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CASE STUDY

CLINICAL AND SURGICAL MANAGEMENT OF AN AGGRESSIVE CHERUBISM

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ABSTRACT

Cherubism is a rare autosomal-dominant inherited syndrome and is usually self-limiting. It starts in early childhood and involutes by puberty. It is a benign fibroosseous disease, characterized by excessive bone degradation of jaws followed by development of fibrous tissue masses. The purpose of this clinical report is to describe a rare and aggressive form of cherubism on a patient that has been treated by gingivectomy and gingivoplasty to correct the gingival defects and the bone defect was allowed to correct by itself to increase the patient's quality of life.

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INTRODUCTION

Cherubism is a rare disease of autosomal dominant inheritance characterized by painless, frequently symmetrical, enlargement of the jaws as a result of the replacement of bone with fibrous tissue in the pediatric population, mostly below five years of age. (Lima G. de *et al*., 2010; Atalar *et al*., 2008) Typically the mandible is primarily affected and in 60% of the cases maxilla is also involved. (Stiller *et al*., 2000) It was first described by Jones (1933) as a "familial multilocular disease of jaw" in three siblings who appeared as though they were "looking towards heaven". This inspired him to call the condition "cherubism", to describe the round appearance of the cheeks, typical of cherubs, resulting from jaw hypertrophy. (Jain *et al*., 2007) The word 'cherubism' refers to the spherical facial appearance of angels painted in the Renaissance era. The characteristic spherical and symmetrical chubby facial appearance observed in cherubism is diagnostic of the condition. (Lima G. de *et al*., 2010; Atalar *et al*., 2008; Silva *et al*., 2007) It is also known as Familial fibrous dysplasia of the jaw/ Disseminated juvenile fibrous dysplasia/ Familial multilocular cystic disease of the jaw/ Familial fibrous swelling of the jaw. Affected children usually present before five years of age with painless progressive swelling of the cheeks, frequently associated with dental malformations. It progresses until puberty, and shows partial or complete spontaneous involution in adulthood, regression is expectedto occur spontaneously by the end of adolescence, resolving by middle age, therefore, management is mostly conservative. (Jain *et al*., 2007; Silva *et al*., 2007) Although the condition is known to be hereditary, in some cases there has been no detectable family history and although it usually occurs bilaterally there have also been cases of unilateral involvement Reade *et al*. (1984) perhaps because of incomplete penetrance or new mutation. (Gomes *et al*., 2011; Reade *et al*., 1984) Cherubism is a rare non-neoplastic hereditary disease related to genetic mutations. It is caused by seven mutations at exon 9 (Etoza *et al*., 2011) in the gene encoding SH3-binding protein SH3BP2 on chromosome 4p16.3. The SH3BP2 mutation is thought to lead to parathyroid hormone receptor (PTHr) signaling and Msx-1 activation. (Lima G. de *et al*., 2010; Silva *et al*., 2007; Gomes *et al*., 2011) The gain-of-function mutation results in a compartmentalization failure of the cap stage during molar development leading to deregulation of bone formation and remodelation, development of multinucleated giant cells and

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abundant deposition of fibrohistiocytic tissues. (Gomes *et al*., 2011) Mutation of the gene encoding for fibroblast growth factor receptor III (FGF-RIII) has also been found in some cases of cherubism. (Peñarrocha *et al*., 2006)

