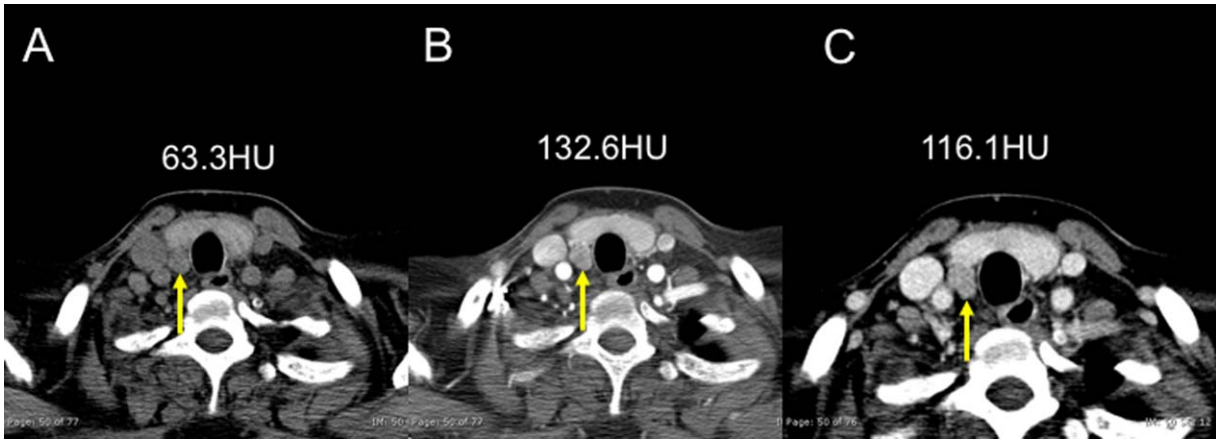

Fig. 3. Four-dimensional (4D) parathyroid computed tomography (CT). (A) Noncontrast axial CT: A 1.5 × 1.2 × 1.2-cm nodule deep to and abutting but separate from the lower pole of the right lobe of the thyroid gland is hypodense to the normal thyroid tissue. (B) Arterial phase axial CT: The nodule demonstrates hyperenhancement (133 HU). (C) Venous phase axial CT: The nodule demonstrates contrast washout with decrease in enhancement (116 HU). Technique: 4D CT images were obtained using a 64-detector row, dual-source CT scanner (Somatom Definition; Siemens, Erlangen, Germany) from the hard palate to the carina from cranial to caudal. Images were acquired without contrast (A), and in the arterial (B) and venous (C) phases at 25 seconds and 70 seconds, respectively, following intravenous injection of 100 mL iodinated contrast (Iohexol, Omnipaque, 350 mg/mL; GE Healthcare, Milwaukee, WI). HU = Hounsfield unit. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

DISCUSSION

Primary hyperparathyroidism is caused by a single parathyroid adenoma 80% of the time, with multiple adenomas seen in 2% to 4% of cases. Fifteen percent of cases are secondary to four-gland disease or hyperplasia.[3] 4D parathyroid CT imaging has dramatically improved our ability to preoperatively differentiate between these conditions. This technique for imaging the parathyroid glands has become the first- or second-line imaging modality for localizing parathyroid adenomas in PHPT. There is less radiation exposure than conventional single photon emission computed tomography/computed tomography imaging. 4D CT sensitivity and specificity for localization of adenoma to the patient's correct side was 84.2% and 81.8%, respectively (quadrant: 76.5%, 91.5%). This technique relies on the unique dynamics of contrast uptake by parathyroid adenomas—rapid uptake followed by washout 1 to 2 minutes later (Fig. 2).[4,5]

Bony changes are a characteristic feature of PHPT, with cortical bone being affected much more than cancellous bone. Among these bony changes are brown tumors, which in a very small percentage of patients may prompt their initial presentation with PHPT.

The treatment of brown tumors consists of reversal of hypercalcemia via parathyroidectomy. The natural history of brown tumors following correction of primary or secondary hyperparathyroidism is regression.[6] Resendiz-Colosia et al. followed 22 patients with brown tumors resulting from primary or secondary hyperparathyroidism. Eighteen cases had complete regression of bony lesions by a mean latency of 10 months following medical and/or surgical management of their disease, with two more patients having partial response by 2 years.[2] More cystic changes and bony destruction tends to portend a worse prognosis for complete resolution of the brown tumors.[7] Older age correlates with an overall longer time to recovery.

