Case Report - Systemic Disorders

A rare case of regression of brown tumors of tertiary hyperparathyroidism after parathyroidectomy and renal transplant: A 5-year follow-up

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ABSTRACT

Tertiary hyperparathyroidism (HPT) is a rare condition that affects patients with secondary HPT, which develop hyperplasia of the parathyroid glands, thus causing an increase in parathyroid hormone levels. Bone alterations are the main consequences of this condition including the development of osteolytic lesions called brown tumor. This article reports an unusual case of brown tumors located in the maxilla and mandible in a 19-year-old man with chronic renal failure with hyperplasia of the parathyroid glands. The lesions regressed approximately 5 months after the parathyroidectomy. At this same time, the patient underwent renal transplant. The patient was followed for 5 years, showing improvement in overall clinical status. There was also improvement of the results of laboratory tests and the pattern of trabecular bone. The correct diagnosis of oral lesions was of great relevance for the conservative treatment could have been chosen.

Keywords: Brown tumor, renal transplant, tertiary hyperparathyroidism

INTRODUCTION

Tertiary hyperparathyroidism (HPT) is a rare condition that affects patients with secondary HPT, which develop hyperplasia of the parathyroid glands, thus causing an increase in parathyroid hormone (PTH) levels, regardless of renal failure. Brown tumors of the bone or osteoclastomas are lesions that occur due to increased osteoclastic activity such as HPT, and it occasionally affects the jaw bones.[1,2] This type of lesion is a nonneoplastic lesion resulting from abnormal bone metabolism that creates this local destructive intraosseous lesion.[2,3] Patients develop brown tumors arising from a group of pathological disorders (primary, secondary, or tertiary HPT) that directly or indirectly result in the hypersecretion of PTH, which results in increased osteoclastic bone resorption, primarily in cortical bone.[4] Their histopathology is characterized by masses of soft tissue composed of giant cells in a fibrovascular stroma, cyst-like spaces lined by connective tissue, and foci of hemorrhage, changes that may be related to microfractures undergoing organization with the release of hemosiderin. These

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features are identical to those found in other giant cell lesions.[2,5] A clinical diagnosis of this lesion is made with the finding of HPT. Parathyroidectomy to control HPT combined with enucleation and curettage of the brown tumors is the treatment of the first choice for brown tumors related to the secondary HPT when the disease is resistant to medical therapy.[6-8] The purpose of this study was to report a rare case of large brown tumors arising in both the maxilla and mandible of a patient with tertiary HPT in whom regressed after parathyroidectomy and renal transplant.

CASE REPORT AND RESULTS

A 19-year-old man, Caucasian, was referred to our Oral and Maxillofacial Surgery Service for evaluation of swellings in the maxilla and mandible. The patient had been diagnosed with secondary HPT due to chronic renal failure in the final stage, whose cause was a urinary tract infection. The patient was in a generally debilitated state, making hemodialysis sessions 3 times a week [Figure 1]. Physical examination revealed that he was short of stature and had vertebral scoliosis. Intraoral inspection revealed an asymptomatic swelling in the anterior palate with a bony consistency, with crackling on some points, measuring approximately 5.0 cm in diameter [Figure 2], which had commenced 2 years previously. Intraoral examination also showed an increase in volume in the anterior region of the mandible with a bony consistency, asymptomatic, measuring approximately 4.0 cm in diameter [Figure 3], also with the same time course. The teeth-related injuries had no mobility, had vitality, no resorption and were displaced. Radiographic examination demonstrated generalized demineralization of the bones. A skull radiograph disclosed a "ground-glass" or "salt and pepper" appearance of the calvarium and loss of cortical lines [Figure 4]. The panoramic radiograph revealed a thinning of the trabecular bone, resulting in an appearance similar to "ground-glass" or "salt and pepper" [Figure 5]. The intraoral radiograph showed a generalized loss of lamina dura of the most teeth of the maxilla and mandible [Figure 6a and b]. The X-rays of hands showed metastatic calcifications in the joints and subperiosteal resorption of the phalanges [Figure 7]. Laboratory tests were abnormal, confirming the diagnosis of HPT. Initial investigations showed elevated levels of PTH 1490 pg/ml, calcium 12.0 mg/dl, phosphate 6.1 mg/dl, and alkaline phosphatase 320 U/L. The hemoglobin level was 6.8 g/dl due to decreased levels of erythropoietin. From the above data, we opted for the incisional biopsy of lesions. The histopathology report showed giant cell lesion (brown tumors of HPT) [Figure 8]. The diagnosis was suggested by the clinical history and confirmed by biochemical, radiological, and histopathologic examinations. Parathyroid glands fine needle aspiration was performed. The result, associated with clinical and laboratory findings, revealed a case of hyperplasia of the parathyroid glands. Because of parathyroidectomy has already been scheduled, it was decided to follow the lesions with the expectation of remission after surgery of the parathyroid glands. Approximately, 2 months after our evaluation, after regression of the symptoms of anemia, the patient underwent parathyroidectomy. The biopsy performed confirmed the diagnosis of glandular hyperplasia. One of the parathyroid glands was reimplanted in the right forearm to maintain PTH levels within normal levels. Laboratory tests were within the normal levels 5 months after parathyroid surgery, with regression of the lesions, and the patient underwent renal transplantation. The patient was followed up for 5 years, showing improvement in overall clinical status [Figure 9]. The pattern of trabecular bone of the jaw has also improved [Figure 10a-d], and the lesions of the maxilla and mandible healed [Figure 11a and b]. We also observed the disappearance of metastatic calcification and supraperiosteal resorption of the phalanges [Figure 12a and b].