Case report

A 11 year old male child reported along with his father with a complaint of missing teeth in both upper and lower jaw along with painless enlargement of the lower face. Patient's history revealed no abnormalities until the age of 3 years, later bilaterally symmetrical swelling of lower face as seen which progressed rapidly till 7-8 year of age (Fig.1). The patient was of non-consanguineous parents, youngest of the two siblings and was born as a full-term normal delivery. On physical examination it was observed that the patient was athletic, active and mentally alert. No abnormality was found on clinical examination of chest, abdomen, cardiovascular system and central nervous system. The patient did not suffer from any mental or physical disability. Both right and left submandibular lymph nodes were palpable, non tender, mobile and firm in consistency. On extraoral examination, no facial or ophthalmic abnormalities were noted. There was asymmetrical enlargement on both sides. Enlargement was firm and non-tender on palpation, extending from anterior border of ramus of mandible to the mandibular premolar region on right side and from anterior border of ramus of mandible to mandibular molar region on left side with well demarcated margins. Intra oral examination revealed the gingiva to be pink, firm and fibromatous. The teeth were almost completely covered by gingiva, bleeding on probing was present in all the teeth and both right and left mandibular buccal vestibular fullness was seen due to the swelling (Fig. 2). Panoramic radiograph revealed extensive involvement of mandible by multilocular cystic lesions, destruction of the alveolar bone, retained deciduous teeth, unerupted and displaced posterior permanent teeth along with small, tightly compressed tubercular pattern giving ground glass appearance (Fig. 3). A biopsy under local anesthesia was performed from right buccal vestibule and a fragment from the lesion was removed. Histological examination revealed a delicate connective tissue stroma with numerous fibroblasts, extravasated RBCs, perivascular eosinophillic cuffing and low density (4 to 6 giant cells per 200 field) of multinucleate giant cells associated with an extensive and dense or highly cellular fibrotic component. (Fig. 4 and 5) Laboratory investigation showed the haemoglobin level to be 13.5gm/dl, hematocrit value of 42.4 (normal 40 to 52%) and serum alkaline phosphate level to be 68 IU/L (normal 56 to 156 IU/L).

The differential diagnoses of cherubism include fibrous dysplasia, gaint cell granuloma of the jaw. Patients with fibrous dysplasia present at a later age, usually between 15 and 30 years of age, and lack the typical "cherubic" look. Also, the lesions do not have a tendency to regress after puberty. On imaging, the multiloculated, ground glass lesions of fibrous dysplasia closely resemble cherubic lesions; however, they are rarely ever bilaterally symmetrical. Giant cell granuloma is a close mimic of cherubism. Histologically, lesions of central reparative granuloma are indistinguishable from those of cherubism; however, radiologically, these lesions have a predilection to involve the anterior mandible. They are rarely bilateral or symmetrical, and it is unusual for them to involve the maxilla, unlike the distribution in cherubism. The age of presentation is also later, usually between 10 and 30 years of age. (Lima G. de *et al*., 2010; Gomes *et al*., 2011; Southgate *et al*., 1998) Based on clinical features and results of lab investigations the lesion was diagnosed as grade I cherubism. (according to the grading system forcherubism by Seward and Hankey, 1957; Seward and Hankey, 1957) Laskin (1985) (Rajendran, 2006) stated, "the treatment of cherubism should be based on known natural course of the disease and the clinical behaviour of the individual case" and the regression of lesion is expected to occur spontaneously by the end of adolescence, resolving by middle age, therefore, management is mostly conservative. (Jain *et al*., 2007; Silva *et al*., 2007)

