RADIOLOGICAL AND EPIDEMIOLOGICAL ASPECTS OF CENTRAL GIANT CELL GRANULOMA*

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Abstract **OBJECTIVE: The present study was aimed at evaluating main radiological and epidemiological aspects of giant cell lesions (central giant cell granuloma and brown tumors of hyperparathyroidism). MATERIALS AND METHODS: The sample consisted of 26 giant cell lesions diagnosed in 22 patients divided into two groups, one of them including 17 patients who were not affected by hyperparathyroidism (group A) and another including five patients with such a disorder (group B). RESULTS: Prevalence was higher in female patients (72.7%). Most frequently, lesions occurred more in the second decade of life (mean age, 27 years). The mandible arc was most frequently involved (61.5%). Radiographically, 57.7% of lesions were multilocular and 42.3% were unilocular with defined limits. All of the 26 lesions caused expansion of bone, 15.4% radicular resorption, 50% dental displacement, and 11.5% produced pain. In the mandible 18.7% of the lesions crossed the midline. Group A showed 66.7% of lesions in the mandible and group B showed an even distribution of lesions between arches. In group A 66.7% of lesions were multilocular, and 33.3% unilocular; in group B 62.5% were unilocular, and 37.5% multilocular. CONCLUSION: Giant cells lesions may present themselves with a wide spectrum, from small, slow-growing unilocular lesions to extensive multilocular lesions. They present features of benignity, though some lesions may demonstrate a locally aggressive behavior.**
Keywords: Central giant cell granuloma; Radiological aspects; Brown tumor; Hyperparathyroidism.

Resumo *Aspectos radiológicos e epidemiológicos do granuloma central de células gigantes.*
OBJETIVO: Este estudo teve como objetivo avaliar os principais aspectos radiográficos e epidemiológicos das lesões de células gigantes (granulomas centrais de células gigantes e tumores marrons do hiperparatireoidismo). MATERIAIS E MÉTODOS: A amostra consistiu de 26 lesões de células gigantes diagnosticadas em 22 pacientes divididos em dois grupos, um deles composto por 17 pacientes que não tinham hiperparatireoidismo (grupo A) e o outro formado por cinco pacientes portadores de tal distúrbio (grupo B). RESULTADOS: O sexo feminino (72,7%) foi o mais acometido. As lesões ocorreram mais freqüentemente na segunda década de vida, com média de idade de 27 anos. A mandíbula (61,5%) foi o arco mais envolvido. Radiograficamente, 57,7% das lesões eram multiloculares e 42,3% eram uniloculares com limites definidos. Todas as 26 lesões provocaram expansão óssea, 15,4% produziram reabsorção radicular, 50% causaram deslocamento dentário e 11,5% produziram dor. Na mandíbula, 18,7% das lesões cruzavam a linha média. O grupo A apresentou 66,7% das lesões na mandíbula e o grupo B mostrou igualdade na distribuição das lesões entre os arcos. O grupo A apresentou 66,7% das lesões multiloculares e 33,3%, uniloculares. O grupo B apresentou 62,5% das lesões uniloculares e 37,5%, multiloculares. CONCLUSÃO: As lesões de células gigantes podem manifestar-se, radiograficamente, com um amplo espectro, desde pequenas lesões uniloculares de crescimento lento até extensas lesões multiloculares. Elas apresentam características de benignidade, embora algumas lesões possam demonstrar um comportamento localmente agressivo.
Unitermos: Granuloma central de células gigantes; Aspectos radiológicos; Tumor marrom; Hiperparatireoidismo.

INTRODUCTION

Many maxillary lesions present similar histological patterns, especially in the presence of giant cells. This group of lesions includes central giant cell granuloma (CGCG), giant cell tumor of long bones, aneurysmatic bone cyst, brown tumor of hyperparathyroidism and the early stages of cherubism. Most of these diseases can be differentiated by the combination of clinical and radiological findings, but differentiation between CGCG and brown tumors of hyperparathyroidism only can be made by means of laboratory tests[1–3].

CGCG is a non-neoplastic lesion of the jaws[4] that can present different radiological features, from small, unilocular radiolucent lesions to extensive multilocular radiolucent areas. Generally, the lesions are well circumscribed, many times presenting with festooned borders. They may present

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a cortical radiopaque halo and cause dental displacement or resorption. Such features are non-specific for confirming the diagnosis, and may be confused with other pathological lesions whose treatment is different[5–9].

