CASE REPORT

Maxillary brown tumor as initial presentation of parathyroid adenoma: A case report

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Abstract Brown tumor is a rare late-stage skeletal change caused by long-term stimulation of excess parathyroid hormone. It is not neoplastic, but a reparative cellular process. Common sites of brown tumor are the ribs, clavicle, long bones and pelvic girdle. Solitary maxillary brown tumor as initial presentation of primary hyperparathyroidism is rare; it is often accompanied by brown tumors of the other facial bones. Here, we present the first case of solitary maxillary brown tumor in a 29-year-old ethnic Chinese woman with initial presentation of a large tumor filling the left maxillary sinus. Underlying long-standing primary hyperparathyroidism caused by a large parathyroid adenoma was finally diagnosed. Brown tumor tends to be misdiagnosed as malignancy, and delayed diagnosis of the underlying hyperparathyroidism is common. Our case validates the suggestion that young women have a higher probability of brown tumor. Biopsy of the suspicious bone tumor and blood tests for calcium and parathyroid hormone level are crucial and essential to reach the correct diagnosis. Most brown tumors show spontaneous regression after parathyroidectomy. However, direct excision of the brown tumor may be indicated to avoid the risk of facial deformity and orbital compression at a special anatomical site, as in our case.

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Introduction

Brown tumor, also called osteitis fibrosa cystica, is an unusual skeletal change with involvement in <2% of cases of primary hyperparathyroidism [1–3]. Brown tumor is not neoplastic, but a reparative cellular process. Long-term increased secretion of parathyroid hormone (PTH) enhances bone mobilization through rapid osteoclast turnover and contributes to the formation of brown tumors. In regions where bone loss is rapid, hemorrhage, hemosiderin deposition, and vascularized fibrous tissue replace the normal bone contents, resulting in a reddish-brown appearance [2]. Common sites of brown tumor are the ribs, clavicle, tibia,
femur and pelvic girdle. Maxillary brown tumor as the initial presentation of primary hyperparathyroidism is rare; it is often accompanied by brown tumors of the mandible, palate or the other facial bone [4–7].

We present the case of a 29-year-old woman with left facial pain caused by left maxillary brown tumor, which was not diagnosed as being related to hyperparathyroidism until surgical removal of the tumor. To the best of our knowledge, this is the first report of solitary maxillary brown tumor as initial presentation of parathyroid adenoma in an ethnic Chinese patient. We also summarize several critical clinical points that are easily missed and should be kept in mind.

Case presentation

A 29-year-old woman visited our neurology clinic with the odd sensation of progressive swelling and pain in the left side of the face, even when washing the face, during the past 3 months. She felt left eye pain when opening the eye. She had no diplopia or blurred vision. Her menstruation was normal and regular. She had had urinary stones and a depressed mood treated by specialists in recent years. She denied a history of trauma to this area, dental problems, or use of drugs. Physical examination revealed tenderness in the left side of the face, near the cranial nerve V-1 and V-2 dermatome area, without motor impairment. She had normal pupil function, eyeball movements and visual field without ptosis or proptosis. Her facial appearance was also normal without asymmetry.

Brain magnetic resonance imaging demonstrated a well-circumscribed large mass measuring $37 \text{ mm} \times 43 \text{ mm} \times 43 \text{ mm}$ in the left maxillary sinus, with bony expansion and remodeling (Fig. 1). The normal residual sinus was severely displaced inferiorly. The left inferior rectus muscle was compressed inferiorly, and the left nasal cavity was obliterated. She underwent a diagnostic biopsy that revealed a tumor characterized by the presence of many multinucleated giant cells with cellular vascular stroma, which suggested central giant cell granuloma, cherubism, or giant cell tumor of the bone.

Blood biochemistry showed an elevated calcium level of 15.9 mg/dL (reference range, 8.7–10.0 mg/dL) and a low normal phosphorus level of 2.6 mg/dL (reference range, 2.5–4.5 mg/dL). The serum alkaline phosphatase level was 712 IU/L (reference range, 36–108 IU/L). Subsequent testing revealed normal renal function tests and a high intact PTH level of 1846 pg/mL (reference range, 12–65 pg/mL), confirming primary hyperparathyroidism. Both kidney–ureter–bladder (KUB) and renal ultrasonography revealed bilateral medullary nephrocalcinosis. Plain radiography of the skull showed a mottled appearance of the calvarium, presenting the characteristic salt-and-pepper pattern of hyperparathyroidism. Ultrasonography of the neck and a parathyroid scan (Tc99 m sestamibi) showed a 35 mm $\times$ 12 mm $\times$ 11 mm solitary mass at the left lower thyroid bed, consistent with a parathyroid tumor. She denied

