

Diagnosis of central giant cell granuloma: a rare case in the mandibular condyle

Diagnóstico de granuloma central de células gigantes: um caso raro no côndilo mandibular

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ABSTRACT

The central giant cell granuloma is an uncommon benign lesion that occurs almost exclusively within the jawbones. This article presents a rare case report of a 15 year-old male patient diagnosed with the pathology after the surgical excision of a lytic lesion of the right condyle. Formalin-fixed paraffin-embedded tissue specimens were stained with histological (hematoxylin and eosin) and immunohistochemical techniques (CD68 and Ki-67). Histologically the lesion was made up of a fibrillar connective tissue stroma with oval and spindle-shaped mononuclear cells, abundant multinuclear giant cells, small capillaries, foci of hemorrhage, and presence of osteoid matrix. There was strong immunoreactivity in giant cells for CD68, with only some of the mononuclear cells exhibiting reactivity for Ki-67. This lesion in the mandibular condyle presents a similar biological behavior to other sites of the gnathic skeleton, therefore requiring the same treatment. Retromandibular incision and resection with margins were chosen for provide the lowest recurrence rates despite the high morbidity.

Keywords: Granuloma, Giant Cell; Mandibular Condyle; Immunohistochemistry

RESUMO

O granuloma de células gigantes central é uma lesão benigna incomum que ocorre quase sempre dentro de ossos gnáticos. Este artigo apresenta um relato de caso raro de um paciente do sexo masculino, 15 anos, diagnosticado com a patologia após a excisão cirúrgica de uma lesão lítica no côndilo direito. Espécimes teciduais fixadas em formol e incluídas em parafina foram coradas com técnicas histológica (hematoxilina e eosina) e imuno-histoquímicas (CD68 e Ki67). Histologicamente, a lesão foi composta por um tecido conjuntivo fibrilar estromal com células mononucleares ovais e fusiformes, abundantes células gigantes multinucleadas, pequenos capilares, focos de hemorragia e presença de matriz osteóide. Houve forte imunoreatividade em células gigantes para CD68, com poucas células mononucleares exibindo reatividade para Ki-67. Esta lesão no côndilo mandibular mostra um comportamento biológico similar a outros sítios do esqueleto gnático, também requerendo o mesmo tratamento. Incisão retromandibular e ressecção com margem foram escolhidas por proverem menores taxas de recorrência, apesar da alta morbidade.

Palavras-chave: Granuloma de Células Gigantes; Côndilo Mandibular; Imunoistoquímica

INTRODUCTION

The central giant cell granuloma (CGCG) was firstly reported to designate the site-dependent giant cell lesions of the jaws in 1953¹. It is an uncommon benign lesion that occurs almost exclusively within the jawbones and only sporadic cases occurring in the extragnathic skeleton (cranial and facial bones) have been reported². The prevalence of this lesion is the anterior mandibular region, in young adult with twice more cases in the female population. There

are wide variation in the clinical presentation and evolution, depending on the degree of aggressiveness.^{3,4} This tumor typically presents itself as a solitary and radiolucent lesion with rare multiple lesions⁵. The atypical condylar lesions are difficult to diagnose because many different lesions may present similar clinical and radiographic findings, emphasizing a detailed histopathology for definitive diagnosis^{3,6}. Histopathologically, it is an intraosseous lesion consisting of fibrous tissue with

multiple foci of hemorrhage, aggregations of multinuclear giant cells and occasionally trabeculae of bone tissue. Multinuclear giant cells, an obvious component of the lesion, seem to have an important role in the progression of bone destruction. The etiology is still uncertain and several theories are proposed as a possible repair process to a hemorrhage or inflammation intraosseous.^{3,7} Although the etiology and pathogenesis of CGCG remains unclear, its histological and clinical features as well as its clinical behavior have been studied in details and are now well established, differentiating the CGCG from other giant cell lesions. The choice of treatment and the recurrence rate are dependent on such factors as patient age, location, extent and clinical behavior of the lesion.³

This article reports the case of a young male patient who had diagnosed presence of CGCG in excised lytic lesion of his mandibular condyle. The biological behavior of the lesion and treatment options are discussed.

CASE REPORT

A 15-year-old white male patient was admitted to the emergency service of the Bonsucesso General Hospital (Rio de Janeiro, RJ, Brazil) reporting a painless swelling in the right preauricular area that had persisted during the past year. He had no history of otitis media or any previous experience of local trauma.