The present study was aimed at evaluating epidemiological and radiological characteristics of 26 giant cell lesions, including CGCG and brown tumors of hyperparathyroidism.

MATERIALS AND METHODS

Epidemiological and radiological aspects of 26 cases of giant cell lesions in 22 patients of the Service of Oral and Maxillofacial Surgery at Hospital Universitário Pedro Ernesto – Universidade do Estado do Rio de Janeiro, were retrospectively evaluated. In the period between January/1990 and June/2004, 2,252 biopsies of maxillary or mandibular lesions were performed, 26 of them (1.1%) corresponding to giant cell lesions. All of the diagnoses were histopathologically confirmed.

The patients were divided into two groups: group A, including patients with no evidence of hyperparathyroidism (n = 17), while group B included those with such a condition (n = 5). For differentiation between groups, the patients were submitted to evaluation of calcium, phosphorus, alkaline phosphatase and parathormone (PTH) serum levels.

As regards epidemiological aspects, the prevalence according to patients´ age and gender, number of lesions, besides the presence of symptoms, was considered.

Regarding radiological aspects, CT studies, extra-oral radiographs (panoramic, posteroanterior view, Water's view), and intraoral radiographs (periapical and occlusal types). Radiographic images were classified according to the presence and number of loculations into unilocular radiolucent or multilocular radiolucent. Also, dental displacement, dental root resorption and cortical bone expansion were evaluated.

RESULTS

Age, gender and symptoms

Prevalence was higher in women (16 patients; 72.7%). In a comparison between groups, 12 patients of group A were women, and five were men. On the other hand, in group B, four patients were women, and one was men. The patients' ages ranged between five and 62 years, with higher incidence in the second decade of life. Mean age was 27 years. The age range of patients with hyperparathyroidism was 22–40 years (mean, 29.6 years). Only three patients (11.5%) presented with painful symptoms.

Localization

Of 26 diagnosed lesions, 16 (61.5%) affected the mandible, and 10 (38.5%) were associated with the maxilla. Of 16 giant cell lesions localized in the mandible, 12 (75%) were found in the mandibular corpus, three (18.7%) in the anterior region, and one (6.3%) in the mandibular ramus. In the maxilla, of 10 giant cell lesions, six (60%) were in the anterior region and four (40%) in the posterior region.

Radiological features

All of the 26 giant cell lesions evaluated in the present study showed up radiographically as a radiolucent image of well-delineated contour. Eleven lesions (42.3%) were unilocular (Figure 1), and 15 (57.7%), multilocular (Figure 2). The mandible presented nine (56.3%) multilocular lesions, and seven (43.7%) unilocular lesions. The maxilla presented six (60%) multilocular lesions, and four (40%) unilocular lesions) (Table 1).

As regards the distribution of images among regions in the maxilla, three (50%) unilocular, and three (50%) multilocular lesions were found in the anterior region, and three (75%) multilocular lesions and only one (25%) unilocular, in the posterior region of the maxilla.

The analysis of the radiographic images distribution between regions of the mandible showed seven (58.3%) multilocular, and five (41.7%) unilocular lesions in the mandibular corpus, and two (66.7%) multilocular lesions and one (33.3%) unilocular in the anterior region of the mandible. The only giant cell lesion in the mandibular ramus presented as a radiolucent multilocular image.

At the level of the mandible, three (18.7%) of the 16 lesions crossed the midline.

All of the lesions caused expansion of at least one cortical bone (Figure 3), 13 (50%) were associated with dental displacement (Figure 4), and four (15.4%) produced dental roots resorption (Figure 5). The evaluation of the involved cortical bone, 13 (50%) of the 26 giant cell lesions resulted in expansion of the internal cortical bone, and 24 (92.3%) in expansion of the external cortical bone.

DISCUSSION

The mandible and the maxilla may be affected by non-neoplastic processes and bone tumors of several lineages[10–14].

Very few bone lesions have caused more controversy than the CGCG, the giant cell bone tumor of long bone and the relationship between them. Before the fifties, the diagnosis of central giant cell tumor was usual for any bone lesion presenting giant cells[4,7,15,16]. Presently, the majority of authors take the biological behavior and histological patterns into consideration in the differentiation between these lesions[1,4,15,17,18]. Giant cell tumors of long bones present larger giant cells with more nuclei and more evenly distributed. Additionally, they present a high rate of recidivation after curettage, besides malignant alterations in about 10% of cases[7,15,17].

