Highly Aggressive Brown Tumor in the Jaw Associated with Tertiary Hyperparathyroidism

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Abstract

The purpose of this paper is to describe the case of a 12-year-old patient with end-stage chronic renal failure. The patient presented with an osteolytic lesion in the mandible with expansion of the buccal, lingual, and occlusal cortical bone, as well as dislocation of the teeth in the area. The calcium, creatinine, and parathormone (PTH) contents of the blood were elevated. A histopathological examination of the jaw lesion revealed the presence of a brown tumor lesion, which is associated with hyperparathyroidism (HPT). An adenoma was found in the upper left parathyroid, a finding compatible with the diagnosis of tertiary HPT. In spite of the continuous ambulatory peritoneal dialysis instituted, the osteolytic lesion kept on growing. A conservative treatment employing an association of intralesional corticosteroid and salmon calcitonin (inhaled) was carried out. After 14 months of therapy, a reduction in size and complete calcification of the lesion were achieved. Aesthetic osteoplasty of the jaw was then performed. (Pediatr Dent 2006;28:543-546)

KEYWORDS: GIANT CELL GRANULOMA, HYPERPARATHYROIDISM, JAW, CALCITONIN, CORTICOSTEROID

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The central giant cell granuloma (CGCG) is a proliferative non-neoplastic lesion that represents less than 7% of all benign jaw lesions.[1] This condition exhibits variable aggressiveness and affects mainly children and young adults, with predominance in women.[2]

Brown tumors are lesions histologically identical to CGCG. They develop, however, as a consequence of undiagnosed or untreated hyperparathyroidism (HPT). HPT may be primary, secondary, or tertiary. In its primary form, hyperplasia or parathyroid neoplasia are responsible for the disease. Secondary HPT occurs mainly as a result of chronic renal insufficiency. The tertiary form is the least common one, attacking patients with secondary HPT who develop autonomous proliferation of parathyroid glands and excessive production of PTH.[3,4] Brown tumors are described in 1.5% to 1.7% of the patients with chronic renal insufficiency.[5] Its treatment is initially based on solving the underlying endocrine abnormality.

In the 1990s, conservative therapeutic approaches of intralesional corticosteroid or calcitonin were introduced to treat CGCG, especially in children or adult patients who presented relapses.[6-8]

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This study's purpose was to describe the case of a preteen patient with an aggressive brown tumor in the mandible associated with tertiary hyperparathyroidism and treated with an association of calcitonin and corticosteroid.

Case description

A 12-year-old female patient diagnosed with end-stage chronic renal failure was sent to the Stomatology Service (São Lucas Hospital, affiliated to Pontifícia Universidade Católica do Rio Grande do Sul in Porto Alegre city, Brazil) for the evaluation of an asymptomatic buccal lesion 3 months into evolution. Facial asymmetry with increased volume in the right posterior jaw area was evident (Figure 1). At the oral exam, an expanding lesion with firm consistency was observed involving the permanent mandibular right premolars, first molar, and second molar (Figure 2). The panoramic radiograph showed a large osteo-

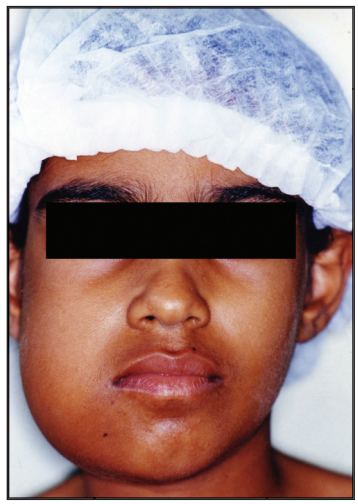

Figure 1. Facial asymetry with increased volume in the right jaw

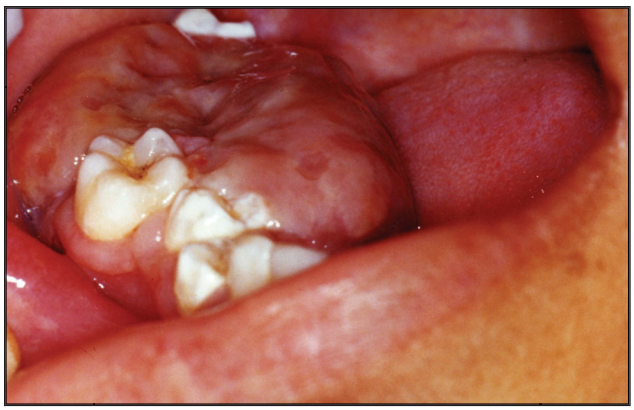

Figure 2. Oral aspect: expanding lesion involving permanent mandibular right premolars, 1st and 2nd molars.

