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UNIVERSIDADE ESTADUAL PAULISTA "JÚLIO DE MESQUITA FILHO"
Instituto de Ciência e Tecnologia
Campus de São José dos Campos

CASE REPORT

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Non-familial Cherubism – Report of a case

Querubim não familiar - Relatório de caso

Cleverson PATUSSI[1], Laurindo Moacir SASSI[1], Regiane Benez BIXOFIX[1], William Phillip Pereira da SILVA[1], Juliana Lucena SHUSSEL[1]

1 – Department of Oral and Maxillofacial Surgery – Erasto Gaertner Hospital – Curitiba – PR – Brazil.

ABSTRACT

Introduction: The Cherubism is a rare disease that affects the middle and lower third of the face in individuals at the time of childhood. It is a rare hereditary benign bone disease with an autosomal dominant inheritance. The familial distribution may affect different generations and isolated non-familial cases have also been reported in literature. Lesions appear as cystic multilocular radiolucencies, histologically, they resemble central giant cell granluloma and hyperparathyroidism brown tumor with numerous randomly distributed multinucleated giant cells and vascular spaces within a fibrous connective tissue stroma. **Objective:** The aim of this study is to report the importance of the diagnosis of this pathology and the variety of treatments available in the literature, thus guiding to an individualized treatment. **Case Report:** Caucasian 8 years-old female, in good general condition, was referred to Service of Oral and Maxillofacial Surgery of Erasto Gaertner Hospital (EGH), Curitiba – PR, Brazil, complaining of bilateral swelling of the maxilla and mandible since 4 years-old. Apparently, the girl is the first one who developed the genetic pathology in at least 4 generations of her family. After biopsy, cherubism diagnosis was confirmed and the treatment of choice was periodic monitoring. **Discussion:** Cherubism studies with long-term follow-up with clinical and radiographic documentation indicate that the spontaneous resolution of bone lesions is rare. Treatment of cherubism is controversial and various modalities have been reported as the use of calcitonin, osseous plasty surgery, curettage, orthognathic surgery, liposuction and palliative treatments. **Conclusion:** cherubism is a rare condition that affects individuals in childhood that lead to some facial alterations, those patients need an special care and an well trained team to treat these

RESUMO

Introdução: O Querubismo é uma doença rara que afeta o terço médio e inferior da face em indivíduos no momento da infância. É uma doença óssea hereditária benigna com herança autossômica dominante sendo que a distribuição familial pode afetar diferentes gerações, todavia casos não-familiares isolados também foram relatados na literatura. As lesões apresentam se radiograficamente como cistos multiloculados radiolúcidos e histologicamente se assemelham ao granuloma central de células gigantes e ao tumor marrom do hiperparatireoidismo com numerosas células gigantes multinucleadas distribuídos aleatoriamente e espaços vasculares dentro de um estroma de tecido conjuntivo fibroso. **Objetivos:** O objetivo deste estudo é relatar a importância do diagnóstico desta patologia e da variedade de tratamentos disponíveis na literatura, orientando dessa maneira a um tratamento individualizado. **Relato de Caso:** Mulher, caucasiana, 8 anos de idade, em bom estado geral. Foi encaminhada ao Serviço de Cirurgia Bucomaxilofacial do Hospital Erasto Gaertner (EGH), Curitiba - PR, Brasil, com queixa de inchaço bilateral da maxila e da mandíbula desde os 4 anos de idade. Em avaliação notou-se que menina é a primeira pessoa que desenvolveu a patologia em pelo menos quatro gerações de sua família. Após biópsia o diagnóstico de cherubism foi confirmado e o tratamento de escolha foi a monitorização periódica. **Discussão**: estudos de cherubism a longo prazo de follow-up com documentação clínica e radiográficas indicam que a resolução espontânea das lesões ósseas são raras. O tratamento do cherubism é controverso e diversas modalidades têm sido relatados como o uso de calcitonina, a cirurgia de plastia óssea, curetagem,

disease more carefully and wisely noting that exist a series of option of new treatments in this cases.

