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Brown tumour of hyperparathyroidism in the mandible associated with atypical parathyroid adenoma

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Abstract
The brown tumour of hyperparathyroidism is a localized bone tumour and an uncommon manifestation of hyperparathyroidism. A 27-year-old woman presented with a mandibular 8 × 10 cm solid mass diagnosed as central giant cell granuloma. Chemical blood analysis revealed increased serum calcium levels of 12.46 mg/dL and the parathyroid hormone level was 124 pg/dL. The patient underwent surgery with removal of a parathyroid mass. Histologically, this parathyroid tissue was seen to be limited by a fibrous capsule with morphological features consistent with atypical parathyroid adenoma. The mandibular tumour has receded and the patient declined further procedures. This is the first case reported of brown tumour as the primary manifestation of an atypical parathyroid adenoma, a lesion that shares some features with parathyroid carcinoma without the unequivocal properties of malignancy.

Key words: Parathyroid diseases; Hyperparathyroidism; Parathyroid neoplasms; Giant cell tumours; Adenoma

Case report

A 27-year-old postpartum woman was referred to our care following biopsy results from another institution of a mandibular lesion, that were consistent with central giant cell granuloma without any evidence of malignancy. The patient presented with a seven-month history of an expanding mass in the left part of the mandible (Figure 1). She also complained of altered teeth position and an ipsilateral numbness of her chin. Physical examination revealed an 8 × 10 cm solid mass on her left mandible. The mass was firm, non-tender, attached to the mandible and the skin on top of it was freely mobile. The mass also involved her left lower gingiva and her 33–35 teeth were anteriorly displaced. The rest of the physical examination was unremarkable. Chemical blood analysis revealed serum calcium levels of 12.46 mg/dL (normal 8.5–10.5 mg/dL), serum phosphorus level of 2.77 mg/dL (normal 4–6 mg/dL), and alkaline phosphatase level of 196 I.U. (normal 30–140 I.U.). The parathyroid hormone (PTH) level was 124 pg/dL (normal 10–65 pg/dL). Urine calcium and phosphorus were normal. A Sestamibi (MIBI) scan was performed with findings consistent with a parathyroid adenoma on the upper left pole of the thyroid gland. Axial computed tomography (CT) scan (Figure 2) showed a large loculated, bone-expanding mass in the anterior left part of the mandible. Contrast enhanced CT scan also showed a 2 cm mass that was consistent with a parathyroid adenoma on the left posterior aspect of the thyroid gland (Figure 3). Abdominal ultrasound revealed bilateral nephrolithiasis.

The patient underwent surgery and the non-adherent parathyroid mass was removed. The tumour measured 1.4 × 0.8 × 0.6 cm and weighed 1.4 g. Biopsy from a second ipsilateral parathyroid gland demonstrated normal parathyroid tissue.

Histologically, the parathyroid tissue was seen to be limited by a fibrous capsule (Figure 4). The cells were arranged in wide sheets with areas of trabecular growth pattern. Broad fibrous bands, in continuity with the capsule, subdivided the parathyroid parenchyma and islands of parathyroid cells were seen within the capsule. Some of the tumour cells showed atypia but no mitotic figures were seen. These morphological features are consistent with atypical parathyroid adenoma.

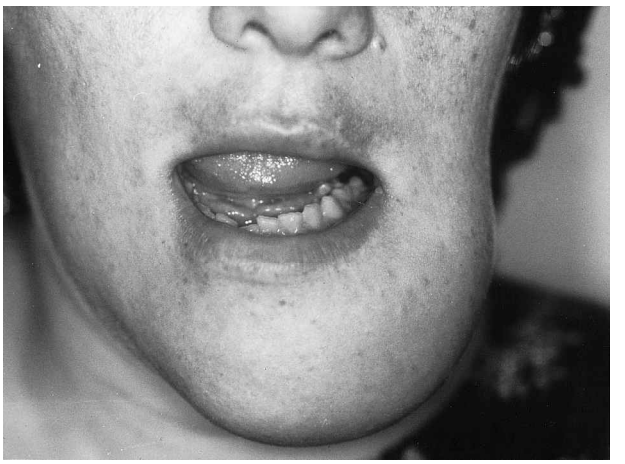

Fig. 1
Large left mandibular tumour.