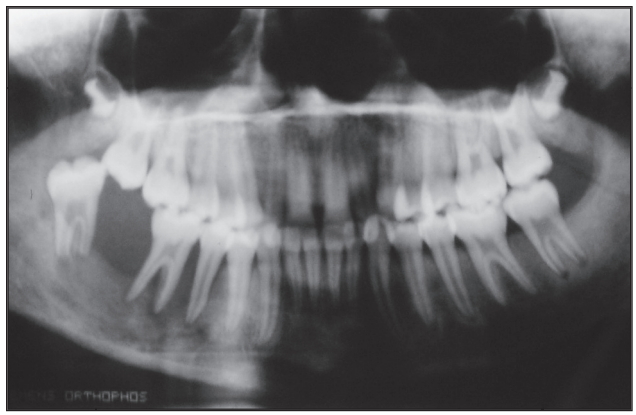

Figure 3. Osteolytic lesion with irregular limits in posterior section of the jaw.

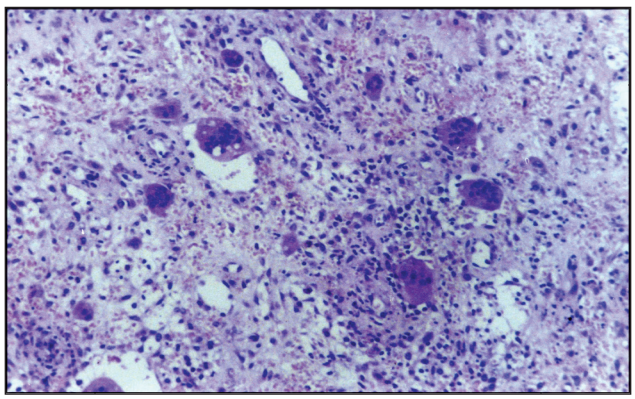

Figure 4. Fibrovascular connective tissue containing giant cells and hemorrhagic areas (HE, 400X).

lytic lesion with irregular contour, located in the right posterior section of the mandible (Figure 3).

Besides the anemia, the patient had elevated blood concentrations of creatinine (4.3mg/dl), PTH (1080 pg/ml), calcium (16 mg/dl) and alkaline phosphatase (8.2 IU/l). After confirmation of HPT, it was suggested that the jaw lesion was actually a brown tumor.

Biopsy samples were obtained from different lesion sites. The histopathological examination confirmed the presence of highly cellularized fibrovascular connective tissue containing numerous multinucleate giant cells and hemorrhagic areas with the formation of hemosiderin deposits (Figure 4). The histological findings were consistent with the diagnosis of brown tumor.

Other radiographic examinations revealed the presence of osteolytic lesions with a regular contour in the left humerus, pelvis, and right femur.

The creatinine blood contents gradually stabilized with the institution of a continuous ambulatory peritoneal dialysis, although the PTH concentrations remained elevated. Cervical area ultrasound and scintillography suggested parathyroid glands hyperplasia. Parathyroidectomy of the upper left gland was performed, and the histological findings were compatible with parathyroid adenoma, characterizing tertiary hyperparathyroidism. The PTH concentration was then gradually reduced to 361 pg/ml after 3 months and to 131 pg/ml after 7 months.

Despite the control of PTH concentrations and due to the extension of the jaw lesion, a treatment combining inhaled salmon calcitonin (100 UI/ml) and intralesional corticosteroid was initiated. A solution containing equal parts of acetonide triamcinolone (20 mg/ml) and lidocaine (0.5%) was injected into the lesion on a weekly basis via disposable syringe with a needle 0.5 mm in diameter. Multiple injections were performed to cover the whole extension of the lesion. Approximately 1 ml of solution per radiotranslucent cm^2 on the panoramic radiograph was applied after each session. After 12 weeks, the penetration of the needle into the overlapping corticals of the osteolytic areas was no longer possible due to the increase in local resistance, which determined the end of the sessions. The patient continued using the salmon calcitonin nasal spray for another 12 weeks. The radiographic controls showed gradual reduction in the lesion's size and an increase in the area's radio-opacity. This clinical and radiographic aspect was confirmed by CT scan.

Considering that the patient's systemic conditions had improved with weight and height gain, a renal transplant was performed. The patient started using systemic corticosteroid as a transplant protocol and continued using inhaled calcitonin for another 6 months. After that period, the lesion presented total calcification. Aesthetic jaw osteoplasty was performed for contour overlay resection. The mandibular right premolars and molars were extracted. The other bone lesions found in the humerus, pelvis, and femur were radiographically controlled and also presented signs of calcification. The patient was followed for 3 years, and no indication of relapse was observed (Figure 5).

Discussion

Brown tumors are uncommon lesions whose name derives from its reddish-brown coloration, resulting from hemorrhages and intralesional hemosiderin deposits.[9] Contrary to idiopathic CGCGs, brown tumors are associated with HPT.

In patients with renal insufficiency, PTH concentrations become elevated as an exaggerated physiological response to hypocalcaemia, hyperphosphataemia, and vitamin D deficiency. Under chronic stimulation, the parathyroid glands increase in size and may occasionally develop neoplasia and autonomous hyper secretion of PTH, as is described in the present case.[10] Milas and Weber[10] recommend subtotal parathyroidectomy in patients with secondary or tertiary HPT. In this study, the surgical excision of the upper left parathyroid, which presented an adenoma, was sufficient to normalize the PTH blood concentrations.