Figure 1. (A) Coronal plain T1-weighted magnetic resonance imaging demonstrated a well-circumscribed large mass (arrow) in the left maxillary sinus, with bony expansion and remodeling. (B) Coronal contrast enhancement with fat saturation on T1-weighted image revealed strong enhancement (arrow). (C,D) T2-weighted magnetic resonance imaging showed multiple hyperintense lesions (small arrows) probably due to the cystic contents of the brown tumor.
Brown tumor is just a reaction rather than a true tumor, but it may be recognized as a primary bone tumor and be excised, as in our case. It has also been mistaken for bone metastases, especially when X-ray films show multiple osteolytic bone lesions [6,9,10]. Although surgical resection may not be necessary, biopsy of the tumor is a crucial and essential step to exclude malignancy and other bone disease, and it helps in avoiding unnecessary extensive operation [2,3]. The differential diagnosis should include giant-cell tumor of the bone, giant-cell reparative granuloma, aneurysmal bone cyst, and osteosarcoma [11]. Pathology cannot distinguish giant cell tumor of the bone from the brown tumor of hyperparathyroidism. However, they can be easily differentiated on the basis of laboratory findings. Blood calcium and PTH levels should both be checked, because a primary hyperparathyroid patient may have a normal blood calcium level due to many factors, such as vitamin D deficiency [3,12]. A higher than expected PTH level with a normal to high blood calcium level is diagnostic for brown tumor caused by primary hyperparathyroidism.

If early diagnosis and treatment of hyperparathyroidism are undertaken, the prognosis is excellent in most patients. Resendiz-Colosia et al. have shown that all of their 20 cases of maxillofacial brown tumor that were followed up for ≥2 years had spontaneous regression after parathyroidectomy. In 90% of the cases, regression was clinically complete and mostly within 4–20 months [6]. Regression in those aged >60 years and with bone lesions located in cancellous bone may take longer, which may reflect differences in the rate of bone turnover [5–7,13]. The first choice in managing brown tumor caused by primary hyperparathyroidism is parathyroidectomy. Most of the bone lesions will regress with time after parathyroidectomy, thus, surgical removal of the brown tumor may not be necessary [2–5]. However, at least two studies have shown that the tumors failed to regress and became even larger after parathyroidectomy. One patient had extensive cystic changes with attendant destruction, and the tissue damage was too great to remodel [4]. The other patient had no conclusive cause, although she was 72 years old [14]. In such cases in which resolution is slow or growth continues, excision of the brown tumor should be performed [5].

In some critical conditions or special anatomical sites, especially the skull base, many patients have been treated with surgical excision of the tumor to avoid facial deformation or damage to vital structures, such as compression of the nerves or eyeball, as in our case [2,15]. The patient’s willingness for a quick resolution of symptoms should also be taken into account. Different management strategies should be used with different bone lesions and different patients [5–7,15,16].

The pathological conditions in primary hyperparathyroidism are more complicated than those in the secondary and tertiary types. Primary hyperparathyroidism is mostly caused by adenoma (>80%), followed by hyperplasia, and carcinoma in fewer than 0.5–4% of patients [5,8,17]. However, Resendiz-Colosia et al. have reported a much higher percentage (13.6%) of carcinoma in their 22 patients with maxillofacial brown tumors [6]. Another case review of orbital brown tumors has shown a similar result [18]. This serves to remind us that a suspicious case should undergo long-term follow-up to rule out malignancy.
Maxillary brown tumor in hyperparathyroidism

Hereditary forms of primary hyperparathyroidism are rare, but should also be considered, including multiple endocrine neoplasia type 1 or 2A syndromes, familial isolated hyperparathyroidism, and hyperparathyroidism—jaw tumor syndrome [5,19].

In our case, the patient’s PTH level decreased to 77 pg/mL 1 week postoperatively, but increased again to 383 pg/mL 4 months after surgery. Does this mean a recurrence? Mittendorf et al. have suggested that it is a compensatory response to remineralization of cortical bone. They have demonstrated that persistently elevated PTH levels occurred in 27% of patients following curative parathyroidectomy. The elevation in postoperative PTH levels was usually transient and resolved within 5 months of surgery [20]. Carty et al. have suggested adequate calcium and vitamin D supplements appear to prevent or normalize the condition [21]. In our case, with an elevated PTH level accompanied with a low blood calcium level, a compensatory response may be a reasonable explanation.

In conclusion, we present a case of maxillary brown tumor in a young woman whose long-standing symptomatic hyperparathyroidism had not been recognized in time. Brown tumor tends to be misdiagnosed as malignancy and delayed diagnosis of underlying hyperparathyroidism is common. A young woman may have a higher probability of brown tumor. We have summarized several critical clinical points in managing brown tumor. A biopsy of the suspicious bone tumor and blood tests for calcium and PTH levels are crucial and essential to reach the correct diagnosis. Direct excision of the brown tumor may be indicated in special anatomical sites, as in our case. A much higher percentage of maxillofacial brown tumors tend to be caused by parathyroid carcinoma, which should always be kept in mind in spite of a benign histopathological report.

References