

## BROWN TUMORS OF THE JAW: AN ATYPICAL MANIFESTATION OF PRIMARY HYPERPARATHYROIDISM

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### Abstract

Brown tumors represent the terminal stage of bone remodeling processes in primary hyperparathyroidism. Currently they are rare, and typically affect long bones, pelvis and ribs. Brown tumors may be not included in the initial differential diagnosis of bone disease, especially when they are present in atypical localizations. We reported two cases of oral brown tumors as the initial presentation of primary hyperparathyroidism. In the first case, a 44-year-old woman presented a painful and sessile lesion of 4x3 cm over the central body of the mandible which progressively increased in 4-month. The second case involved a 23-year-old woman who was referred with a 3-month history of a painful and ulcerated mass of 2 cm arising from left maxilla, episodes of gingival hemorrhage and difficulty of breathing. Both cases were solitary tumors with no evidence of palpable cervical lymphadenopathy. Incisional biopsy of oral tumors resulted in giant cell and primary hyperparathyroidism was confirmed by laboratory tests. After parathyroidectomy, histology confirmed adenoma in both cases. Although this type of clinical presentation has almost disappeared in the recent decades, brown tumors should be considered in the differential diagnosis of bone oral masses.

**Key words:** primary hyperparathyroidism, brown tumors, palate tumor, jaw tumor

Los tumores pardos son raros y, por lo general, afectan huesos largos, pelvis y costillas. Pueden no estar incluidos en el diagnóstico diferencial inicial como manifestación de enfermedad esquelética, especialmente cuando se presentan en localizaciones atípicas. Comunicamos dos casos de tumores pardos orales como presentación inicial de hiperparatiroidismo primario. En el primer caso, una mujer de 44 años presentó una lesión dolorosa y sésil de 4 x 3 cm sobre el cuerpo central de la mandíbula que aumentó de tamaño progresivamente en 4 meses. El segundo caso corresponde a una mujer de 23 años que acudió por presentar una masa dolorosa y ulcerada de 2 cm en maxilar izquierdo de 3 meses de evolución, episodios de hemorragia gingival y dificultad para respirar. Todos fueron tumores solitarios sin evidencia de linfadenopatía cervical palpable. La biopsia incisional de los tumores orales resultó en células gigantes, y las pruebas de laboratorio confirmaron el hiperparatiroidismo primario. Tras la paratiroidectomía, la histología confirmó adenoma en ambos casos. Los tumores pardos representan la etapa terminal de los procesos de remodelación ósea en el hiperparatiroidismo primario. Aunque este tipo de presentación clínica casi ha desaparecido en las últimas décadas, los tumores pardos deben ser considerados en el diagnóstico diferencial de las masas óseas orales.

**Palabras clave:** hiperparatiroidismo primario, tumores pardos, tumor de paladar, tumor de mandíbula

### Resumen

**Tumores pardos de mandíbula: una manifestación atípica de hiperparatiroidismo primario**

Oral tumors are a relatively common pathology that can present at different ages. Its clinical presentation is characterized by tumor mass, facial deformity and bone pain. In these cases, the differential diagnoses are multiple, from infectious diseases, malignant tumors such as lymphomas and soft tissue sarcomas. However, they occasionally may be the manifestation of advanced hyperparathyroidism<sup>1</sup>.

Primary hyperparathyroidism (PHPT) is characterized by elevated serum parathyroid hormone (PTH) and calcium. PHPT is caused by a solitary or multiple parathyroid adenomas in 80-85% of the cases<sup>2</sup>. In the last decades, given the advent of the routine measurement of serum calcium in periodic health examination, the classical manifestation of PHPT as nephrolithiasis and nephrocalcinosis or skeletal disease has nearly disappeared. Actually the PHPT is often diagnosed by mild symptoms of hypercalcemia or incidental finding of asymptomatic high serum calcium levels<sup>2</sup>.

The typical bone manifestation of PHPT is the osteitis fibrosa cystica. It is characterized clinically by bone pain and radiographically by subperiosteal bone resorption, osteolysis of the distal clavicles, a "salt and pepper" appearance of the skull, bone cysts and brown tumors<sup>3</sup>. Brown tumors (BT) represent approximately 10% of all skeletal injuries caused by PHPT and typically affect ribs, clavicle, tibia, femur and pelvic girdle, being the jaw involvement of 0.1% to 4.5% of cases<sup>3,4</sup>. As BT are rare, they may be underdiagnosed or even be mistaken for malignant lesions<sup>5</sup> and they are not included in the initial differential diagnosis of this manifestation of skeletal disease, especially when are present in atypical localizations.