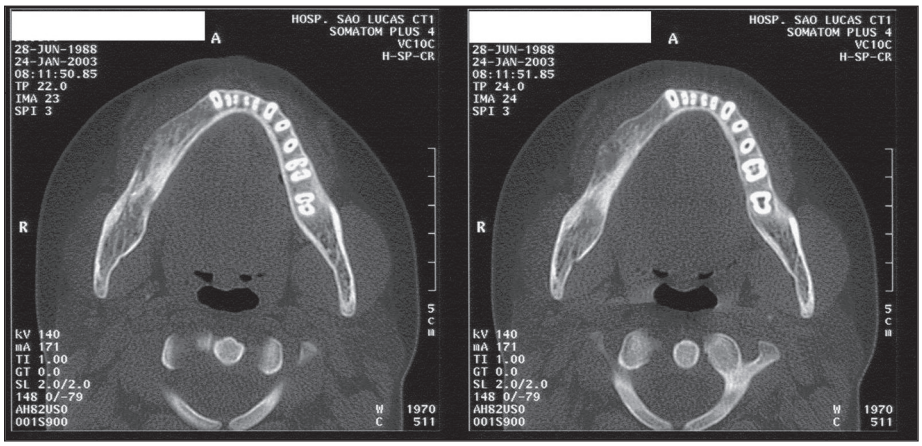

Figure 5. Computerized tomography: calcification in jaw on area of the lesion.

The diagnosis of a brown tumor as a first indication of HPT is rare.[11] In the present case, the patient presented multiple bone lesions which were part of the severe renal osteodystrophy picture. Gomez et al[12] reported a similar case in which the bone lesions were treated only through the normalization of calcium and PTH levels via a subtotal parathyroidectomy. Brown tumor management depends on the severity of the lesions present. As previously described in this study, some brown tumors may exhibit: (1) aggressive clinical behavior with rapid growth; (2) expansion of cortical bones; and (3) dental dislocation. The jaw lesion continued growing even after the beginning of the dialysis. Therefore, drug-based therapy was the option taken.

Throndson et al[4] performed a surgical resection of a large brown tumor in the jaw of a patient with secondary hyperparathyroidism. Other surgical treatments such as enucleation and curettage have also been described. Non-surgical treatments employing calcitonin or intralesional injection, however, have been showing excellent results in the treatment of CGCG, especially when associated to HPT.[6-8,13-16] This study describes the first case in which both drugs were administered for the treatment of a brown tumor.

The intralesional corticosteroid promotes the inhibition of osteoclast-type giant cells present in CGCG. Abdo et al[8] and Sezer et al[15] successfully treated patients presenting jaw CGCG via intralesional injection of corticosteroids. The authors suggest that the nonsurgical treatment should be the first choice for the treatment of this lesion, particularly in the case of children. According to the authors, this therapy: (1) is simple; (2) is low-cost; and (3) allows for the preservation of anatomical structures.

Calcitonin inhibits bone reabsorption by inhibiting the local mediators of the calcium metabolism in the lesion, thus acting in an antagonistic way to PTH. On the other hand, its long-term usage does not alter the biochemical parameters in the bone tissue metabolism, such as the calcium and alkaline phosphatase concentrations in serum.[7]

The optimal dosage and period of the treatment with calcitonin and corticosteroid for CGCG are still under study. In the case reported, the employed therapeutic approach made it possible to preserve the anatomical structures and avoid extensive facial deformity. The patient has been under control for 3 years, without clinical or radiographic signs of relapse.

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Abstract of the Scientific Literature

Oral Manifestations and Coeliac Disease

Coeliac disease is characterized by malabsorption resulting from inappropriate T-cell-mediated immune response against ingested food in genetically predisposed people. The objective of this study was to compare the prevalence of enamel defects and recurrent aphthous stomatitis (RAS) between coeliac disease patients and healthy controls. Seventy-two coeliac patients were divided into 2 subgroups based on dentition. One hundred sixty-two healthy patients were used as controls. Based on oral examination, defects of the dental enamel were found in 14 of 70 coeliac patients and 9 of 159 controls. Thirteen of 53 coeliac patients with mixed or permanent dentition and one of 17 coeliac controls children with deciduous dentition had enamel defects. Overall, 9 of 145 controls with mixed or permanent dentition had dental enamel defects, while no control with deciduous dentition had enamel defects. Therefore, enamel defects occurred more frequently in coeliac patients (P<.001). There was no statistical difference, however, between coeliac patients and controls subjects having aphthous ulcers. Though the cause of enamel defects associated with coeliac disease is uncertain, the authors conclude that the disease does predispose patients to enamel defects. Furthermore, for at least one third of the coeliac subjects, the presence of gluten in the diet influenced the recurrence of oral ulcers.

Comments: The findings from this study suggest that coeliac patients are at a higher risk of having enamel defects when compared to healthy controls. Furthermore, the prevalence of recurrent aphthous stomatitis between the 2 groups was not statistically significant. Interestingly, a gluten-free diet was beneficial for many coeliac patients suffering from RAS. **THB**

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