doi: 10.7213/archives.08.003.RC02 ISSN 2236-8035
Archives of Oral Research, v. 8, n. 3, p. 249-53, Sept./Dec. 2012

Case report on cherubism: non-familial variant

Relato de caso de querubismo: uma variante não familiar

Shelly Arora[a], Aadithya B. Urs[b], Jeyaseelan Augustine[c], Priya Kumar[d], Ashi Singh[e]

[a] MDS, senior resident, Department of Oral & Maxillofacial Pathology, Maulana Azad Institute of Dental Sciences, New Delhi - India, e-mail: arorashells76@yahoo.co.in
[b] MDS, professor, Department of Oral & Maxillofacial Pathology, Maulana Azad Institute of Dental Sciences, New Delhi - India, e-mail: draadithya@sify.com
[c] MDS, assistant professor, Department of Oral & Maxillofacial Pathology, Maulana Azad Institute of Dental Sciences, New Delhi - India, e-mail: j_augustine@gmail.com
[d] MDS, assistant professor, Department of Oral & Maxillofacial Pathology, Maulana Azad Institute of Dental Sciences, New Delhi - India, e-mail: drpri_kumar@yahoo.com
[e] BDS, intern, Department of Oral & Maxillofacial Pathology, Maulana Azad Institute of Dental Sciences, New Delhi - India, e-mail: drsingh.ashi@gmail.com

Abstract

Introduction: Cherubism is a rare, non-neoplastic, self-limiting, fibro-osseous disease, characterized by painless expansion of the maxilla, mandible or both. It usually develops in the first and second year of life. The radiographic appearance presentation is ordinarily bilateral, multilocular appearance in the mandible. To the best of our knowledge, very few cases (less than ten) of non-familial cherubism have been reported in the English literature. **Objective**: To describe non-familial case of cherubism in a 10-year-old child. **Materials and methods**: The current case was clinically, radiographically and histopathologically analysed for confirmatory diagnosis. **Results**: H & E stained section showed vascular and cellular stroma containing numerous multinucleated giant cells. **Conclusion**: Correlating radiographically and histopathologically the case was finally diagnosed as non-familial variant of cherubism.

Keywords: Cherubism. Mandible. Multilocular lesion.

Resumo

***Introdução**: Querubismo é uma doença rara, não neoplásica, autolimitada, fibro-óssea, caracterizada pela expansão indolor da maxila, mandíbula ou ambas. Ela geralmente se desenvolve no primeiro e no segundo*

ano de vida. A aparência radiográfica é normalmente bilateral, multilocular e localizada na mandíbula. Para melhor conhecimento, poucos casos (menos de dez) de querubismo não familiar foram relatados na literatura. ***Objetivo****: Descrever um caso de querubismo não familiar em uma criança de 10 anos.* ***Materiais e métodos****: Para confirmação do diagnóstico, foram realizadas avaliações clínicas, radiográficas e histológicas deste caso.* ***Resultados****: Seção corada de H & E mostrou estroma vascular e celular contendo numerosas células gigantes multinucleadas.* ***Conclusão****: Na correlação radiográfica e histológica, ficou confirmado diagnóstico de variante não familiar de querubismo.*

Palavras-chave*: Querubismo. Mandíbula. Lesão multilocular*

Introduction

Cherubism is a rare, hereditary, non-neoplastic, self-limiting, fibro-osseous childhood disease, characterized by bone degradation and fibrous tissue replacement at the angles of the mandible and at the tuberosity areas of maxilla that leads to prominence of lower face (1). It was first described by Jones, in 1933, as "a familial multilocular cystic disease of the jaw". He later coined the descriptive term "cherubism" when he likened the classical characteristics of full round cheeks and upward cast of eyes to the angelic look of the cherubs immortalized by Renaissance art (2). It usually develops in the first and second years of life and it is characterized by bilateral expansion of the maxilla and mandible, which becomes progressively pronounced till puberty, with gradual involution by middle age. The radiographic presentation is unique because of its diffuse, bilateral, multilocular appearance (3–6). To the best of our knowledge, very few cases (less than ten) of non-familial cherubism have been reported in the English literature. Due to its rarity, it's difficult to determine a disease frequency for this disorder. The purpose of this case report is to present a case of cherubism in a 10-years-old child with no apparent familial involvement.