DISCUSSION

HPT is a pathological disorder caused by high levels of PTH. It is classified into 2 types: Primary, due to hyperplasia or neoplasia of one or more of the parathyroid glands; and secondary, when the parathyroid glands are stimulated to produce increased amount of PTH to correct abnormally low serum calcium levels in different physiologic or pathologic processes, resulting in parathyroid hyperplasia.[2] In most cases, the cause of low levels of calcium is a chronic renal failure. Sometimes, in long-standing secondary HPT cases, the parathyroid glands gain an autonomous character, which are known as tertiary HPT.[6]

Patients with chronic renal failure show changes in their mineral metabolism and bone structure resulting in renal osteodystrophy.[9] Overt findings of osteitis fibrosa cystica include generalized demineralization of bone, "ground-glass," or "salt and pepper" appearance of the bones, including the skull; bone cysts; subtle erosion of bone on the subperiosteal surfaces of the phalanges; and brown tumors.[10] Brown tumors are an extreme form of osteitis fibrosa cystica, in which bone turnover is increased due to secondary HPT. These lesions represent the terminal stage of HPT. In the past, bone lesions were recognized in 80–90% of patients with primary or secondary HPT. Currently, these rates have been declined in 10–15%. This is because of early diagnosis (new and more objective PTH radioimmunoassay techniques) and successful treatment of the disease.[8] The ribs, clavicles, pelvic girdle, and mandible are the most often involved bones.[2] The maxilla is not frequently involved.[5,10] The case reported in this study showed the mandible and the maxilla affected by brown tumors.

The brown tumor presents itself as a friable red browned mass, representing the final stage of HPT.[2,8] The name "brown tumor" derives from the color, which is caused by the vascularity, hemorrhage, and deposits of hemosiderin. Painful usually is present, as well as hard, clearly visible, and palpable swelling. Long-term injures commonly produce a significant expansion of cortical.[3,5,7] Radiographically, brown tumors appear as well-demarcated monolocular or multilocular osteolytic lesions.[2,5] In the mandible, the cortical bone is expanded and thinned. These lesions occasionally cause root resorption and widespread loss of the lamina dura, and changes in the pattern of trabecular bone of the jaws.[5] The loss of the lamina dura was a common radiographic feature in 40% of the patients in their study[8] Based on those radiographic characteristics, in the diagnosis of chronic renal failure, and the result of incisional biopsy, the jaw bone lesions presented in this case was diagnosed as brown tumors. In our case report, the teeth-related injuries had no mobility, had vitality, no resorption and were displaced.

The histopathological examination of brown tumors is characterized by an abundant stroma, consisting of bundles of the spindle or