KEYWORDS

Jaw Diseases; Cherubism; Jaw abnormalities; Familial Benign Giant-Cell Tumor of the Jaw

cirurgia ortognática, lipoaspiração e tratamentos paliativos.

PALAVRAS-CHAVE

Edema bilateral da mandíbula, Querubismo, anormalidades mandibulares, múltiplas lesões de células gigantes.

INTRODUCTION

The Cherubism is a rare disease that affects the middle and lower third of the face in individuals at the time of childhood. It was first described by Jones (1933) as "familial multilocular cystic disease of the jaws with the eyes looking towards heaven appearance". [1] It is a rare hereditary benign bone disease with an autosomal dominant inheritance. The family distribution may affect different generations and isolated non-familial cases have also been reported in literature. [2-4]

This disease is characterized by bilateral expansion of the mandible and maxilla bones that starts in childhood and presents progressive growth until puberty, when lesions seem to stabilize. The injury received this named because of patient's appearance that are alike the "cherubs" of Renaissance paintings with round faces with eyes directed to heaven. [5,6]

Radiographically, lesions appear as cystic multilocular radiolucencies, often beginning near the angle of the mandible and spreading to the mandibular ramus and body. Histologically, it resembles central giant cell granuloma and brown tumor in a patient with hyperparathyroidism with numerous randomly distributed multinucleated giant cells and vascular spaces within a fibrous connective tissue stroma. [3,6]

Conservative curettage and patient monitoring are the most commonly treatment of choice. Surgical recontouring should, therefore, be postponed until after puberty, except for very severe cases where functional and aesthetic problems are present. [7,8] The successful use of subcutaneously administered synthetic human calcitonin and salmon calcitonin in the treatment of cherubism has been reported in literature. [6]

CASE REPORT

Caucasian 8 years-old female, in good general and cognitive condition, was referred to Service of Oral and Maxillofacial Surgery of Erasto Gaertner Hospital (EGH), Curitiba – PR, Brazil, complaining of bilateral swelling of the maxilla and mandible bones since 4 years old. It was mentioned recurrent infections in the same region since was noted volume increase with consequent swelling of the region. The patient had laboratory values within normal limits, eliminating the possible origin of systemic pathology.

On clinical examination it was observed bilateral volume increase of maxilla and mandible bones at height and depth, presenting flaccid consistency to palpation and painful symptoms to touch, it was not possible to see mucosa alterations or spontaneous blending is the nodular regions. The presence of teeth marks on the volume increased regions are highlighted in de mandible.(Figures 1 and 2)

The Computed Tomography (CT) showed an expansive and hypodense lobulated lesion

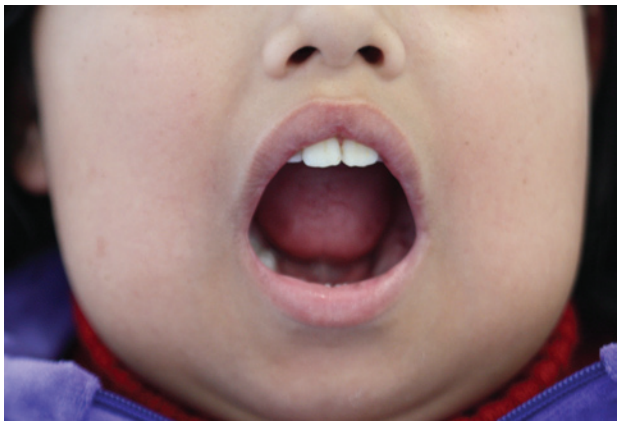

Figure 1 - Extra oral appearance showing bilateral swelling.