Case report

A 10-years-old male reported to the Outpatient Department of the hospital, with a chief complaint of swelling on the left side of the cheek for the past six months. There was no evidence of pain/pus discharge or dysphagia. There was no family history of a similar condition. On extraoral examination, a bilateral swelling was observed in the lower border of the mandible, which was asymmetric and more prominent towards the left side (Figure 1). The swelling on this side extended from lip commissures to the ear, mesiodistally. The superior-inferior extent of the swelling was from the floor of the orbit to the inferior border of the mandible and measured approximately 5 × 6 cm. The right side swelling extended from the angle of the mandible to the front of the ear. The swelling was hard and bony on palpation. The right and the left submandibular lymph nodes were palpable but not tender.

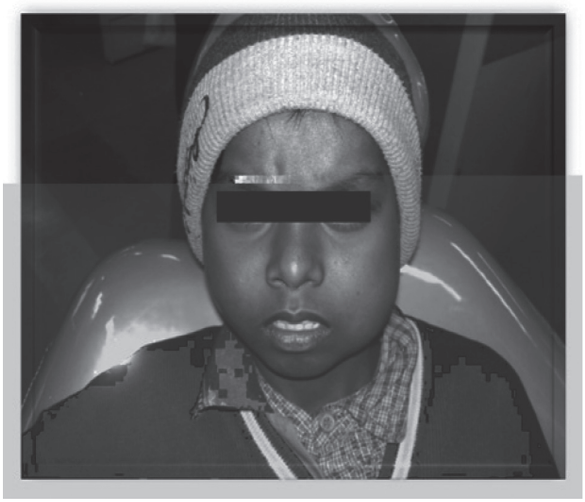

Figure 1 - Picture showing extraoral swelling on left side of the face
Source: Research data.

On intraoral examination, a firm swelling was seen distal to mandibular left first molar along with the expansion of the buccal cortical plate. Premature eruption of all premolars was noted.

Panoramic radiograph revealed a bilateral multilocular cystic radiolucency with ragged borders,

posterior to the first molar and extending up to the condyles, involving the angle of the mandible and the rami as well (Figure 2).

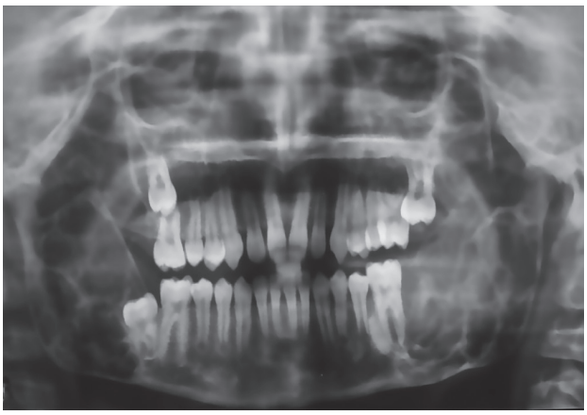

Figure 2 - Panoramic radiograph showing multilocular cystic appearance with ragged borders in mandible, bilaterally
Source: Research data.

Fine needle aspiration cytology from bilateral cervical lymph nodes showed features of reactive lymphadenitis. A non-contrast scan of the head and neck, done on 128-slice CT scanner, revealed an expansible multiloculated lesion, causing cortical thinning and endosteal scalloping with soft tissue attenuation involving the body and ramus of the mandible. Maxillary involvement was seen in the region of posterior aspect of the alveolar arch and the maxillary sinus, bilaterally (Figure 3). Malocclusion and displacement of the involved premolar and molar teeth was noted. Both temporomandibular joints appeared normal and no involvement of the orbital floor was seen. The disease was provisionally diagnosed as a fibro-osseous lesion.

