Case Report

A rare complication of secondary hyperparathyroidism

Brown tumor of the maxilla and mandible

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ABSTRACT

Brown tumors are focal bone lesions caused by increased osteoclastic activity and fibroblastic proliferation encountered in primary or more rarely secondary hyperparathyroidism. Ninety-two percent of the patients undergoing dialysis develop secondary hyperparathyroidism. Of these, approximately 1.5% develops brown tumors. Brown tumors of hyperparathyroidism may appear in any bone but are frequently found in the facial bones and jaws, particularly in long-standing cases of the disease. As it becomes common for hyperparathyroidism to be detected earlier during the disease, the bony manifestations of the disease are rarely seen. The following report describes a case of brown tumor of the maxilla and mandible in a patient with renal insufficiency. This patient presented multiple skeletal lesions, which are uncommonly seen nowadays.

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Secondary hyperparathyroidism results from a compensatory increase in the output of parathyroid hormone (PTH) in response to hypocalcemia. The underlying hypocalcemia may result from inadequate dietary intake or poor absorption of vitamin D or from deficient metabolism of vitamin D in the kidney. This condition produces clinical and radiographic effects similar to those of primary hyperparathyroidism.[1] Parathyroid hormone induces simultaneous trabecular expansion and cortical regression, the combination of which allows contours of the jaws to change.[2] Brown tumors are a local bone destructive phenomenon which is accounted for by rapid osteoclastic bone turnover resulting from severe hyperparathyroidism.[3] This unusual complication of secondary hyperparathyroidism is more commonly seen with increased longevity of hemodialysis patients and can be found in any bone. The tumor is called "brown" because of its color, which is a result of vascularity, hemorrhage and deposits of hemosiderin.[4] Histopathologically, it is difficult to differentiate from other giant cell lesions. A clinical diagnosis of this tumor is reached with the finding of hyperparathyroidism. A brown tumor often develops at multiple sites, including the ribs, clavicle, and pelvic girdle, but maxillofacial brown tumors are rare.[5] Our patient highlights the presentation of hyperparathyroidism as a localized brown tumor of the mandible and maxilla which are unusual locations for brown tumors.

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Case Report. A 41-year-old woman was admitted to our university hospital because of progressive difficulty in walking in December 1998. Her medical history disclosed that she had been on a regular hemodialysis program 3 times a week because of chronic kidney failure for 10 years. Her laboratory findings were as follows; intact PTH 1250 pg/ml (9-78 pg/ml), calcium 10.4 mg/dl (8.1-10.7 mg/dl), phosphate 2.7 mg/dl (2.3-4.7 mg/dl), alkaline phosphatase 2427 u/L (95-280 u/L). Thyroid ultrasonography detected 2 possible parathyroid nodules in the parathyroid region. Parathyroid scan with 99mTc-sestaMIBI showed no abnormal staining in the parathyroid tissue. Radiologic studies indicated multiple bone locations of brown tumors in ribs. Following the medical therapy including parenteral vitamin D plus oral calcium salts, hypercalcemia developed within a few weeks. Consequently, subtotal parathyroidectomy was performed in January 1999. After operation, serum iPTH levels decreased to 101 pg/ml and the surgical intervention was regarded as successful. Unfortunately, despite the successful operation, the clinical condition did not improve significantly. We thought that delayed parathyroidectomy might be the main reason for clinical failure.

During the follow-up period, she came to the clinic with a gradually progressive mandibular swelling 3 years after the operation. Oral examination revealed a 3.5x3 cm hard, nontender, nonpulsatile, mandibular swelling with nonadherent normal overlying skin (**Figure 1**). Computerized tomography (CT) revealed 2 cystic formations, in the anterior mandibular region and the maxillary region (**Figures 2 & 3**). A curettage biopsy of the mandibular lesion was taken. Microscopic examination showed many multinucleated giant cells arranged in groups adjacent to hemosiderin granules, within a fibrovascular hemorrhagic stroma (**Figure 4**). This pathologic picture was consistent with a brown tumor, in the context of the patient's severe hyperparathyroidism.

Repeated laboratory examination showed high iPTH level again at 754 pg/ml. Recurrence of secondary hyperparathyroidism was diagnosed. Ultrasonographic examination of parathyroid glands showed nodular enlargement of both inferior parathyroid glands. She refused all the invasive interventions for enlarged parathyroid glands.

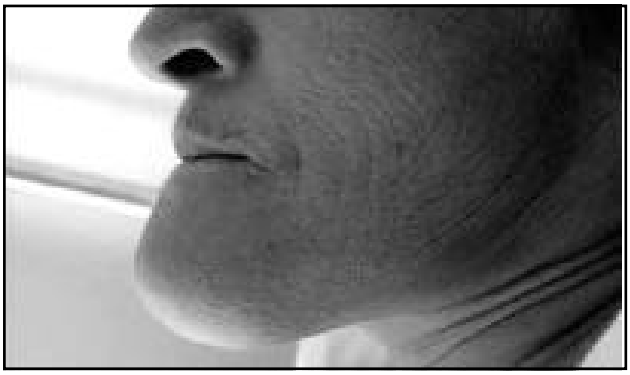

Figure 1 - Clinical view of mandibular brown tumor.