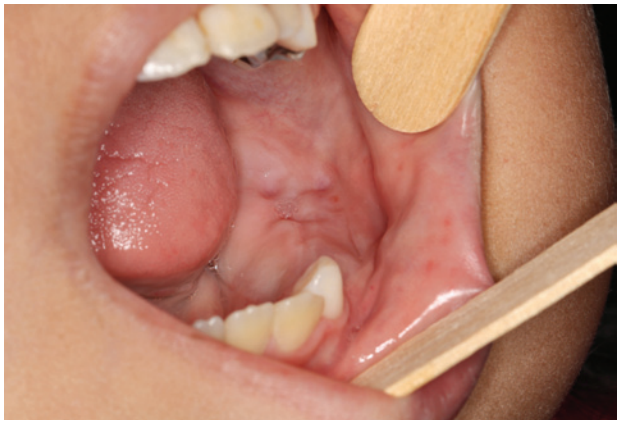

Figure 2 - Intraoral aspect, evidencing dentitions marks at the oral mucosa.

in maxilla and mandible, bilaterally. (Figure 3) On radiographic study it was possible to observe the alteration of the bone pattern and the occlusal disorder occasioned by the pathology. Radiolucent lesions are observed with lobed pattern of radiographic images. (Figure 4 and 5)

The patient was submitted to incisional biopsy under general anesthesia, which confirmed the diagnosis of Cherubism. Histologically, it presented numerous randomly distributed multinucleated giant cells and vascular spaces within a fibrous connective tissue stroma (Figure 6). There is no history of diagnostic of Cherubism in her family. The girl is the first one who developed the genetic pathology in at least 4 generations of her family.

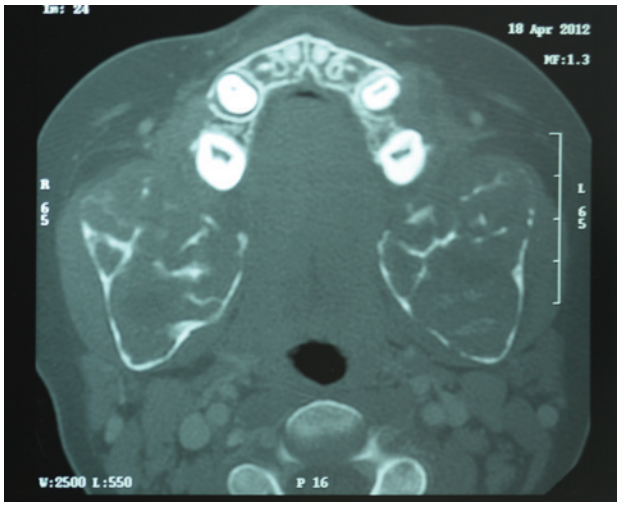

Figure 3 - Fan Beam Computed Tomography showing hypodensity and expansion of the jaw.

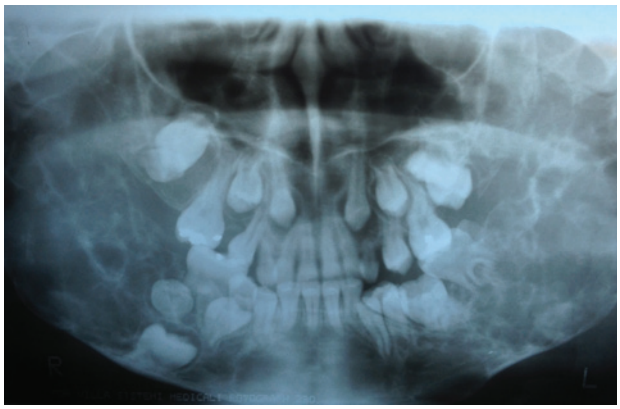

Figure 4 - Panoramic radiograph showing complete compromising of the jaws.

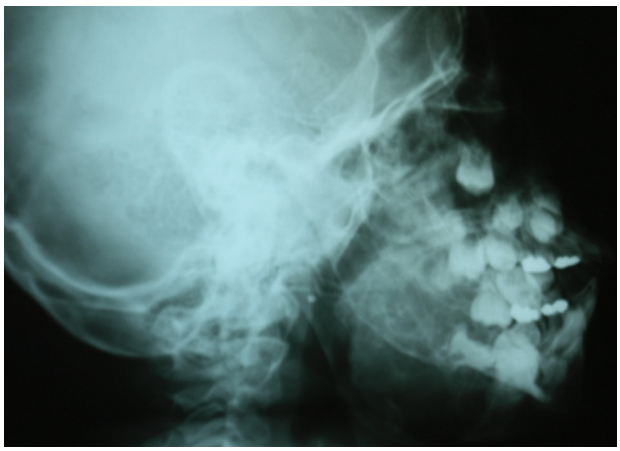

Figure 5 - Lateral radiograph of the face where it can be noted alteration in the pattern of tooth eruption.