An incisional biopsy was performed and the soft tissue specimens received were routinely processed and stained with hematoxylin and eosin. Microscopic examination showed vascular and cellular stroma containing numerous multinucleated giant cells. Abundant plump fibroblasts were present in a loosely collagenous background showing whorling arrangement at areas. Foci of extravasated blood were also evident (Figure 4).

The differential diagnosis could be central giant cell granuloma and hyperparathyroidism. But keeping in mind patients' age, clinical appearance and normal serum calcium level, confirmatory diagnosis of cherubism was given. Due to the expected tendency of these lesions to regress with time, no surgical intervention was undertaken and the patient was kept on follow-up.

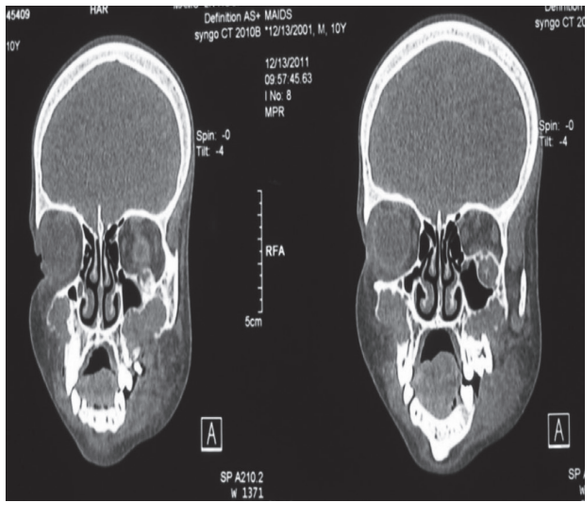

Figure 3 - Micro-tomographic image showing expansive multiloculated lesion, causing cortical thinning and endosteal scalloping with soft tissue attenuation involving the body and ramus of the mandible
Source: Research data.

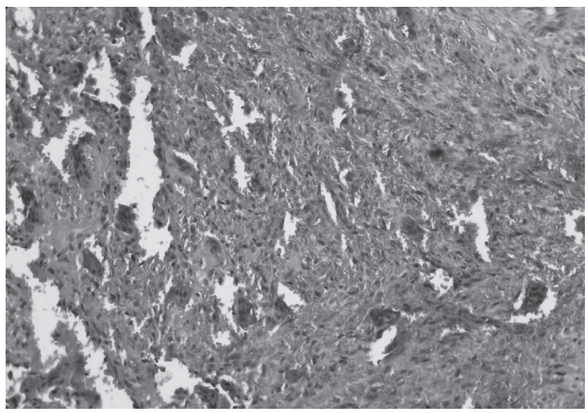

Figure 4 - Numerous multinucleated giant cells with abundant fibroblasts are seen with moderate vascularity
Source: Research data.
Note: H&E × 200.

Discussion

Cherubism is a rare, non-neoplastic, self-limiting, fibro-osseous disease, characterized by painless

expansion of the maxilla, mandible or both (7, 8). It is diagnosed early in childhood, often in the first decade of life. The disease is more active between the ages of 3 and 7 and increases till puberty, after which spontaneous involution may occur (3-5). The age of presentation in this case was slightly higher than usual, 10 years. Many other authors have also reported a higher age of presentation, ranging from 1 to 19 years (9-11). There was no family history of similar disease in this case, thus adding to the list of non-familial cases that have now been reported in literature (1, 8, 11).

The pathogenesis of cherubism remains controversial. No cause and effect relationship with trauma, infections or haemorrhage has been verified. Most cases are familial and inherited as autosomal dominant pattern, with high prevalence and penetrance of 100% in males and 50-75% in females (12, 13).