Physical examination revealed a mass with slight tenderness to palpation in the right preauricular area expanding toward the right temporomandibular joint region. The overlying skin appeared normal, and there were no palpable nodes in the neck. At the open mouth position, there was mandibular deviation to the right side. The intraoral examination was noncontributory and the patient was in good general health. (Figure 1)

Different imaginological analyses were performed to elucidate the correct diagnosis. Both panoramic radiograph (Figure 2A) and computed tomography scan (Figure 2B) showed a round-shaped lytic lesion inside the right condylar area causing marked bone destruction to medial bone cortical. Structures of the right temporomandibular joint and the right external auditory canal were not affected. A technetium bone scan (or bone scintigraphy) of the mandible showed no other lesions (Figure 2C). The

diagnosis hypotheses were: giant cell granuloma, eosinophilic granuloma, condylar lesions and ganglion cyst in the temporomandibular joint.



Figure 1: Initial clinical aspect, with mild augmentation of the right preauricular area.

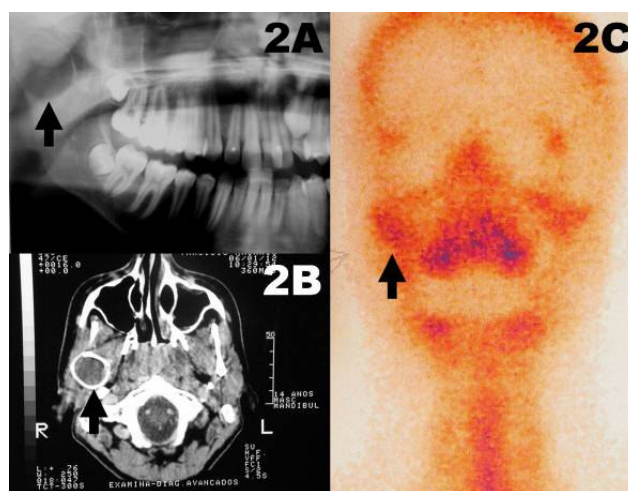


Figure 2: Imaginological analysis. Panoramic radiograph (A), computed tomography (B) and bone scintigraphy (C) indicating the presence of a lytic lesion inside the right mandibular condyle (black arrows).

Under general anesthesia, the lesion was exposed through a retromandibular approach, and an unencapsulated granulation tissue mass could be observed. A right condylectomy (remotion of the condilar process and a piece of mandibular ramus) was then performed. A surgical specimen with at least 35mm diameter was obtained. Postoperative healing was uneventful.

Biopsied tissue specimens were fixed in 10% buffered formalin, processed (dehydration in graded ethanol serial washings, clarification in xylol, embedding and including in paraffin), and microtomed sections (4µm thickness) of these samples were deposited upon glass slides for microscopic examination. For the descriptive histological analysis, slides with tissue samples were stained with the routine hematoxylin and eosin method to general lesion identification carried out by a trained examiner pathologist. For the immunohistochemical analysis, paraffin cuts mounted on electrostatically charged glass slides (Colorfrost/Plus, Fisher Scientific, USA) were immunostained with mouse antihuman macrophage monoclonal anti-CD68 antibody (clone PG-M1, dilution 1:100, Dako, USA), using the standard streptavidin-biotin-peroxidase complex method (LSAB System Universal Kit, Dako, USA), 0.3% diaminobenzidine solution (Dako, USA) and counterstained with Harris hematoxylin (Merck, Brazil) in the investigation the presence of macrophages or multinuclear giant cells in the abnormal tissue; and other tissue samples mounted on poly-L-lysine coated glass slides were immunostained with mouse antihuman monoclonal anti-Ki-67 antibody (clone MIB-1, dilution 1:1000, Dako, USA) using an automated immunostainer (i6000 Automated Staining System, Model 1.0, Bio-Genex, USA), to investigate the proliferative behavior of the condyle lesion.

Histological analysis demonstrated in the external tissue region of the biopsy the normal composition of a health young mandibular condyle: proliferative layer compound by mesenchymal stem cells in mitogenic activity, thick cartilaginous layer and subcondral trabecular bone (Figure 3A). Well delimited by bone walls, the internal tissue region of the biopsy was made up of numerous and dispersed multinuclear giant cells in the connective tissue background. These giant cells varied in shape and size.

Foci of hemorrhage were evident (Figure 3B). The stroma was compounded by a fibrillar connective tissue with oval and spindle-shaped mononuclear cells and small capillaries, and signs of hemosiderin (Figure 3C). Amorphous osteoid matrix or ectopic bone was the less frequently seen feature (Figure 3D). All these findings did help in the diagnosis of the lesion as central giant cells granuloma.