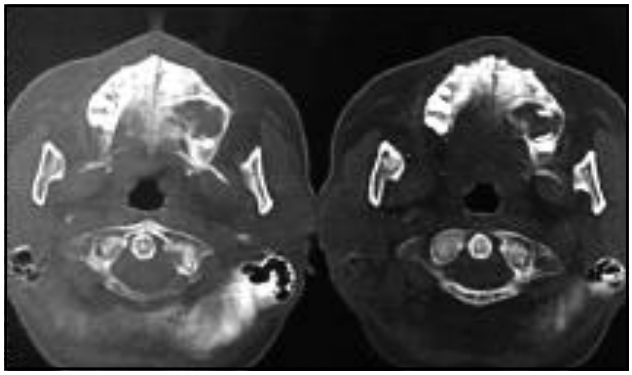

Figure 3 - Computed tomography scan of the maxilla; osteolytic area with irregular margins in the left maxilla.

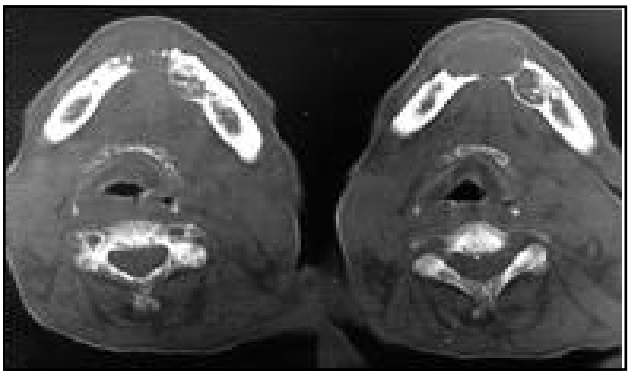

Figure 2 - Computed tomography scan of the mandible; osteolytic area with irregular margins in the midline of mandible.

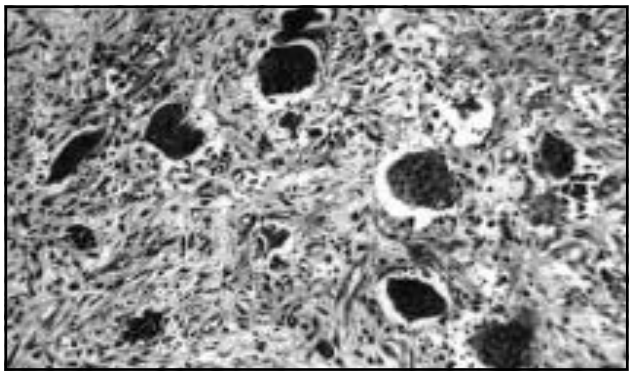

Figure 4 - Histopathologic features of the mandibular lesion. Many osteoclast-like multinucleated giant cells arranged in groups adjacent to fibrovascular hemorrhagic stroma.

Discussion. Early diagnosis and successful treatment of hyperparathyroidism have made clinical evidence of bone disease uncommon.[6] The earliest and most reliable changes of hyperparathyroidism are subtle erosions of bone from the subperiosteal surfaces of the phalanges of the hands. Osteitis fibrosa cystica are localized regions of bone loss produced by osteoclastic activity resulting in a loss of all apparent bone structure. Brown tumors occur late in the disease and in approximately 10% of cases.[1] Grossly, a brown tumor appears as a mass with partly cystic and partly solid areas.[7] The lesion results from a change in bone metabolism and presents clinically and radiologically as an expansile mass.[4] Clinically they are slow-growing lesions that can be locally destructive, resulting in a variety of symptoms, such as significant bone pain and pathologic fractures.[7] In our case, the patient was asymptomatic. At radiography, the lesions have variably well- or ill-defined margins and may cause cortical expansion.[8] On plain films, a brown tumor appears as a radiolucent, expansile, and somewhat cystic lesion. Computed tomographic scans typically show a lytic lesion that may erode the bony cortex.[9]

Concurrent bone changes associated with hyperparathyroidism, such as generalized demineralization of the medullary bones of the jaw and loss of lamina dura around the roots of teeth, can help differentiate brown tumors from other processes.[8] Histologic examination demonstrates a dense fibrovascular stroma with focal areas of osteoid, numerous osteoclastic type giant cells arranged in groups, and hemosiderin-laden macrophages with associated hemorrhage.[10] Brown tumors are histologically indistinguishable from the other giant cell-containing lesions, such as true giant cell tumor, aneurysmal bone cyst, and giant cell reparative granuloma.[4,5,7] Unlike brown tumors, these other lesions are not seen in the clinical setting of hyperparathyroidism.[5,11]

Parathyroidectomy to control hyperparathyroidism is the treatment of first choice for brown tumor in patients resistant to medical therapy including vitamin D and oral calcium salts because the normalization of parathyroid function should lead to a reduction in size or disappearance of the tumor.[5] A review of the literature has shown that parathyroidectomy is usually curative. After successful surgical removal of the causative parathyroid adenoma, almost all radiographic changes revert to normal. The only exception may be the site of a brown tumor, which often heals with bone that is radiographically more sclerotic than normal.[1] Tumor recurrence can result from persistent or recurrent hyperparathyroidism.[4] Sometimes, surgery in the form of excision of the brown tumor may be required.[7] Resulting from recurrence of secondary hyperparathyroidism that our patient demonstrated, 3 years after the parathyroid surgery, there was growth of the mandibular and maxillare tumor. She refused all the invasive interventions for enlarged parathyroid glands and brown tumors.

Despite parathyroidectomy, patients must be followed up for recurrence of hyperparathyroidism and occurrence of brown tumors of the maxilla and mandible which are rare complications of secondary hyperparathyroidism.

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