

CASE REPORT

Non-hereditary cherubism

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ABSTRACT

Cherubism is a self-limiting non-neoplastic autosomal dominant fibro-osseous disorder of the jaw usually found in children between 2-5 years of age. It occurs predominantly in boys and is characterized clinically by bilateral swelling of cheeks due to bony enlargement of the jaw that gives the patient a typical cherubic look. Cherubism may occur as solitary cases or in many members of family, often in multiple lesions. Radiographically the lesions appear as multilocular bilateral radiolucent areas. The present case report describes a 13-year-old female cherubic child with progressive swelling of cheeks.

Key words: Fibro-osseous disorders, multinucleated giant cells, osteoclastic lesion

INTRODUCTION

Cherubism is a benign self-limiting fibro-osseous disorder characterized by bilateral expansion of the mandible, maxilla or both.^[1] It was first described by Jones in 1933. The jaw lesions of cherubism are characterized by bilateral symmetrical swelling of lower face and because of this prominence of lower face, patient gives an appearance reminiscent of the 'cherubs' portrayed in Renaissance art, thus, this disease has been known as cherubism.^[2] It is one of the very few genetically determined osteoclastic lesions. Cherubism is generally diagnosed in children aged 2-7 years. Stabilization or even regression of the disease after puberty may occur. The incidences of males getting affected are more than female in 2:1 ratio.^[2]

Its gene is mapped on chromosome band 4p16.3^[3] and is called SH3BP2^[4] (for SH3 domain binding protein 2) and possible degradation of the Msx-1 gene, which is involved in the regulation of mesenchymal interaction during craniofacial morphogenesis. Although the condition is known to be hereditary, in some cases there has been no detectable family history. In such cases, it results from new mutations in the gene and occurs in people with no history of the disorder in their family.

Clinically the patients typically present with marked fullness of the jaws and cheeks with upward gazing of the eyes.^[5]

Although extragnathic skeletal involvement is rare, Davis *et al.*,^[6] reported some rare occurrences in other bones, i.e. ribs, humerus and femur. Radiologically, it appears as multilocular cystic lesion. This case report presents a rare case of female aged 13 years presenting with classical picture of cherubism.

CASE REPORT

A 13-year-old female child of non-consanguineous parents, youngest of siblings [Figure 1a and b] reported to our department with a complaint of painless, progressive and bilateral enlargement of lower face and jaws. There was no history of similar disease in any of the siblings and parents of the affected child.

The history of present illness revealed that the patient had been born as a full-term normal baby and showed no abnormalities until about the age of 2 years, but later bilateral symmetrical prominence of lower face was seen. This enlargement had stopped at age of two and half years and remained the same in size for the subsequent years. Since 3-4 months her parents observed that it gradually increased to present size. On physical examination it was seen that patient was well built, active and mentally alert. No abnormality was found on clinical examination of the chest, abdomen, cardiovascular and central nervous system. No cutaneous pigmentation or other congenital abnormality was present and there was no evidence of endocrinal disturbance.

Extraoral examination revealed normal expression and color of the face with no ophthalmic abnormality. Diffuse enlargement on both right and left side of face extending till the inferior border and angle of mandible region bilaterally was noticed. It was roughly round in shape and hard in consistency with ill-defined margins. The swelling was fixed

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Figure 1: (a and b) Clinical image shows bilateral diffuse enlargement, which was more prominent on right side of face. (c and d) Clinical image shows no disturbance of occlusion and no midline shifting

with no secondary changes. Swelling on the right side was slightly larger as compared with left [Figure 1a and b]. On palpation, temperature of the overlying skin was normal and no tenderness was elicited. Submandibular lymph node was palpable on right side, single in number, measuring approximately 1 cm in diameter, firm in consistency, non-tender and mobile in nature.

Intraoral examination revealed that patient was in permanent dentition stage with absence of mandibular left second permanent molar. There was no disturbance in occlusion or shift in midline [Figure 1c and d]. Based on history and clinical examination, a provisional diagnosis of cherubism was given, with the differential diagnosis of mumps, fibrous dysplasia, bilateral masseter dystrophy, central giant cell granuloma, infantile cortical hyperostosis and human immunodeficiency virus parotitis. To differentiate from the various disorders, blood, radiographic, histopathologic investigations and computed tomography (CT) scan was performed.

Blood investigations

Serum alkaline phosphatase, serum glutamic oxaloacetic transaminase (SGOT) (17 IU/l), serum glutamic-pyruvic transaminase (SGPT) (20 IU/l), calcium (8.6 mg/dl) and phosphorus level assessment (5.40 mg/dl) were conducted and all were within the normal range except serum alkaline phosphatase levels (260 IU/l), which was found to be highly raised.