### Clinical case 1

A 44-year-old woman presented to the dentist with swelling over the central body of the jaw. She noticed the swelling 4 weeks earlier. The size of the mass had progressively increased, causing mobility of central incisor, canine and first premolar teeth and functional problems with chewing and speech. On initial intraorally examination an expansive, painful, hard, hyperpigmented and sessile lesion of 4 × 3 cm was noted (Fig. 1A). There was no cervical palpable lymphadenopathy. Her medical his-

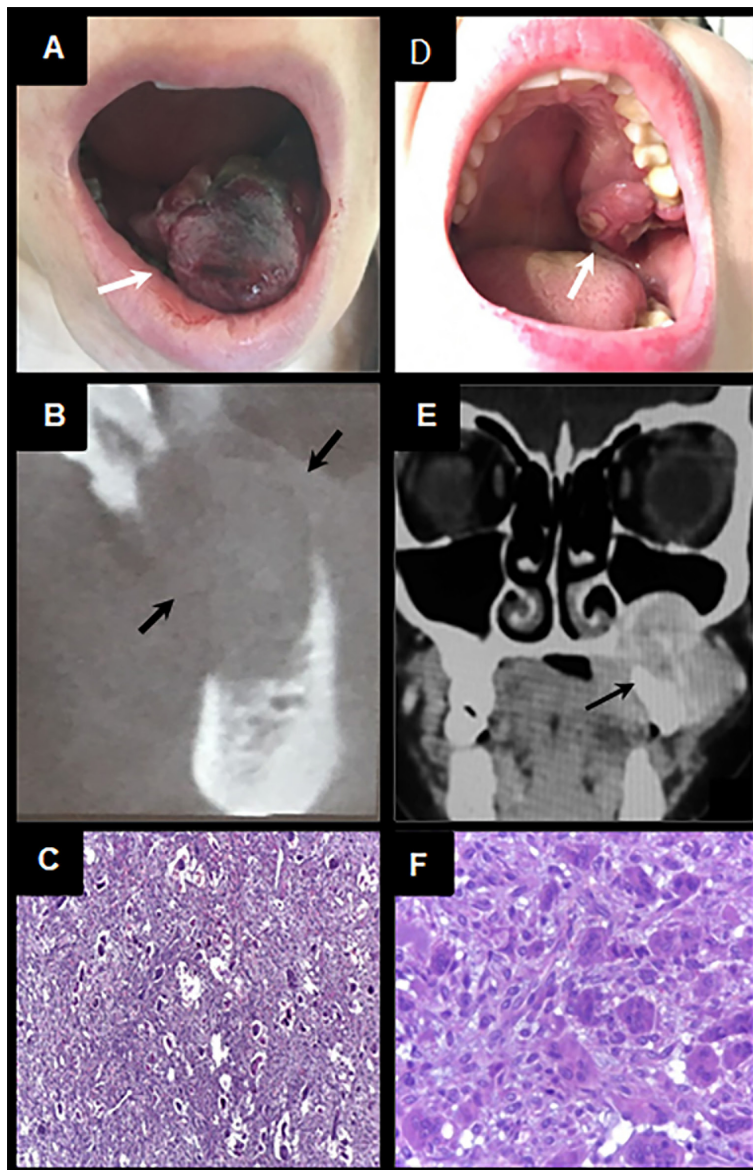
tory revealed left nephrolithiasis diagnosed 1-year-ago. A maxillofacial computed tomography (CT) showed an osteolytic lesion (Fig. 1B). An incisional biopsy was done on the mandibular tumor and the result was reported as giant-cell tumor (Fig. 1C). 99mTc-Sestamibi bone scintigraphy showed no bone lesions except in the mandible. On the other hand, bone densitometry revealed low bone mass. The mass was removed before performing imaging of the neck. Serum biochemistry was compatible with PHPT (Table 1). Ultrasound (US) revealed a large solid lesion with a central cystic area on the right inferior parathyroid gland measuring 2.1 × 2.6 cm. 99mTc-Sestamibi scan of the parathyroid showed uptake at the inferior of the right thyroid lobe. The patient underwent right inferior parathyroidectomy and histopathology of the lesion confirmed a parathyroid adenoma. The patient recovered without complications and normalized biochemical parameters (Table 1).