Curettage or local excision for improved contouring and aesthetics may be warranted down the road. If the lesion is symptomatic, providing gross unacceptable aesthetic deformation, or fails to regress after correction of hypercalcemia, surgical resection of the brown tumor should be reconsidered. However, some have reported up-front removal of brown tumor, mainly curettage, with some success in lieu of waiting. Some clinicians also advocate for intralesional corticosteroid injections or even systemic steroids as a means of reducing the tumor

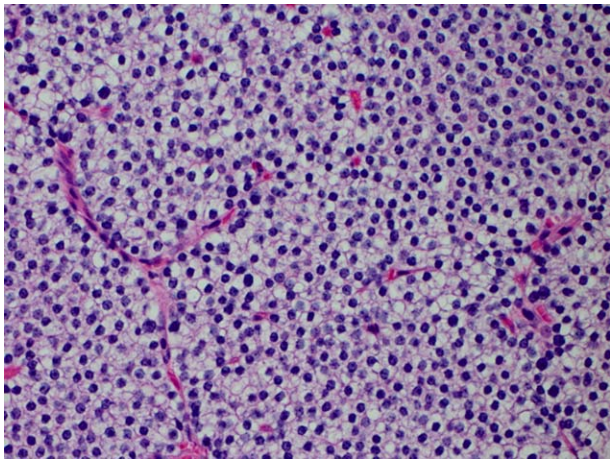

Fig. 4. Right inferior parathyroid excisional biopsy. Gross specimen received as ovoid encapsulated pink-tan tissue, 1.8 cm in maximal dimension, weighing 1.5 grams. Hematoxylin and eosin–stained slide shows evenly distributed monotonous cells with features of a classic parathyroid adenoma. Magnification: 40×. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

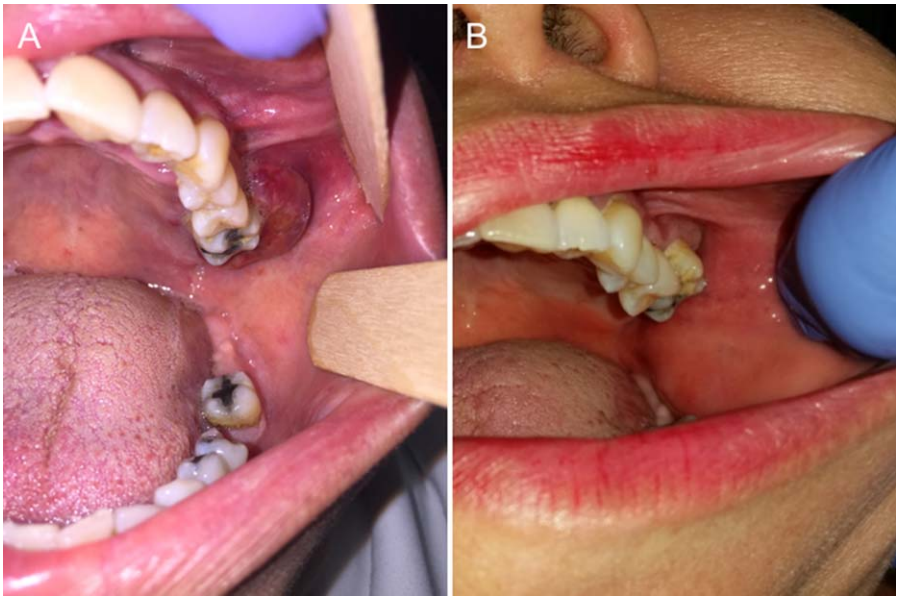

Fig. 5. Clinical presentation and resolution of a maxillary lesion. (A) Presentation at first visit. Maxillary and malar prominence, 1-cm exophytic, erythematous mass centered about tooth 16. Tender to touch with some bleeding. (B) Six months following treatment of primary hyperparathyroidism. Previous left maxillary lesion is now resolved. Dentition remains intact and region is no longer tender. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

size and possibly improving surgical resection if necessary at a later time.[1,8] In this case, correction of hypercalcemia via removal of the parathyroid adenoma led to near complete resolution of the clinically visible maxillofacial lesions and her bony symptoms at 6 months.

Most importantly, in this case, the patient got the right treatment in a timely fashion. A patient whose physical exam could have easily been mistaken for head and neck cancer could have been subject to thousands of dollars of diagnostic testing and even worse, unnecessary surgery and the associated unwarranted morbidity.[9] As healthcare providers in a climate of healthcare reform, aimed to better balance and validate the growth of healthcare expenditures with better outcomes, we must always consider the big picture in a patient-centric manner. We must evaluate all available data, plan and justify our diagnostic and therapeutic proceedings, while staying true to the Latin dictum, *primum non nocere*.

CONCLUSION

As a clinician we are trained to recognize patterns of data. In regard to brown tumors as a primary presentation of PHPT, it is critical to consider the entire dataset. No one piece of information is singularly adequate. We desire to hasten treatment but must ensure we hasten what is right and best for the patient.

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