Radiographic investigations

Panoramic radiograph revealed diffuse multiple cystic areas involving body, ramus, angle and coronoid process of the mandible bilaterally. The tooth bud of mandibular left second permanent molar was seen floating in multilocular radiolucent areas conferring so called 'floating tooth' appearance [Figure 2].

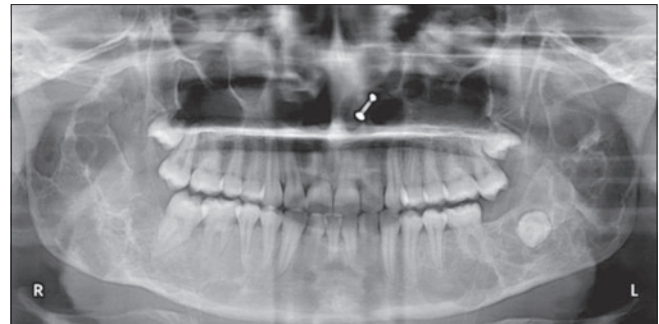


Figure 2: Panoramic radiograph showing diffuse multiple cystic areas involving body, ramus, angle and coronoid process of mandible

A posteroanterior view of skull revealed multilocular radiolucency extending bilaterally on both sides of mandible [Figure 3].

To confirm radiographic findings, CT was performed on Siemens Sensation 40 slice modified discrete cosine transform (MDCT) using 50 ml of intravenous (IV) contrast. The sections of 0.6 mm thickness were obtained and reconstructed at 1.0 and 3.0 mm thickness. There was evidence of bilaterally symmetrical osseous expansile lesions involving body, angle and rami. It revealed bone remodeling, cortical thinning, multilocular contour with coarse trabecular pattern. Multiple cystic/lucent areas were seen within the lesion, which contains low attenuation materials [Figure 4a-c].

CT-axial and coronal contrast images showed symmetric expansion of the mandible with "ground glass" appearance.

Different CT-Axial sections from symphysis region, body, ramus and angle of mandible were taken [Figure 5a-d]. The multilocular radiolucency was found to be gradually increasing in size from body to angle of mandible.

Histopathological investigations

Histopathological examination revealed multinucleated giant cells (up to 10 nuclei) with interlacing bundles and whorls of spindle cells and moderate vascular stroma. It also showed an eosinophilic perivascular cuffing of collagen [Figure 6a and b].

Differential diagnosis

Asimilarity with central giant cell lesions and hyperparathyroidism was found to be present in the histological findings. In cherubism, multinucleated giant cells are found scattered throughout collagenous and vascularized fibrous connective tissue. There was presence of dense connective tissue that is highly or poorly cellularized, with a smaller or larger number of collagen fibers, depending on the progression of the lesion.

Furthermore, central giant cell lesion can be excluded on the basis of clinical background, as it is not bilateral in nature and does not regress in adulthood. It can be distinguished

by radiological findings as most lesions are unilocular in nature.

Hyperparathyroidism can be excluded on the basis of laboratory tests as serum calcium and parathyroid hormone (PTH) levels are found to be increased and phosphorus levels are found to be normal or reduced. In present case, laboratory investigations showed normal calcium and phosphorus level with increased levels of alkaline phosphatase.

DISCUSSION

Cherubism is a rare autosomal dominant benign lesion of childhood. It appears as bilateral painless swellings of mandible and maxilla, which progresses until puberty and

then spontaneously abates. To date, many cases have been added to the literature without restriction to any one country or ethnic group. Cherubism appears to be uncommon in India as compared with the incidence in other countries. Here, a case of a 13-year-old Indian cherubic child is reported.

According to World Health Organization (WHO), cherubism belongs to a group of nonneoplastic bone lesion that affects only the jaws. It is also considered a member of the family of fibrous osseous diseases and some authors refer this disorder as familial fibrous dysplasia.^[7]

In 1978, Arnott,^[8] suggested a grading system for the lesions of cherubism. Cherubism is divided into grades I, II, III and IV, depending on location and the severity of involvement of jaws. These classifications are based on extent of lesion at the time of evaluation. Our case falls under grade I of this classification, i.e. involvement of both the mandibular ascending rami.