The CGCG affects children and young adults, with more than 60% of cases occurring before 30 years of age[7,9]. The majority of CGCGs is found in women[2,7,9]. Our

Table 1 Distribution of radiographic images in the maxillas.

	Mandible		Maxilla		Total	
Lesion	N	%	N	%	N	%
Multilocular	9	56.3%	6	60%	15	57.7%
Unilocular	7	43.7%	4	40%	11	42.3%
Total	16	100%	10	100%	26	100%

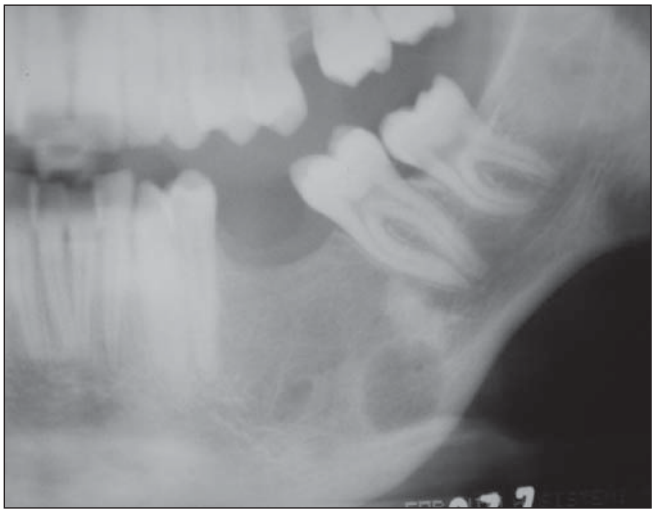

Figure 1. Detail of a panoramic radiograph showing CGCG in the left mandibular corpus, as an unilocular, radiolucent image with well-defined limits.

Figure 2. Computed tomography showing CGCG as a multilocular image in the left anterior region of the maxilla.

Figure 3. Occlusal radiograph of mandible demonstrating CGCG as cause of expansion of internal and external cortical bones.

Figure 4. Brown tumor of hyperparathyroidism (group B) in right mandibular corpus, showing up as a well-delimited, unilocular radiolucent image, causing displacement of the first right lower premolar.

casuistic demonstrated prevalence in female patients in 72.7% of cases. Ages ranged between five and 62 years, with a higher incidence in the second decade of life, and mean age of 27 years, very similar to the literature[1,6,19–21].

The CGCG is considered as an uncommon lesion of maxillas[7,22,23]. Minić & Stajčić[19] have found 31 cases of CGCG (0.1%) in 29,134 biopsies performed in the period between 1970 and 1990. Waldron & Shafer[8] diagnosed 36 cases of CGCG (0.16%) in 22,000 specimens received by their laboratory. In the present study, 26 giant cell lesions (1.1%) were found in 2,252 biopsies performed in the period between Januray/1990 and June/2004. Eight (0.3%) of these 26 lesions were associated with patients affected by hyperparathyroidism (brown tumor) and 18 (0.8%), not.

Mandible is more affected than maxilla, with the majority of lesions being found in the anterior region. The present study demonstrated that the mandible presented 61.5% of lesions diagnosed, and the maxilla, 38.5%, a result similar to the results presented in the literature[1,2,9,18–20,24].

Bataineh et al.[20] reported that the molar/ramus (37%) is the most affected region, followed by the incisive/canine teeth region)28%), premolar/molar teeth region (22%), and premolar teeth region (11%). Cohen & Hertzanu[5] have reported the mandibular ramus (31%) as the most affected region, followed by the mandibular corpus (25%) and anterior (25%) regions. Our study demonstrated that of 16 mandibular lesions, 12 (74%) were in the region of the corpus, three (18.7%) were in the region of the symphysis, and one in the mandibular ramus (6.3%). Considering the corpus and ramus regions described as posterior in our sample, our results are similar to those reported in the literature[6,21,24,25].

Figure 5. CGCG in left mandibular corpus showing up as a well-delimited multilocular radiolucent image, and causing second left lower molar roots resorption.

Cohen & Hertzanu[5], in a sample of 16 cases of CGCG, reported three (18.7%) lesions in the maxilla, with two of them (66.4%) in the posterior region, and one (33.3%) in the anterior region, a result similar to the one reported by Sidhu et al.[25]. On the other hand, in our study, of the 10 maxillary lesions (38.5%), six (60%) were in the anterior region, and four (40%), in the posterior region, a prevalence similar to the ones reported by other authors[24,26].