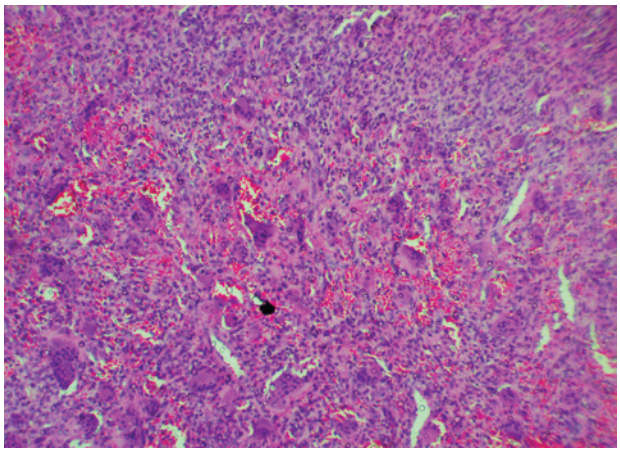

Figure 6 - Histological characteristics similar to giant cell lesion.

After diagnosis confirmation, the treatment of choice was periodic monitoring. After 18 months of follow-up, it was not observed episodes of infection or any alterations of the child condition.

DISCUSSION

Cherubism is a rare non-neoplastic hereditary disease affecting the two lowers thirds of the face and is related to genetic mutations. It is transmitted in an autosomal dominant fashion with 100% penetrance in males and 50% to 70% penetrance in female, however several cases have been reported isolated in literature, called non-familial cherubism. [6,8,11] The patient reported has no familial history of cherubism, been classified as non-familial disorder.

Most patients with cherubism have germline mutations in the gene encoding SH3BP2, located at 4p16.3 chromosome, this may cause the deregulation of MSX-1 gene, that it is involved with the craniofacial morphogenesis. Affected individuals have an increase of bone activity that occurs between the ages 2.5 to 10 years due to an up-regulation of MSX-1. This genetic disorder stops by the end of molar development, leading to osteolytic lesions remineralization, suggesting that the underlying cause for cherubism is a systemic autoinflammatory response to physiologic changes despite the localized.

It usually occurs between 2 years and 5 years of age followed by a phase of rapid growth until 7-8 years of age, a phase of slow growth until 12 or puberty, a phase of stabilization of lesions at or after puberty and finally a phase of remission at about 25-30 years. According to recent literature exist approximately 150 cases of cherubism reported. This pathology is typically limited to the craniofacial region. However, there are some reports in the literature that refer to involvement of the ribs. [13]

Cherubism is often accompanied by abnormalities of the dental arch, abnormal pattern of teeth eruption, agenesis. Patients with this condition have round face by swelling of gnathic bones. The substitution process of healthy bone by hypervascular fibrous tissue and immature bone can extend up to the infra-orbital region, stretching cheeks skin and lowering eyelid slightly down with sclera exhibition below the pupil and appearing the eyes are facing up. [8,9] Affected children appears normal at birth, have no mental dysfunction and facial alteration becomes apparent early in life, becoming progressively higher until puberty, and it is expected that lesion regression occurs spontaneously by the end of adolescence. [9]

In general, cherubism does not affect other parts of the skeleton or osseous metabolism; bone markers such phosphorous, serum calcium, and alkaline phosphatase are usually at normal levels. Significant ocular disturbances, such as proptosis, superior globe displacement, visual loss, and exposure of the inferior part of the sclera can be noted. Often ocular alterations occur after puberty and require ophthalmologic support for best multidisciplinary treatment. [9,14]

Some studies have suggested that cherubism may be associated with other genetic diseases such as Noonan syndrome, Ramon syndrome and also gingival fibromatosis. [15-17] The differential diagnosis is multilocular cyst, central giant cell granuloma, hyperparathyroidism brown tumor, odontogenic

myxoma, aneurysmal bone cyst, metastatic tumors of jaws and central hemangioma of bone. [13]

The hyperparathyroidism brown tumor and the central giant cell granuloma are particularly important because they present histological characteristics equal to cherubism, the clinical and complementary assessment by blood tests will lead to the correct diagnosis.