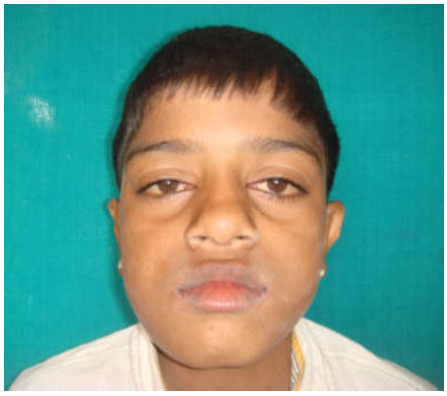

Figure 1. Bilaterally symmetrical swelling of lower face

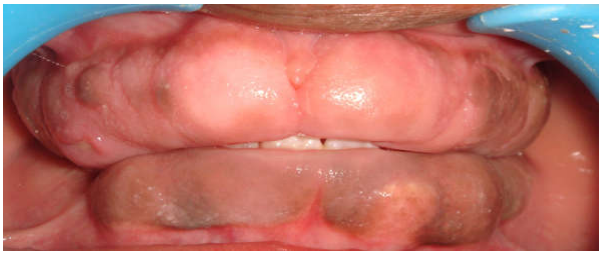

Figure 2. Right and Left Mandibular Buccal Vestibular Fullness

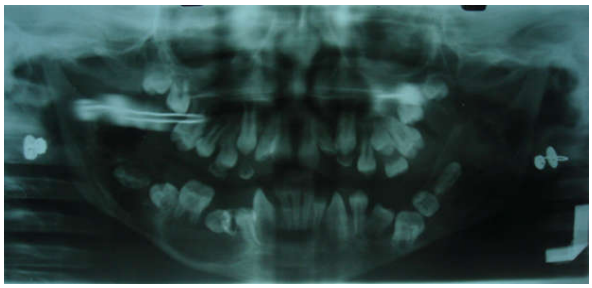

Figure 3. Panoramic Radiograph

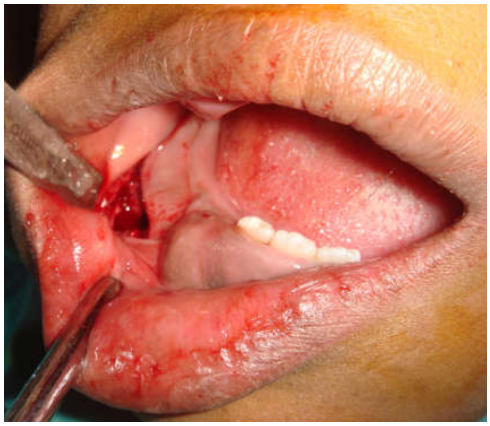

Figure 4. Biopsy

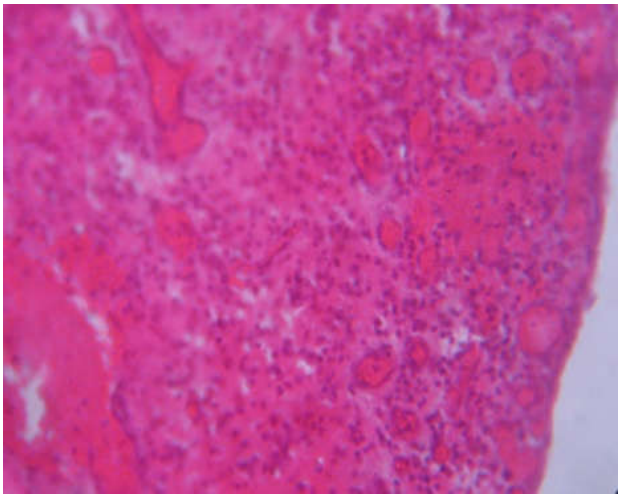

Figure 5. Histological Examination of the Lesion

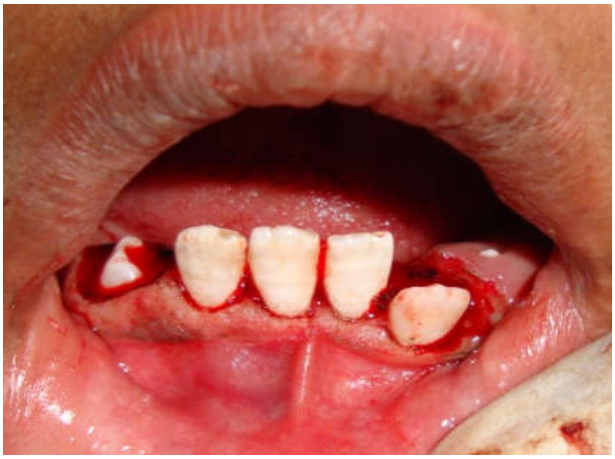

Figure 6. Post Operative view after Gingivectomy and Gingivoplasty

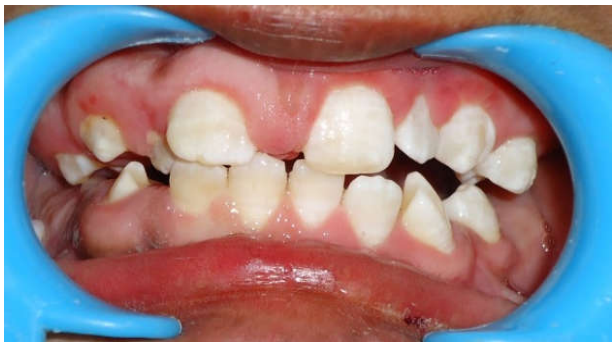

Figure 7. Post operative view

Hence in the present case, gingivectomy and gingivoplasty to correct the gingival defects was performed and the bone defect was allowed to correct by itself. Gingivectomy and gingivoplasty using electrocautery under local anesthesia was planned. Under standard betadine and towel preparation, the pocket on each surface were explored with a periodontal probe and marked with a pocket marker. Each pocket was marked in several areas to outline its course on each surface. Scalpel with 15 number surgical blade was used for incision on both facial and lingual surface and distal to terminal tooth in each arch. The incision was started apical to the points marking the course of pockets and was directed coronally to a point between the base of the pocket and the crest of the bone. Continuous incision was used, and the incision was bevelled approximately 45 degree to the tooth surface and the normal festooned pattern of the gingiva was recreated, as far as possible. (Fig. 6 and 7)

DISCUSSION

Cherubism is a rare hereditary autosomal dominant benign lesion of childhood. It appears as bilateral painless swelling of mandible and maxilla which progress until puberty and then spontaneously abates. Cherubism appears to be uncommon in India compared with the incidence in other countries. (Niranjan *et al*., 2014) Here a case of a 11 year old Indian male cherubic child is reported. According to the WHO, cherubism belongs to a group of non-neoplastic bone lesion (K10.80) that affects only the jaws. (World Health Organization, 1995) It is also considered member of the family of fibrous osseous diseases and some authors refer this disorder as familial fibrous dysplasia. (Southgate *et al*., 1998)