Researchers have described seven mutations in the gene encoding SH3-domain binding proteins SH3BP2 on chromosome 4p16.3 that cause cherubism. The SH3BP2 gene provides instructions for making a protein that plays a role in transmitting chemical signals within cells, particularly the ones involved in the replacement of old bone tissue with new bone (bone remodelling) and certain immune system cells. Mutations in the SH3BP2 gene lead to the production of an overactive protein, which causes inflammation in jaw bones and triggers the production of osteoclast (excess of the bone resorbing cells that contribute to the destruction of bone in the upper and lower jaws). A combination of bone loss and inflammation most likely causes the cyst-like growth characteristic of cherubism (12, 13).

The clinical signs and symptoms depend upon the severity of condition. The patients usually have a symmetrical swelling in the mandible or mandibular protrusion only, and exhibit "eye to heaven appearance", as described by Jones (2). It may also show diffuse maxillary involvement and unilateral in some cases (3). In the current case, the swelling was asymmetric and more prominent on the left side. Widening of the alveolar ridge is also common with the maxillary involvement, resulting in alveolar widening and a narrow V-shaped palate, which sometimes causes backward displacement of the tongue. In severe cases, the palatal vault may be obliterated, causing dysarthria, dysphagia and dyspnoea (3).

Painless enlargement of submandibular lymph nodes frequently occurs in children with cherubism (3). It is probably a reactive hyperplasia with fibrosis, which has been confirmed by microscopic examination of lymph node biopsy specimen from cherubic patients. The same features were noted in this case.

The severity of cherubism was graded by Seward and Hankey, citados por Meing et al. (6), as follows: (i) Grade I – Involvement of bilateral mandibular molar region and ascending rami, mandibular body or mentis; Grade II – Involvement of bilateral maxillary tuberosities as well as the lesion of Grade I, diffused whole mandible; Grade III – Massive involvement of the entire maxilla and mandible, except the condyles; Grade IV – Involvement of both jaws with condyles.

The patient reported in this case study falls into grade II of this classification.

Radiographically, a unilocular or multilocular, bilateral radiolucent lesion with ragged, poorly defined borders, in the mandible is usually seen (3, 6, 9). Similar features are discussed in the present case. In adults, the multilocular rarefactions are replaced by irregular patchy sclerosis with progressive calcification. There is a classical ground glass appearance as a result of small tightly compressed trabecular pattern (6). Cortical bone at the mandibular base is thin but not disrupted, even though there is expansion of bone, indicating the benign behaviour of the lesion. Another factor that could sustain the benignity of the lesion would be the integrity of the mandibular nerve (14).

On histological evaluation, the normal bone is partly replaced by pathological tissue. It contains numerous randomly distributed multinucleated giant cells and vascular spaces within a fibrous connective tissue stroma. The abundant multinucleated giant cells are osteoclasts which synthesize tartrate-resistant acid phosphatase and express vitronectin receptor, in addition to resorbing bone. Eosinophilic collagen perivascular cuffing is reported by some authors. An increase in osteoid and newly formed bone matrix is found in the peripheral region of fibrotic stroma (15).

The biochemical markers such as serum calcium, serum phosphorus, serum alkaline phosphatase and parathormone are increased in hyperparathyroidism but not in cherubism, so the latter can be differentiated from hyperparathyroidism. Other differential diagnosis in this case could be central giant cell granuloma, but this lesion is generally anterior to lower first molar and more vascular.

Treatment of cherubism has not been standardized; often the disease involutes spontaneously when the child reaches puberty. The reason why

this happens is not clear, but it is postulated that osteoclast formation is reduced by the increased plasma concentration of sex steroid hormones estrogen and progesterone at puberty. Genetic defect may be responsible for the localized increase in osteoclasts in cherubism because of physiological increase in the synthesis of sex steroid hormone (6).