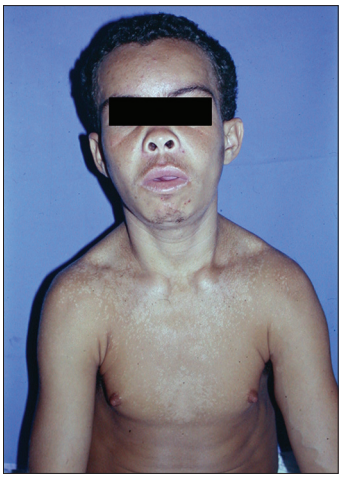

Figure 1: Full-face photograph showing a generally debilitated state

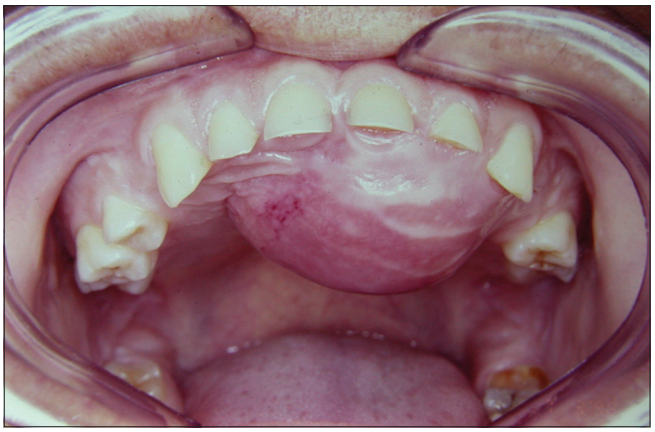

Figure 2: Intraoral photograph showing anterior palatal enlargement. Note displacement of the teeth in the related area

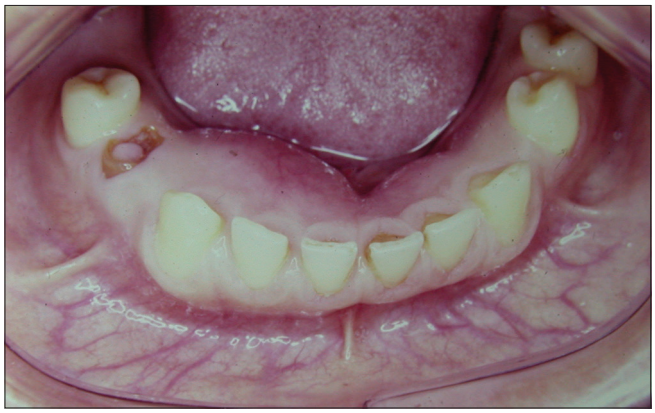

Figure 3: Intraoral photograph showing swelling of the anterior alveolar part of the mandible and spacing of incisors are evident

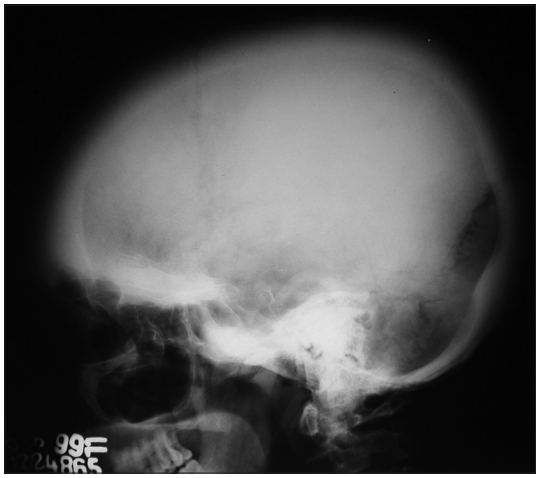

Figure 4: Radiograph of skull demonstrates "ground-glass" appearance of calvarium

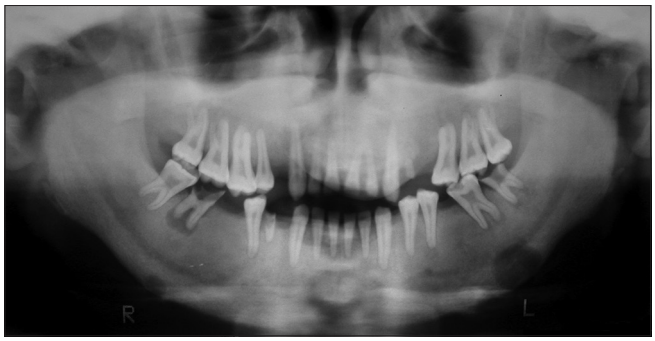

Figure 5: Panoramic radiograph showing expansion of both jaws with nearly homogenous or "ground-glass" trabecular pattern. Note the loss of cortical outline for the incisive nerve canal, poor definition of crestal bone, and inferior cortex of the mandible. The maxillary and mandibular lesions are not clearly distinguishable on this panoramic radiograph