Seward and Hankey (1957), suggested a grading system for the lesion of cherubism as follows:

Grade I: Involvement of bilateral mandibular molar regions and ascending rami, mandible body, or mentis.
Grade II: Involvement of bilateral maxillary tuberosities (in addition to grade I lesions) and diffuse mandibular involvement.
Grade III: Massive involvement of entire maxilla and mandible, except the condyles. Grade IV: Involvement of both jaws, including the condyles.

Histologically, it is characterised by presence of numerous multinucleated giant cells. These multinucleated cells show strong positivity for tartarate-resistant acid phosphate, which is characteristic of osteoclast. The collagenous stroma, which contains a large number of spindle shaped fibroblast, is considered unique because of its water logged, granular nature. Numerous small vessicals are present and the capillaries exhibit large endothelial cells and perivascular cuffing. The eosinophilic cuffing appears to be specific to cherubism. However, these deposites are not present in many cases and their absence does not exclude the diagnosis of cherubism. Older resolving lesion of cherubism shows an increase in fibrous tissue, a decrease in number of giant cell and formation of new bone. Based on presence of giant cells and fibrous tissue, Peñarrocha *et al*. (2006) described the types for cherubism as follows (Peñarrocha *et al*., 2006) –

- Subtype I: High cell density: 160 to 180 giant cells per 200 field, intermingling with small areas of interstitial microhemorrhage.
- Subtype II: Low cell density: 10 to 15 giant cells per 200 field, intermingling with inflammatory and interstitial microhemorrhagic areas.
- Subtype III: Low cell density: 5 to 8 giant cells per 200 field, associated to an extensive and often dense or highly cellular fibrotic component.