Radiographically, lesions appear as cystic multilocular radiolucency, often beginning near the mandibular angle and spreading to the mandibular ramus and body. Maxillary and mandibular lesions may occur at the same time. Frequently, ectopic unerupted teeth are involved in the lesions. [18] The remission of facial bone enlargement seemed to occur later in the maxilla than in the mandible. Radiographic follow-up showed that multilocular radiolucent areas gradually filled in with osseous structure, sometimes within a short period. [8,9] However in the case described it was not possible to observe amendment of bone pattern in the course of time.

Histologically, cherubism resembles central giant cell granuloma and hyperparathyroidism brown tumor with numerous randomly distributed multinucleated giant cells and vascular spaces within a fibrous connective tissue stroma, [9,19] being impossible to distinguish these pathologies by microscopic examination.

Seward and Hankey [20] suggested a grading system for cherubism that has been modified by other authors. The classical grading system is based on the radiographic location of the lesions. Grade 1: with mandibular but no maxillary involvement at the time of examination; Grade 2: with full mandibular involvement and maxillary involvement only in the tuberosities and Grade 3: with both jaws diffusely affected. Remission of signs of cherubism occurs most rapidly in grade 1, although it is expected to occur in almost all patients, independent of the classification. [9]

Cherubism studies with long-term follow-up with clinical and radiographic documentation indicate that the spontaneous resolution of bone lesions is rare in the literature. [7,9] However, de Lange et al. [6] related that in adult life, the patients may exhibit normal facial appearance, and radiographs showed almost complete involution of the lesions.

Treatment of cherubism is controversial and various modalities have been reported as the use of calcitonin, osseous plasty surgery, curettage, orthognathic surgery, liposuction and palliative treatments. The more accepted approach for the treatment of cherubism is the monitoring of patients in order to prevent permanent conditions such as malocclusion or edentulism. Biopsies with diagnostic purposes may be performed and extractions of impacted or ectopic teeth as well. [4,6,8,9,19,21] The treatment should be determined individually for each patient, considering the clinical course of the disease and the individual behavior; a possible surgical intervention can be justified on aesthetic conditions or severe functional problems, such as alterations in swallowing, breathing or vision. [8,9,19] When discussing treatment, we must consider the psychological problems associated with an unattractive cherubic appearance in young patients. [9]

Some authors have suggested combination of orthognathic surgery and use of calcitonin. The surgery is indicated in patients affected with severe malocclusions and esthetic compromising. It is proved that this modality of treatment can be successful, but bleeding control and skeletal fixation can present a challenge. [4,8] In another hand, systemic treatment with hormonotherapy (human synthetic calcitonin and salmon calcitonin) is used for conservative treatments to cherubism, where calcitonin promotes an inhibition of the osteoclastic activity of the giant cells, preventing the development of bone lesions. [6]

Patient care by a multidisciplinary team using gold standard treatment is important

for sustained treatment results. The treatment should be reasonably programed and analysed - patient's age, sequel, technical difficulty of surgery, symptoms, location of disease, presence or not of multidisciplinary time and also the surgeon's skill in handling this type of condition - these factors must be taken into account for choice of treatment this kind of lesion. Although cherubism is rare alteration, there is a need to be listed as a differential diagnosis from other lesions of similar characteristics, with this would be possible to avoid surgical risks to the patient and a plan of treatment of the lesion can be done in a better way.

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Cleverson Patussi
(Corresponding address)
Department of Oral and Maxillofacial Surgery,
Erasto Gaertner Hospital
Rua Dr. Ovande do Amaral, 20. Curitiba, Brazil
81520-060
E-mail – cleversonpatussi@hotmail.com

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