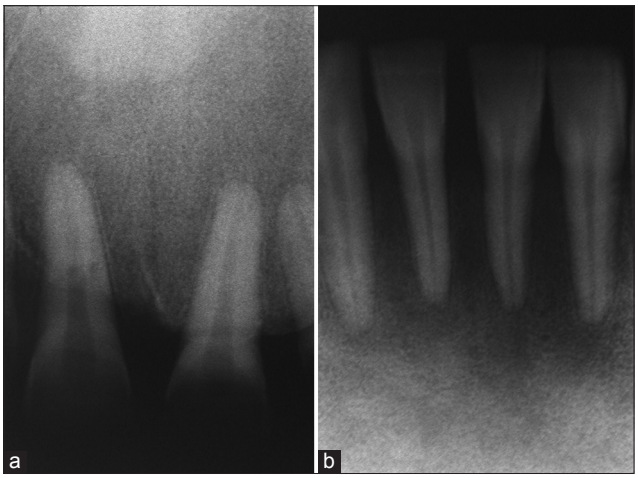

Figure 6: (a) Intraoral radiograph showing loss of lamina dura of maxillary anterior teeth; (b) Intraoral radiograph showing loss of lamina dura of mandibular anterior teeth

oval cells, and several multinucleated osteoclast-like giant cells. Calcified material can be found, as well as areas with extravasation of red blood cells and pigmentation by hemosiderin.[2] These findings are not pathognomonic, making it necessary to perform a differential diagnosis with other lesions such as the early stages of cherubism, aneurysmal bone cyst, and central giant cell granuloma (CGCG). Most of these diseases can be differentiated by the combination of clinical and radiological findings, but differentiation between CGCG and brown tumors of HPT only can be made by means of laboratory tests including PTH level.[3,5]

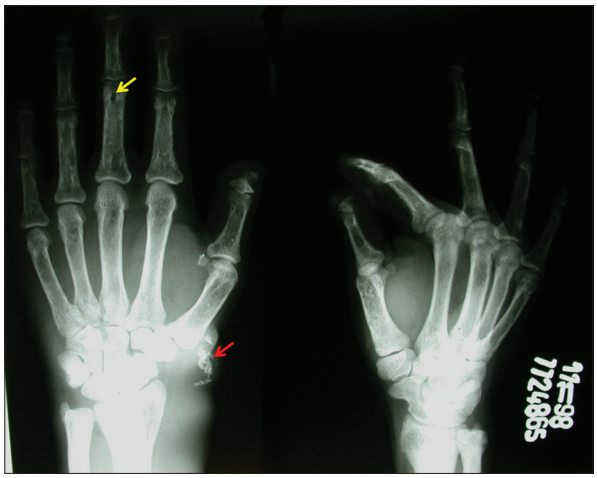

Figure 7: Radiograph showing metastatic calcifications in the joints (red arrow) and subperiosteal resorption of the phalanges (yellow arrow)

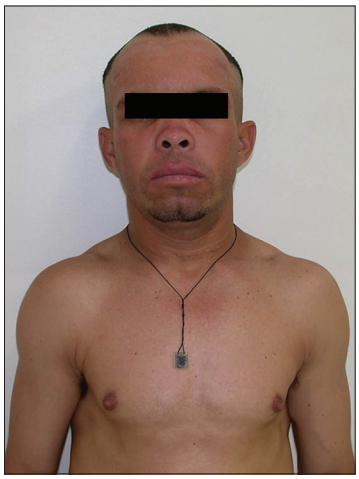

Figure 9: Full-face photograph showing improvement in overall clinical status

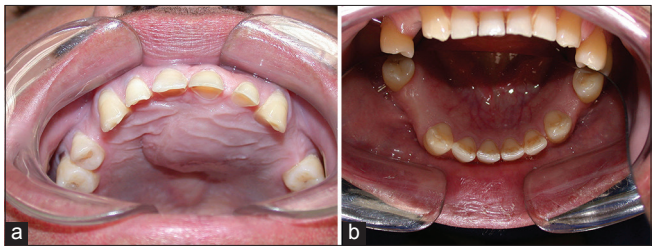

Figure 11: (a) Intraoral photograph of maxillary lesion showing healing with a small residual deformity; (b) Intraoral photograph of mandibular lesion showing healing

In patients with a brown tumor, HPT should first be treated before considering resection of the tumor. Some studies[1] have indicated a total parathyroidectomy to treat tertiary HPT, to restoring normal serum PTH values, and increasing bone mineral density. Krause *et al*.[9] have reported that they resected any remaining brown tumor after PTH resolved. In our case, it was decided by the implantation of one of parathyroid glands in a patient's forearm to maintain PTH levels within the normal levels, although Kebebew *et al*.[6] advocate that patients

