



## CHERUBISM : A CASE REPORT WITH REVIEW OF LITERATURE

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### ABSTRACT

#### Keywords:

#### INTRODUCTION:

Cherubism – first described by Jones – is a benign fibroosseous disorder of childhood involving the lower two-thirds of the face<sup>1</sup>. The true incidence is unknown but the age of onset is between 2 to 10 years<sup>2,3,4</sup>. It is a rare disease of autosomal dominant inheritance characterised by painless, frequently symmetrical, enlargement of the jaws as a result of the replacement of bone with fibrous tissue<sup>5</sup>. It has been associated with mutations in SH3BP2 gene, which has been mapped to locus 4p16.3. The SH3BP2 mutation is thought to lead to parathyroid hormone receptor signalling and Msx-1 activation<sup>6</sup>.

It is characterised by swelling of submandibular lymph nodes in the early stages that contributes to the fullness of the face. As the soft fibrous dysplastic tissue in the lesions expands, the protuberant can infiltrate the orbital floor and cause the characteristic upward tilting of the eyes, exposing the sclera below the iris. Cherubism lesions are limited to the jaws and in most cases the dysplastic expansile masses begin to regress with the onset of puberty<sup>7</sup>. Boys are more affected than girls at the proportion of 2:1<sup>8,9</sup>.

#### CLINICAL PRESENTATION:

The hallmark of cherubism is the development of symmetrical multilocular radiolucent expansile lesions in the mandible and/or the maxilla, which typically first appear at the age of 2 to 7 years. Submandibular and cervical lymph nodes are enlarged during the early stages of the disease. Patients with mild form of cherubism may develop only small symmetrical lesions in the mandible. The more progressive form manifests with multiple symmetric lesions in the mandible or involves the maxilla and mandible with singular or multiple lesions<sup>7</sup>.

Although cherubism lesions are usually limited to the mandible and the maxilla, there are rare reports of involvement of the zygomatic arches and condyles<sup>10,11</sup>. Lesions in patients with the progressive form of cherubism result in extensive bone resorption and leave only a fenestrated shell of cortical bone. Fibrous tissue masses can expand the cortical bone and lead to facial swelling. When expansile fibrous tissue masses invade the floor and walls of the orbits they can cause upward tilting or displacement of the globes. Most cases regress spontaneously after puberty. There are rare instances when lesions persist or actively grow in young adults<sup>12,13</sup>.

#### DENTAL ALTERATIONS:

The impact of cherubism lesions on development and eruption of the primary and permanent dentition varies depending on the time of onset and severity of expansile lesions. The arrangement of primary teeth can be disturbed. There is impaction and/or displacement of teeth, which radiographically seem to float in radiolucent areas conferring the so called “floating tooth appearance”<sup>8,14</sup>. In addition, ectopic tooth eruption, agenesis of permanent teeth and root resorption of existing teeth are observed. These alterations result in malocclusion as well as problems of phonation and swallowing, the latter being exacerbated by flattening or inversion of the palatal cleft<sup>10,12,15,16</sup>. In more severe instances, children may require prosthesis that need to be adjusted as the child grows or swelling within the oral cavity changes. A dental prosthesis may improve the ability to chew and increase the self esteem of the child. Orthodontic treatment is appropriate after growth is completed and when cherubism is regressing<sup>5</sup>.

#### BIOCHEMICAL CHANGES:

Mineral metabolism is normal in patients with cherubism and serum levels of calcium, parathyroid hormone related peptide, calcitonin and alkaline phosphatase are typically within normal range. Urine markers of bone remodelling such as pyridinium and deoxypyridinium crosslinking, hydroxyproline and calcium/creatinine have been reported to be at the upper limits of normal in some children<sup>17</sup>. Serum levels of alkaline phosphatase may be increased during the active stages of the disease<sup>18</sup>.

#### HISTOLOGICAL FEATURES:

Cherubism lesions resemble giant cell tumours because they contain many giant cells and mononuclear or stromal cells. The fibrotic lesions are non-neoplastic. Cherubism cannot be diagnosed by histology alone because they are not distinguishable from other giant cell lesions of the bone<sup>19</sup>. Chomette and colleagues describe 3 distinct stages in cherubism lesions<sup>20</sup>. In the first, osteolytic stage the authors found numerous round, fusiform and multinucleated giant cells. The tissue of the lesion is well vascularised. Fibroblastic cells with fewer giant cells can be found in the periphery of the lesions. Hemosiderin, a breakdown product of haemoglobin is observed in endothelial cells and some surrounding fibroblasts.

The second stage is characterised by proliferative spindle cells. Fibroblastic nodules with central vessels dominate the lesion while some osteogenesis can be observed near the cortex of the

bone. The tissue

An important component in the management is the differential diagnosis which includes brown tumour of hyperparathyroidism, giant cell lesion, Noovam/multiple giant cell lesion syndrome, fibrous dysplasia, aneurysmal bone cyst and the hyperparathyroidism- jaw tumour syndrome. The limited and symmetrical distribution of the cherubism lesions can often facilitate distinction of cherubism from these other conditions<sup>7</sup>.

#### **TREATMENT OPTIONS:**

Once the diagnosis is established, therapeutic management should be evaluated. Treatment options include waiting for stabilization and spontaneous remission of the disease, tooth extraction in areas showing fibrous alterations, cosmetic osteoplasty of the affected jaws after regression of the disease activity or, in case of functional impairment, curettage of the lesion and treatment with calcitonin<sup>21,22,23</sup>. The policy of waiting for disease regression, followed by the evaluation of physiological bone remodelling is the most recommended.