The present case was reported with chubby facial appearance, gingival fibromatosis, Radiographically lesion shows ground glass appearance that involving both mandibular ascending rami and histological features suggested Grade I subtype III cherubism. Early studies reported cherubism to be a familial disease with autosomal dominant inheritance and a variable degree of penetrance and expressivity. There was no history of a similar disease in any of the family members of our patient,

thus adding to the list of non-familial cases that have now been reported in literature. (Jain *et al*., 2007) Clinical and radiographic finding of cherubism are not evident until the age of 12 months to 36 months of age. (Jain *et al*., 2007) Typically, the earlier the lesion appears, the 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. Atalar *et al*. (2008) found 60% cases of cherubism shows involvement of mandible. (Atalar *et al*., 2008) 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 the present case and was 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 occurs. The signs of condition range from clinically, radiologically undetectable features to grossly deformed jaws, upright palate, respiratory obstruction, 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. Jaw and face lesions with displaced teeth were the only clinical abnormalities present in the present case. Radiographically, it is characterised by bilateral multilocular cystic expansion of jaws. Cystic areas in the jaws become reossified resulting in irregular patchy sclerosis. The presence of numerous unerrupted teeth and the destruction of the alveolar bone may displace the teeth, producing an appearance referred as 'floating tooth syndrome'. (Atalar *et al*., 2008) Classic ground glass appearance because of compressed trabecular pattern is seen but is nonspecific as in our case. In few cases radiographic examinations of other areas of the patient sometimes reveals peculiar cyst like changes in the ribs, humerus, femur and tibia. The treatment of cherubism depends on the rate of progressionof the lesion, extension of tissues involved and emotional state of the patient. The general recommendation from previous studies is to postpone the treatment until after puberty, unless severe psychological and physiologic dysfunctions impose an early intervention. (Gomes *et al*., 2011)

Treatment options suggested are

- Provide no treatment- As the regression of lesion is expected to occur spontaneously by the end of adolescence, resolving by middle age, therefore, management is mostly conservative. (Lima G. de *et al*., 2010; Jain *et al*., 2007; Silva *et al*., 2007) It is better if surgical intervention is delayed until after puberty. (Atalar *et al*., 2008) The clinicians choice in monitoring the patient´s condition was based on routine observation and literature data. (Teixeira *et al*., 2004) Surgical treatment is unnecessary unless functional or emotional disturbances develop.
- Surgical curettage and medical therapy with calcitonin - Curettage has been suggested to be as a good approach since this intervention stimulates bone replacement. (Lima G. de *et al*., 2010) Some authors point medical therapy in the form of calcitonin as a possibility to curtail the disease and obviate the need for surgery. (Lima G. de *et al*., 2010; Etoza *et al*., 2011) Gomes *et al*. (2010), managed a case of aggressive cherubism with autogenous bone graft and salmon calcitonin by nasal sprayand after 4-year follow up, confirmed the stomatognathic system improvement and esthetic rehabilitation. (Gomes *et al*., 2011)
- Contouring / osteotomy- There is general agreement that in extreme cases in which important functions are impaired, surgical intervention should be performed as early as possible. (Lima G. de *et al*., 2010) Curettage alone or in combination with surgical contouring has been considered the treatment of choice and some authors have reported a massive growth of the lesion after surgery, especially when this is performed during active growth phase. (Stiller *et al*., 2000)
- Liposuction- Liposuction has been used to change the contour of the jaws in patients with cherubism. (Stiller *et al*., 2000)
- Radiation therapy- It has been abandoned as a treatment of cherubism because of the potential risk of osteoradionecrosis or even malignant transformation of the process resulting in osteosarcoma. (Lima G. de *et al*., 2010)

Conclusion

In general, cherubism has a good prognosis. Cherubism does not progress after puberty and as the patient grows to adulthood, the entire jawbone lesion tends to develop a more normal configuration. Surgery is not a treatment of choice. But in case of expansion of tissue resulting in difficulty with airway or chewing capacity, biopsy and surgical intervention can be done. Medical attention for aesthetic and functional concern is required.

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