### Clinical case 2

A 23-year-old woman was referred to us by an otorhinolaryngologist. She presented with a 3-month history of a painful mass in left maxilla bone. The size of the mass progressively increased. She complained about nocturnal episodes of gingival hemorrhage and bad breath. Her past medical history was unremarkable. Examination of oral cavity demonstrated a firm, non-fluctuant, ulcerated lesion of 2 cm arising from left maxilla (Fig. 1D). CT showed a well-defined osteolytic lesion of the left maxillary sinus and palatine bone (Fig. 1E). An incisional biopsy of the tumor resulted in a giant-cell tumor (Fig. 1F). Laboratory evaluation revealed that the patient had PHPT (Table 1). Calcitonin and prolactin were in normal range. Cervical US showed a large solid lesion with macrocalcifications on the right inferior parathyroid gland measuring 3.1 × 1.2 cm. 99mTc-Sestamibi scan of the parathyroid showed MIBI uptake at the inferior of the right thyroid lobe. Systemic impact of hyperparathyroidism resulted in low bone mass, bilateral renal staghorn calculi and a 99mTc-ses-tamibi bone scintigraphy, which showed hypermetabolic foci in the superior left maxilla, inferior right maxilla and skull. The patient underwent right inferior parathyroidectomy and histopathology confirmed a parathyroid adenoma. She recovered without complications and normalized biochemical parameters (Table 1). Two weeks after surgery, she referred no pain on her oral lesion and a reduction of its size was evident. She was lost to follow up.

Both cases were solitary tumors with no evidence of palpable cervical lymphadenopathy.

**Figura 1** | In intraoral photographs white arrows show a solitary exophytic lesion arising from the mandible (A) and maxilla (D). CT scans show hypodense osteolytic lesions that infiltrate the jaw (B-E) as indicated by black arrows. Biopsy images of brown tumor: (C-F) staining shows a brown tumor with multinucleated giant cells in a hypervascular fibroblastic stroma (H&E; 100 x). (F) Numerous osteoclast-like multinucleated giant cells (H&E; 250 x)



**Tabla 1** | Laboratory findings before and after parathyroidectomy in two patients with facial brown tumors

	Reference range	Case 1		Case 2	
		Before PTX	After PTX	Before PTX	After PTX
Ca	8.6-10.5 mg/dl	12.1	9.6	11.1	9.1
P	2.5-4.5 mg/dl	1.3	3	2.6	3.6
PTH	15-65 pg/ml	239	77	606	78
ALP	35-104 U/L	86	91	155	115
Cr	0.5-1.2 mg/dl	0.96	0.91	1.38	1.4

Ca: serum calcium; P: serum phosphorus; PTX: parathyroidectomy; PTH: parathyroid hormone; ALP: alkaline phosphatase; Cr: creatinine

## Discussion

BT are slow-growing lesions that can be locally destructive resulting in significant bone pain and pathologic fractures<sup>6</sup>. The name BT refers to the brown appearance of the lesion as a consequence of local hemorrhage produced by an imbalance of osteoclastic and osteoblastic activity, causing high bone resorption with fibrous connective tissue proliferation replacing the normal content of bone marrow and thinning the cortex<sup>6</sup>. It needs to be emphasized that BT are non-neoplastic lesions and represent a reparative cellular process.

The facial BT occur most frequently in the mandible whereas maxilla or both jaw bones are less commonly affected. The appearance of oral BT is more prevalent in the third decade of life and has a little female predominance<sup>7</sup>. As evidenced in our case series, BT generally appear as a hard and painful palpable swelling, with or without facial deformity<sup>7</sup>.

Typical radiological findings of BT are well-defined radiolucent lesions that do not affect the cortical layer and with no evidence of periosteal reaction or inflammatory signs<sup>8</sup>. On CT images, BT usually appear as a multiloculated lesion with "ground glass opacification"<sup>9</sup>. It is important to remark that BT are frequently associated with other bone changes due to general bone compromise of PHPT such as demineralization or subperiosteal resorption, salt-and-pepper radiographic appearance of skull bones<sup>10</sup>. In our patients, diffuse bone involvement was confirmed by low bone mass in bone densitometry.

BT may be histologically indistinguishable from central giant cell granuloma and giant cell tumor<sup>11</sup>. Thus BT are only differentiated by a clinical and biochemical context of PHPT as was evident in the cases described.

The first option in the management of the BT caused by PHPT is the parathyroidectomy<sup>12</sup>. Most bone lesions will regress with time after parathyroidectomy, therefore, surgical removal of the BT may not be necessary<sup>13</sup>. However, if the lesion continues to grow despite treatment, persists for more than six months or is locally disfiguring, the surgical excision of the BT may be indicated<sup>14</sup>. The two cases presented illustrate these possible treatments. In case 1, surgical removal of the mass was required due to the local symptoms she presented. On the other hand, in case 2 the parathyroidectomy resulted in improvement of the size and symptoms of the BT.

In conclusion, PHPT is currently diagnosed more frequently by the coincident finding of asymptomatic hypercalcemia in the laboratory. BT represent the terminal stage of bone remodeling processes in this disease. Although this type of clinical presentation has almost disappeared in the recent decades, these cases highlight the fact that BT should be considered in the differential diagnosis of bone oral masses.

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**Conflict of interest:** None to declare

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