Surgical intervention is recommended when aesthetic or functional concerns arise including nasal obstruction, proptosis or facial deformity. Options for surgical management include partial resection, contour resection, curettage or a combination of these. Surgical procedures should be performed after puberty when the lesions are quiescent. Severe aesthetic or functional problems may justify intervention prior to puberty<sup>24</sup>. Curettage has been suggested to be a good approach since this intervention stimulates bone replacement. Radiation therapy has been described in the literature for the management of cherubism. However, radiation therapy is contraindicated in this benign condition because of the potential for long term adverse consequences such as retardation of jaw growth, osteoradionecrosis and increased incidence of induced malignancy<sup>7</sup>.

Calcitonin has been used for the treatment of central giant cell granuloma with successful outcome and experimental use of calcitonin for the treatment of cherubism has been suggested. Carvalho Silva and colleagues describe that the cherubism lesions in 7 of 8 of their patients stabilized by age of 12 years and regressed thereafter<sup>25</sup>.

#### **CASE REPORT:**

Siblings aged 6 years and 4 years reported to the department of Pediatric and preventive dentistry, PGIDS, Rohtak with the chief complaint of bilateral swelling of face which was painless and slowly progressive. The history revealed that none of their parents had any history of swelling on their face in their childhood. On clinical examination the faces of both the siblings had severe bilateral expansion. Bilaterally submandibular lymph nodes were enlarged. On general physical examination, no abnormality was detected in any system. On clinical examination, the swellings were bony hard with obliteration of the buccal vestibule. There was widening of the alveolar processes and displacement of teeth. A panoramic radiograph revealed extensive bone destruction involving the mandibular body, angles and both ascending rami with multilocular radiolucent areas and marked bony expansion. The lesions spared the mandibular condyles, but concerned the

alveolar processes and maxillary tuberosities. There was also associated thickening of cortices. The displacement of the teeth was less marked in case of younger sibling. The maxillary sinuses were surrounded by modified tissue, yet with aerial space. The body of the maxilla presented bilateral overgrowth. On the basis of family history, it might be presumed that this was probably non-familial case of the disease because there was no other member of the family with similar condition, such as an autosomal dominant inherited genetic disease. Laboratory tests which included serum calcium and phosphorus levels were normal. Histopathological evaluation of an incisional biopsy showed giant cell, dysplastic cystic bone tissue. Because of the self limiting nature of the disease, active phase of the disease and absence of any disturbances, there was no need to perform any surgery and the patients were scheduled for regular follow up for 20 years.

#### **DISCUSSION:**

Cherubism is a rare, painless, self limiting osseous disorder in children and adolescents. The radiologic characteristics of cherubism are not pathognomic but the diagnosis is strongly suggested by bilateral relatively symmetric jaw involvement that is limited to the maxilla and mandible. Imaging typically shows expansive remodelling of the involved bones, thinning of the cortices, multilocular radiolucencies with a coarse trabecular pattern and absence of periosteal reaction<sup>26,27</sup>. This is a genetic disease in which the trait is transmitted in an autosomal dominant pattern with a marked variation in clinical expression. It is known to be related to the mutations in the gene encoding the binding protein SH3BP2 on chromosome 4p16.3G<sup>27,28</sup>. Affected children appear normal at birth. Bilateral painless swelling tends to begin usually within the first several years of life. The lesions characteristically continue a pattern of variable enlargement of the jaws until puberty and does not progress later. During the late teens, the disease may undergo spontaneous, gradual, partial, or complete involution, leading to remineralization of the lesions and sclerotic remodelling in adulthood. Facial appearance may return to normal by the fourth or fifth decade of life. However some patients request surgical recontouring of their residual deformity during their twenties<sup>26-28</sup>.

Radiographically, it is characterised by bilateral, well defined, multilocular radiolucent areas within jaw bones. The lesions usually originate in the area of mandibular angle and spread to ascending rami and body of the mandible. Maxillary involvement is less frequent and less extensive but always accompanies mandibular involvement. The lesions in cherubism may cause abnormal patterns of tooth eruption, as well as tooth agenesis, premature loss of deciduous teeth and the presence of ectopic or retained teeth<sup>28</sup>. Widening of alveolar ridges is common. Expansion of the maxillary alveolus sometimes resembles V-shaped palatal arch. As cherubism is generally a self limiting condition and regresses with age, treatment depends on the clinical course of the disease and is indicated only in the cases of aesthetic or functional problems. Most investigators prefer waiting until the end of puberty before performing a surgery. Surgery is indicated only in more aggressive cases characterised by functional impairment such as speech, chewing, or swallowing, and ocular disturbances, or with the presence of major deformities that may cause

psychological problems for the patient. Surgical removal of the fibrotic lesions does not modify the natural course of the disease and gives temporary relief, but may provoke rapid recurrence or exacerbate the disease if the patient is operated on during the active phase<sup>29</sup>.

### CONCLUSION:

Despite the expectations, cherubism is a clinically well-characterised disease which confers to the patient the appearance of a baroque cherub, therefore, derived the name of the disease. In case of suspicion of cherubism, radiographic examination is essential since the clinical presentation and location and distribution of lesions may define the diagnosis. Histopathological examination is complementary.

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