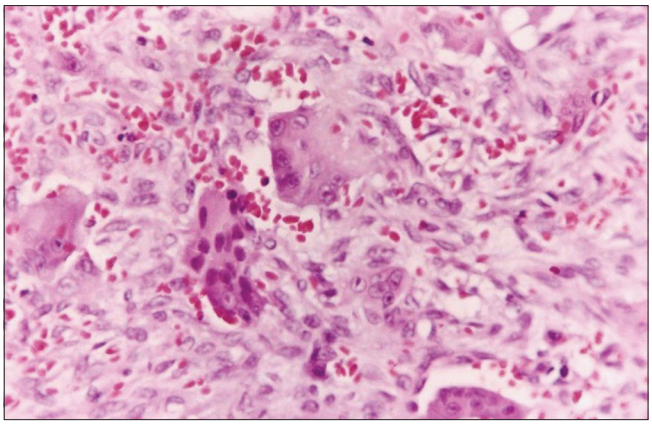

Figure 8: Histopathologic photomicrograph of the biopsy specimen from the maxillary lesion showing multinucleated osteoclast-like giant cells (H and E, ×40)

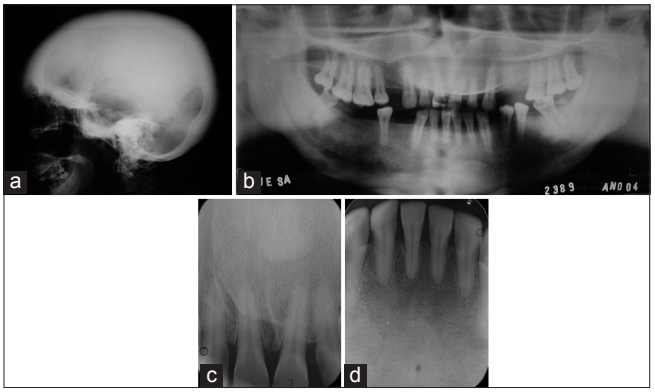

Figure 10: (a) Radiograph of skull showing improvement of the "ground-glass" appearance of calvarium; (b) Panoramic radiograph showing improvement of the pattern of trabecular bone; (c) Intraoral radiograph showing restoration of lamina dura of maxillary anterior teeth; (d) Intraoral radiograph showing restoration of lamina dura of mandibular anterior teeth

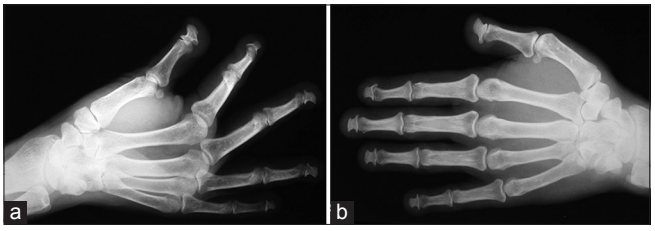

Figure 12: (a and b) Radiograph showing resolution of metastatic calcifications and resolution of subperiosteal resorption of the phalanges

who underwent partial removal of the glands are more likely to remain in HPT. Normalization of PTH levels will often cause the brown tumors to regress or sometimes even resolve spontaneously.[10] De Oliveira *et al*.[11] described a case of a big brown tumor regression after surgical removal of parathyroid adenoma, which measured 8.1 cm × 6 cm × 5.1 cm, which invaded the orbital cavity on the left side and a large part of the nasal cavity. Nabi *et al*.[12] also reported the same experience of spontaneous regression after a parathyroidectomy. As the patient in this study had a chronic renal failure in the final stage, we opted for the renal transplant to prevent recurrent HPT. Enucleation and curettage of the brown tumors are

indicated if bone healing does not occur, despite treatment of the parathyroid glands. The surgical removal of brown tumors is sometimes necessary because of the functional problems that these tumors create for the patients. Pinto *et al*.[3] advocate that in aggressive lesions, conservative therapies are reported in the literature, such as the use of intralesional corticosteroids and calcitonin, requiring only a possible osteoplasty after the recalcification of the osteolytic sites.

Large lesions may resolve very slowly or may regress with resultant facial asymmetry. Surgery in the form of excision of the brown tumor and recontouring of the bone should, therefore, be done in such cases.[3] The brown tumor of the maxilla resulted in a residual deformity after its resolution. The patient refused the suggestion of osteoplasty to improve the contour of the palate.

CONCLUSION

The result obtained in this study, as well as other reports has encouraged us to follow the brown tumors associated with tertiary HPT in expectations for resolution of the lesions after normalization of PTH levels. Surgical removal of lesions would be reserved for cases with functional or esthetic problems and for cases when the bone healing does not occur, despite treatment of the parathyroid glands.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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