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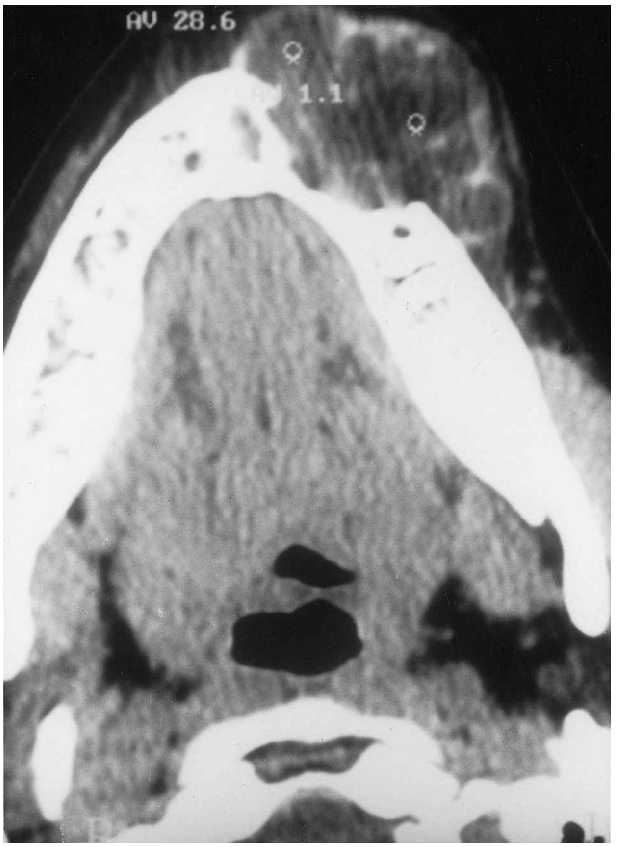

FIG. 2
Axial CT scan depicting large expansible mandibular mass.

The post-operative course was uneventful and calcium levels normalized following a two-week period of mild, transient hypocalcaemia. The mandibular tumour has significantly receded six months after the procedure and the patient has declined a curettage procedure.

Discussion

The role of PTH is to control calcium and phosphorous levels in the plasma and in the extracellular fluid and this is done partly by modulating the balance between osteoblastic and osteoclastic activities. Primary hyperparathyroidism results from overproduction of PTH, most commonly by a single adenoma. It can also be a manifestation of two or more adenomas, primary hyperplasia or rarely, carcinoma. Secondary hyperparathyroidism results from compensatory hyperplasia, usually of all four glands, a condition seen most commonly in renal insufficiency. It can also be seen in conditions such as calcium malabsorption and forms of osteomalacia.

Tertiary hyperparathyroidism represent those cases of secondary hyperparathyroidism, which lead to development of autonomous parathyroid tissue. In hyperparathyroid states, an imbalance exists between osteoblastic and osteoclastic activity. Lamellar bone is being constantly resorbed while woven bone is laid down to replace it. Occasionally soft tissue proliferation replaces the lost bone.

The full manifestations of this process, including reduced bone density and generalized osteoporosis, have traditionally been known as osteitis fibrosa cystica or Von Recklinghausen disease. There is also subperiosteal bone resorption of phalangeal tufts and clavicle, absence of lamina dura of teeth and a 'salt and pepper' radiological appearance of demineralization in the skull.[1,2]

The skeletal changes of hyperparathyroidism are never localized and those that seem so are the more difficult to diagnose because they present clinically and radiologically as expansile multilocular masses.[3]

The brown tumours are non-neoplastic lesions found only in the presence of hyperparathyroidism. The lesion results from a change in bone metabolism and presents clinically and radiologically as an expansile mass. They are very similar histologically and radiologically to other giant cell lesions and differential diagnosis includes giant cell reparative granuloma, cherubism, true giant cell tumour and aneurysmal bone cyst.[1,2]

Over the past two decades brown tumour has been a rare manifestation of primary hyperparathyroidism.[4] The growing use of biochemical assays has led to an earlier diagnosis of the disease as asymptomatic hypercalcaemia. However, brown tumour can be the first manifestation of hyperparathyroidism, usually incurred in the ribs, clavicle and pelvic girdle. Less commonly there is facial bone involvement, and mandibular and maxillary bones are the facial bones that are commonly involved.[1,2,6]