The indication for treatment is based on the rate of lesion progression, the extent of its involvement and the emotional state of the patient. Sufficient removal of tissue by enucleation or curettage of tumoral tissue appears to be useful in more aggressive cases. Radiation therapy is ineffective and contraindicated, considering the risk of osteoradionecrosis and interference with dentofacial growth and development (6, 16). In this case, the patient has been put on wait and watch approach until puberty.

References

1. Gomes MF, de Souza Setúbal Destro MF, de Freitas Banzi EC, dos Santos SH, Claro FA, de Oliveira Nogueira T. Aggressive behaviour of cherubism in a teenager: 4-years of clinical follow-up associated with radiographic and histological features. J. Dentomaxillofac Radiol.2005;34(5): 313-8. PMID:16120883

2. Jones WA. Familial multilocular cystic disease of the jaws. Am J Cancer. 1933:17:946-50. doi:10.1158/ajc.1933.946

3. Katz JO, Underhill TE. Multilocular radiolucencies. Dent Clin North Am. 1994;38(1):63-81. PMID:8307237

4. Carroll AL, Sullivan TJ. Orbital involvement in cherubism. Clin Experiment Ophthalmol. 2001;29(1): 38-40. PMID:11272784

5. Silva EC, de Souza PE, Barreto DC, Dias RP, Gomez RS. An extreme case of cherubism. Br J Oral Maxillofac Surg. 2002;40(1):45-8. PMID:11883969

6. Meing XM, Yu SF, Yu GF. Clinicopathologic study of 24 cases of chrubism. Int J Oral Maxillofac Surg. 2005;34(4):350-56. PMID:16053841

7. Jones WA, Gerrie J, Pritchard J, Cherubism – a familial fibrous dysplasia of the jaws. Oral Surg Oral Med Oral Pathol 1952;5:292-305. PMID:16053841

8. Von Wowern N. Cherubism: a 36 year long term follow up of 2 generations in different families and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radio Endod. 2000;90(6):765-72. PMID:11113824

9. Reade PC, McKellar GM, Radden BG. Unilateral mandibular cherubism: brief review and case report. Br J Oral Maxillofac Surg. 1984;22(3):189-94. PMID:6234934

10. Kaugars GE, Niamtu J 3rd, Svirsky JA. Cherubism: diagnosis, treatment,and comparison with central giant cell granulomas and giantcelltumors. Oral Surg Oral Med Oral Pathol 1992;73(3):369-74. PMID:1545971

11. Beaman FD, Bancroft LW, Peterson JJ, Kransdorf MJ, Murphey MD, Menke DM. Imaging characteristics of cherubism. AJR Am J Roentgenol. 2004;182(4):1051-4. PMID:15039186

12. Tiziani V, Reichenberger E, Buzzo CL, Niazi S, Fukai N, Stiller M, et al. The gene for cherubism maps to chromosome 4p16. Am J Hum Genet. 1999;65(1):158-66. PMID:10364528

13. Ueki Y, Tiziani V, Santanna C, Fukai N, Maulik C, Garfinkle J, et al. Mutations in the gene encoding c--Abl-binding protein SH3BP2 cause cherubism. Nat Genet. 2001;28(2):125-26. PMID:11381256

14. Faircloth WJ Jr., Edwards RC, Farhood VW. Cherubism involving a mother and daughter: case report and review of the literature. J Oral Maxillofac Surg. 1991;49(5):535-42. PMID:2019904

15. Regezi JA, Sciubba JU. Oral pathology: clinical-pathologic: correlations. 2nd ed: Philadelphia: WB Saunders Company; 1993.

16. Lannon DA, Earley MJ. Cherubism and its charlatans. Br J Plast Surg. 2001;54(8):708-11. PMID:11728115

Received: 07/25/2012
Recebido: 25/07/2012

Accepted: 10/29/2012
Aceito: 29/10/2012