Horner[24], Bodner & Bar-Ziv[22], and Cohen & Hertzanu[5] have reported that all of the lesions evaluated were radiolucent, with respectively 77%, 60% and 56,2% presenting well-defined limits. On the other hand, Stavropoulos & Katz[26] have studied 20 cases and observed that 55% of the lesions were radiolucent, 45% presented a mixed aspect, and 65% presented well-defined limits. Kaffe et al.[6] have observed 87.5% of studied CGCG as radiolucent images, 10% with mixed aspect, and 2.5% radiopaque. Although the literature demonstrates varied results, the present study demonstrated that the lesions presented radiographically as radiolucent images and with well-defined limits.

Horner[24] and Austin et al.[1] have found, respectively, 85% and 97.1% of unilocular lesions. We observed that 15 (57.7%) of the 26 giant cell lesions of our sample produced multilocular images, and 11 (42.3%), unilocular images, a result similar to those of some authors[6,19,21]. In the present study, nine (56.3%) of the 16 giant cell lesions in the mandible presented a multilocular image, and seven (43.7%), unilocular. In the maxilla, six lesions (60%) were multilocular, and four (40%), unilocular.

In the case of unilocular lesions, they may look like periapical lesions, such as periapical cysts and granulomas[7,27].

The literature highlights the possibility of radicular resorption as a result of CGCG[1,7,9,24]. Horner[24], Kaffe et al.[6] and Stavropoulos & Katz[26] have found, respectively, 7.7%, 12% and 37% of radicular resorption. Our sample showed dental roots resorption in 15.4% of cases.

The majority of CGCGs are asymptomatic, and usually are discovered during routine radiological examinations or because of the asymmetry caused by cortical bone expansion[2,7,9,24,25]. In our sample, all of the 26 lesions caused expansion of at least one cortical bone, a result similar to the results presented in the literature [5,6,19,24,25].

CGCGs present a tendency to cross the midline, principally when the lesion is in the mandible[7,9,21,28]. In the present study, we observed that 18.7% of lesions crossed the midline, a result similar to those reported by some authors[5,20,25].

Goaz & White[9] have pointed out that CGCG affecting the maxillary sinus may expand or erode bone walls, and are confused with tumors or mucoceles. The literature[5,9,22] advises the utilization of computed tomography in these cases, aiming at evaluate more accurately the limits and the extension of the lesion through adjacent tissues.

Painful symptoms are usual in cases de CGCG[6,9,21,24]. Austin et al.[1] and Bodner & Bar-Ziv[22] have observed that, respectively 25% and 30% of their cases presented pain. In our study, we observed that 11.5% of cases presented painful symptoms.

Dental displacement is a sign frequently associated with CGCG[2,5,21,22,25]. Our sample demonstrated that 50% of cases produced adjacent teeth displacement, a result similar to those reported by some authors[6,24,26].

Clinical, radiological and histological features of CGCG are identical to those found in brown tumors associated with hyperparathyroidism. These later may generate uni- or multilocular radiolucent images, showing up in approximately 10% of patients with hyperparathyroidism. The differentiation between these lesions depends on laboratory tests for investigating serum levels of calcium, phosphorus and alkaline phosphatase which, in cases of hyperparathyroidism, present alterations[3,9].

Mandible and/or maxilla are sites where giant cell lesions develop in cases of hyperparathyroidism, many times as the first clinical manifestation of this disorder[28,29]. Our sample demonstrated that 80% of patients with hyperparathyroidism were asymptomatic. Regezi[2] reports that hyperparathyroidism should be considered whenever facial bones are involved, in cases of recurrence, and in cases of multiple lesions.

In the five patients affected by hyperparathyroidism, eight lesions were diagnosed. Three patients presented only one lesion. This demonstrates that not always will the patient with hyperparathyroidism present multiple lesions, and a patient may rarely present more than one lesion without hyperparathyroidism[28,29].

Neville et al.[7] have reported that hyperparathyroidism affects women about two to four times more than men. Our sample demonstrated that four of five patients with hyperparathyroidism were women. The ages of patients with hyperparathyroidism ranged between 22 and 40 years (mean, 29.6 years).

Evaluating the most affected maxilla in each group, we have found that 66.7% of lesions in group A were in the mandible. On

the other hand, in group B, we have observed an even distribution — 50% for each arch.

Based on the present data, we conclude that the knowledge about the variation of radiological images of CGCGs and brown tumors associated with hyperparathyroidism is extremely important. In case of patients with diagnosis of CGCG, the possible presence of parathyroid disorders should not be disregarded.

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