Ueki *et al.*,^[4] have previously proposed possible explanations of the pathogenic mechanism. Hyckel *et al.*,^[9] have also reported

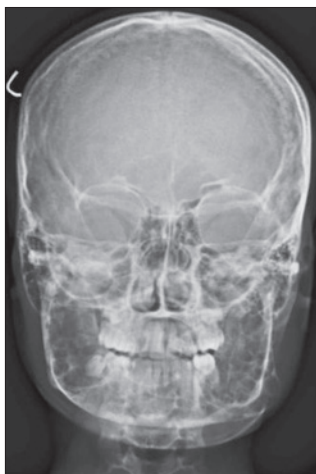


Figure 3: Postero-anterior view of skull shows multilocular radiolucency extending bilaterally on both sides of mandible

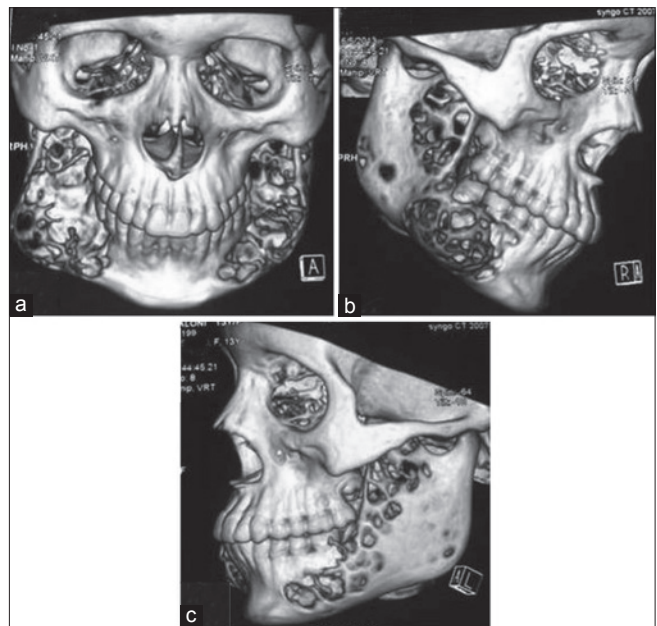


Figure 4: (a-c) CT 3D reconstruction image shows osseous expansile lesion

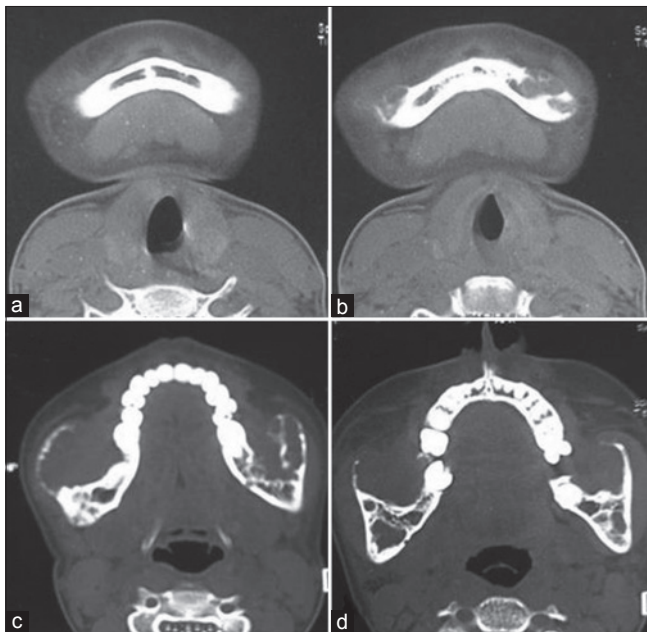


Figure 5: (a-d) Different CT axial sections from symphysis, body, ramus and angle region

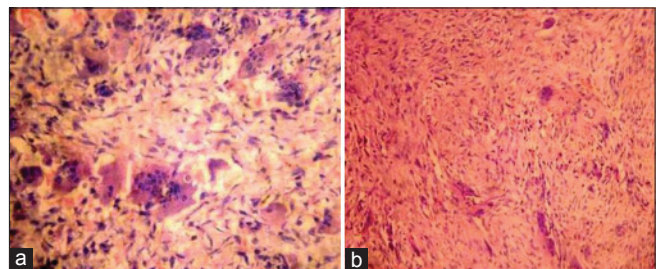


Figure 6: (a and b) Histopathological images showing multinucleated giant cells with spindle cells arranged in bundles (H&E stain, ×400 and ×100, respectively)

a case study to advance the understanding of the etiology and pathogenesis of cherubism. It is hypothesized that the development of the lesions in cherubism might be linked to the development of the second and third molars because these molars are frequently missing or displaced in cherubism.^[9] Furthermore, the lesions in cherubism are always located in the jaw, where the second molar starts mineralizing at 2- or 3-years-old and the normal odontogenesis stops at adolescence.