Because of an increasing number of dialysis patients and their increased longevity, brown tumour is seen more often as a result of secondary hyperparathyroidism.[1,7] Patients

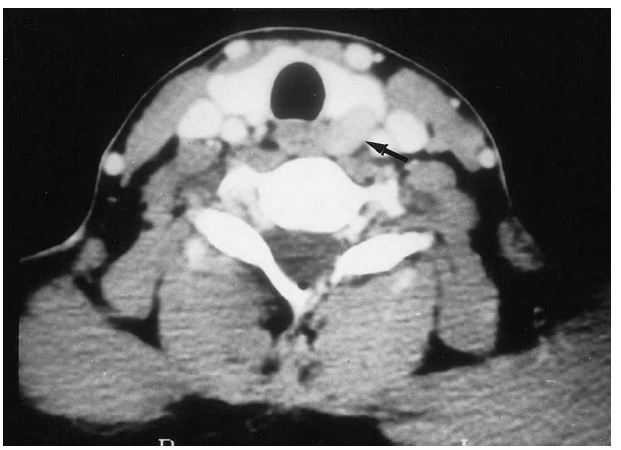

FIG. 3
Axial contrast enhanced CT scan demonstrating an enlarged parathyroid mass on the left posterior aspect of the thyroid gland (arrow).

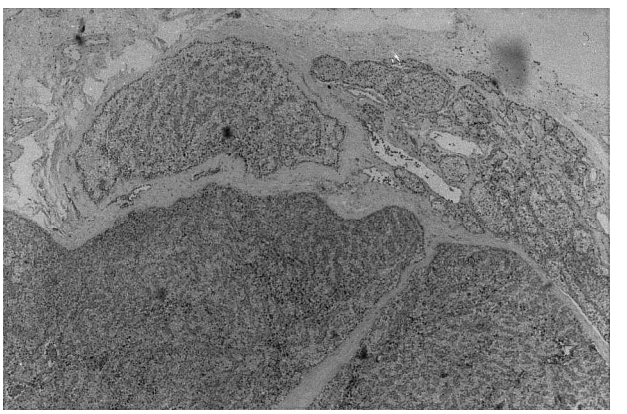

FIG. 4
Histological section showing parathyroid tissue limited by a fibrous capsule. The cells are arranged in wide sheets with areas of trabecular growth pattern. Broad fibrous bands in continuity with the capsule subdivide the parathyroid parenchyma and islands of parathyroid cells are seen within the capsule (H & E; × 250).

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have to be screened for parathyroid function incorporating both blood tests and imaging in selected cases prior to embarking upon local radical surgery of the tumour. Indeed, curettage or resection are warranted mostly in persistent or large destructive tumours.[1] Grossly brown tumour appears as a mass with partly cystic and partly solid areas. Microscopically, there is a combination of osteoblastic and osteoclastic activity, often associated with cyst formation. Clusters of haemosiderin-laden macrophages, giant cells and proliferating plump fibroblasts fill the lytic lesions.[3] The name 'brown' comes from its colour a result of vascularity, haemorrhage and deposits of haemosiderin.

Most brown tumours are associated with primary hyperparathyroidism but none have been reported to be associated with hyperparathyroidism due to atypical adenoma.

Treatment of hyperparathyroidism is the first step of management. Tumour regression and healing are expected, although tumour recurrence can occur because of persistent or recurrent hyperparathyroidism. There have been a few cases reported in which there was rapid tumour growth after parathyroidectomy without any evidence of hyperparathyroidism.[4,6,7] Sometimes, a persistent or large brown tumour should be removed.

Clinically the excised tumour had some of the properties of adenoma i.e. it was not adherent to surrounding tissue and was not associated with very high calcium levels. Pathologically the tumour had some histological features of parathyroid carcinoma including a trabecular growth pattern. There was thick fibrous bands and entrapment of parathyroid cells within the capsule, that could mistakenly be interpreted as capsular invasion. No mitotic activities, no vascular invasion nor obvious capsular invasion were seen however with the lack of clear evidence of malignancy, a diagnosis of atypical adenoma was made. This implies that the behaviour of the neoplasm is unpredictable with respect to recurrence and metastasis.[8] Because of the uncertain behaviour of the tumour, follow-up of the patient should include periodic serum calcium and PTH measurements.

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