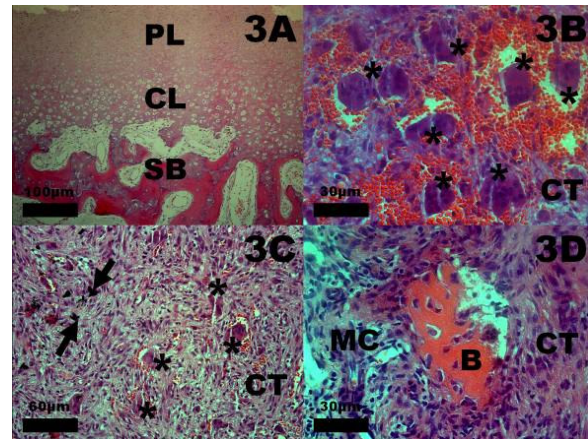


Figure 3: Histological analysis of the right mandibular condyle. External tissue region: proliferative layer (PL), cartilaginous layer (CL) and subcondral bone (SB) (A). Internal tissue region: abundant multinuclear giant cells (asterisks), hemorrhagic areas, connective tissue (CT) (B-C), hemosiderin signs (arrows) (C), mesenchymal cells (MC) and amorphous osteoid matrix or ectopic bone (B) (D).

Immunohistochemical analysis confirmed with strong cytoplasmatic positivity for CD68 the presence of giant cells in this lesion, with only some mononuclear cells exhibiting moderate reactivity (Figure 4A). Some Ki-67-positive nuclei were seen almost exclusively in the mononuclear cells, without reactivity in giant cells, in this way indicating low mitotic activity in the lesion (Figure 4B).

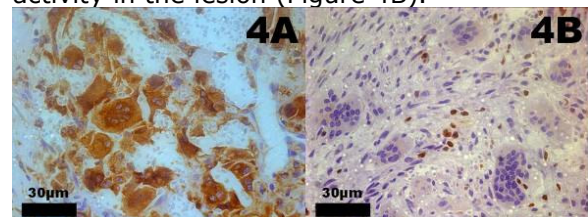


Figure 4: Immunohistochemical analysis of the right mandibular condyle. Strong presence of CD68-positive multinuclear giant cells (A) and low reactivity of Ki67-positive mononuclear cells (B).

At 36-months follow-up there was no sign of recurrence of the lesion and the patient wait soonly the bone maturation or end of growing period for definite installation of the right temporomandibular joint prosthesis and his complete functional rehabilitation.

DISCUSSION

Giant cells are the most prominent histopathological feature of central giant cell granuloma so many investigative studies has been directed to the role of the originary mononuclear cells in its pathogenesis⁸. The mononuclear cells can form osteoclast-like giant cells *in vitro* by their fusion, event associated clinically to the development of osteolytic lesions⁹. Besides osteoclasts, the mononuclear cells can differentiate themselves in macrophages which play a critical role in the course of multinuclear giant cells in connective tissue during inflammatory and reparative processes, due to their abundance and to their activation status by overexpression of CD68^{7,10}, proinflammatory cytokines¹¹, matrix-degrading enzymes¹² and angiogenic factors (VEGF, FGF-2, TGF- β , PDGF)^{13,14} which stimulate the proliferation of endothelial cells forming new blood vessels and fibroblasts increasing the collagen matrix synthesis¹⁵.

This biological behavior can explain the exuberant vascularization and stromal tissue presents in the lesion. Therefore in the present study, the overexpression of CD68 might be associated specially to bone resorption. The expression of Ki-67, a nuclear antigen expressed in all active phases of the cell cycle (except G0 phase)⁹, in our analysis can suggest a mild increase in the tissue mitotic activity. The slow growing rate can corroborate this result as a favorable indicator of the benign clinical course of this lesion.

Intralesional applications of medicamentous therapies are widely used to decrease giant cell granulomas and inhibit osteoclastogenesis using respectively steroids¹⁶⁻¹⁸ and calcitonin^{19,20} or still to promote initial antiangiogenic effect and direct bone repair using interferon²¹, but all these therapies demonstrated heterogeneous or delayed results. In the present case report, these procedures were not conducted due to the unappropriated application in a central lesion and the still doubtful effectiveness of the treatment.

Radiotherapy is contraindicated as the treatment of CGCG because of the potential for sarcomatous transformation that has been reported²². Surgery is considered the traditional treatment and it is still the most accepted one, however in the literature not all authors agree on the type of procedure which should be performed²³. Excision via curettage has been associated with a low rate of recurrence in small lesions²⁴. In case of recurrences, curettage associated to peripheral ostectomy and bone resection should be performed^{25,26}. Some authors proposed the creation of safety margins by microdrilling of the surgical field with a diamond bur²⁷. In general destructive surgery (en bloc surgical resection with 5mm margins) seems to be the safest option for the control of recurrences but it may result in high morbidity and facial deformities which are obviously of great concern. There are some case reports that describe the use of this technique followed by favorable reconstruction with iliac crest graft^{28,29}. In the present patient, a retromandibular incision and en bloc resection with margins was chosen based in the lesion size and to decrease the recurrence risk. If soft tissues and periosteum are preserved, and only the bony component is excised, then it is possible to reconstruct the surgical defect with autogenous bone grafts. By doing this, bone continuity is maintained and the future rehabilitation of the present patient can be performed satisfactorily.

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Recebido em 29/08/2010
 Reformulado em 12/12/2010
 Aprovado em 13/12/2010