Clinical or radiographic findings of cherubism are not evident until the age of 14 months to 3 years of age. This disease tends to show variable degree of remission or spontaneous involution after puberty; nevertheless, some facial deformity may persist. In rare cases, the disease remains active during adulthood.^[10] Typically, earlier the lesion appears, more rapidly it progresses. The progressive swelling of the face, with marked increase in fullness of cheeks and jaws, is common to all cases and is due to enlargement and expansion of the underlying bony structures, the skin and subcutaneous tissue being normal. The bilateral enlargement of maxilla when present contributes to cherubic analogy by causing stretching of skin of the cheeks, thus exposing a thin line of sclera causing eyes raised to heaven look. This was not reported in this case and is rarely encountered in other case reports.

Frequently cherubism is accompanied by abnormalities in the configuration of dental arch and dental eruption. In severe cases, tooth resorption also occurs. Such findings were absent in present case except for absence of mandibular left second permanent molar and tooth bud was displaced in panoramic radiography.

The signs and symptoms of disease depend on the severity of the condition, range from clinically, radiologically undetectable features to grossly deformed jaws, upright palate, respiratory obstruction and impairment of vision and hearing. In few cases, cherubism has been described as being connected with other diseases and conditions such as Noonan's syndrome.

In the present case, there was no association with the syndrome.

Raposo-Amaral *et al.*,^[11] speculated that cherubism is a disease of odontogenic origin and suggested a hypothesis that condyles and zygomatic arches are not affected because tooth buds do not develop in these skeletal segments. The SH3BP2 mutation leading to PTH chaperone protein disruption of normal tooth germ development lends additional support to this hypothesis.^[11]

Radiologically it is characterized by bilateral multilocular cystic expansion of the jaws. Cystic areas in the jaws become reossified resulting in irregular patchy sclerosis. The borders are distinct and divided by bony trabeculae. In mandible, it causes thinning and expansion of the cortical plates with occasional perforation. Displacement of the inferior alveolar canal may be noted.^[12] The presence of numerous unerupted teeth and

the destruction of the alveolar bone may displace the teeth, producing an appearance referred as 'floating tooth syndrome'.

With the adulthood, the cystic areas in the jaws become re-ossified, which results in irregular patchy sclerosis and gives a classical 'ground glass' appearance,^[2] but is nonspecific as in our case. Plain radiographs and CT scans are sufficient for diagnosis of cherubism. Marck and Kudryk^[13] reported that conventional radiography provided a limited image because it is only two dimensional. On the other hand, CT provided a realistic picture of the lesions, showing some aspects that otherwise would not be demonstrable due to superimposition and the anatomical complexity of the jaws. CT scan contributes to the diagnosis at all stages of cherubism. CT is considered as a useful tool for the assessing the damage caused by the process either during the analysis of disease progression or during surgical planning.^[14] Advancements in virtual three-dimensional (3D) reconstruction of anatomic structures based on CT or cone beam CT data helps to provide more predictable individual treatment planning.

Histopathologically, the lesion can be characterized into three subtypes: I—predominance of multinuclear cells, II—predominance of inflammatory activity and III—predominance of fibrosis.^[12] Our case falls under subtypes-I in histopathologic findings. An eosinophilic perivascular cuffing of collagen is considered characteristic of cherubism; this feature was present in our case.

The clinical and histological features of cherubism may sometimes present problems in diagnostic distinction from giant cell granuloma, giant cell tumor, ossifying fibroma, fibrous dysplasia of the jaw and Paget's disease of bone. Giant cell granuloma, in particular, can only be distinguished by radiological findings because most lesions are unilocular, whereas in cherubism the lesions are multilocular.^[15] If the mandible alone is involved and there is no family history, it is impossible to differentiate on clinical grounds between cherubism and multiple granulomas in the jaw.

As Laskin (1985) stated "the treatment of cherubism should be based on the known natural course of the disease and the clinical behavior of the individual case."^[2] Treatment protocols for cherubism are not well established because the disease does not progress after puberty and, as the patient grows into adulthood, the bone lesion tends to develop a normal contour. However, in severe cases, when there is functional and esthetic impairment, surgical intervention becomes necessary. Various treatment plans for cherubism have been reported that ranges from no treatment, extraction of teeth or surgical contouring of the expanded lesion to complete curettage or enucleation.

Surgical interventions are advised to be performed on individuals between 5-15-years-old with disfiguring enlargement of jaws or locally aggressive lesions associated with complications.

Early treatment (orthodontic and surgical reconstruction of the jaw) may reduce the risk for secondary complications like upper airway obstruction, obstructive sleep apnea and tooth displacement. An attitude of wait-and-see is also preferred mode of treatment.

A pharmacological modulation of bone metabolism could be a therapeutic option in the future.^[16] During recent years, experimental use of calcitonin in the treatment of cherubism has been described.

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