CASE REPORT

CHERUBISM: REPORT OF A CASE

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ABSTRACT

Cherubism is a non-neoplastic fibro-osseous lesion that is diagnosed among children based on its characterization by bilateral painless enlargement of jaws that offers a cherubic appearance to the affected persons. The treatment of such lesion is combative, it may regress during puberty leaving some facial deformity and malocclusion. Cherubism may occur in solitary cases or in many members of the family. In this case report we are presenting such a case in which 9yr old cherubic male child, with positive family history describing the clinical, biochemical and radiographic features.

KEY WORDS

Cherubism, familial multilocular cystic disease of jaws, floating teeth

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INTRODUCTION

Cherubism is an inherited disorder that is transmitted as an autosomal dominant, benign self-limiting fibrosseous bone disease, but sporadic cases have also been documented. It was first recognized as a separate entity in 1933 by William A. Jones a Canadian radiologist in family of jews affecting three siblings. The name "cherubism" is so accurately captured because of the clinical features of the disease and it became the standard nomenclature (plump cheeked little angels (cherubs). Mutation of the SH3BP2 gene on chromosome 4 (SH3-domain binding protein) is the main etiology of the occurrence. The protein encoded by SH3BP2 is essential for bone metabolism. Because of the presence of the full round cheeks and the upward cast of the eyes give the children a peculiarly" cherubic appearance.[1,2]

Although penetrance of cherubism is known to be 100% for males and 50% to 70% for females, some clinical studies have shown that mutation in this gene does not have 100% penetrance in males.[3] The disease is characterised by presence of symmetrical, painless bilateral expansion of the jaws as a result of the replacement of normal bone by proliferation of fibrovascular tissue containing multi nucleated giant cells, displaced and/or missing teeth or tooth germs.[1]

Radiographic findings include multilocular, radiolucent lesions of the mandible and/or the maxilla. The enlargement of the jaw bones occurs as an isolated finding and affected children do not have other mental or physical abnormalities. However, it has been occasionally associated with other genetic disorders, such as Noonan-like syndrome or Noonan-like/multiple giant-cell-like lesion syndrome.

It is classified as quiescent, non-aggressive and aggressive on the basis of clinical behaviour and radiographic findings. Quiescent cherubic lesions are usually seen in older patients and do not demonstrate progressive growth. Non-aggressive lesions are most frequently present in teenagers. Lesions in the aggressive form of cherubism occur in young children and are large, rapidly growing and may cause tooth displacement, root resorption, thinning and perforation of cortical bone.

Motamedi[3] proposed a grading system for cherubism in 1998 which was modified by Raposo-Amaralet al[4] in 2007. Table: 1

This article highlights the case of grade 2 class 2 type cherubism

CASE REPORT

A 9 year old male referred to the department of pedodontics and preventive dentistry with chief complaint of painless, progressive bilateral symmetric thickening of the lower jaw since 3 years. There was discrepancy in normal teeth eruption pattern.

On extraoral examination normal expression and colour of the face was seen. There was no ophthalmic abnormality. There was symmetrical enlargement of both sides of mandible. Enlargement which was non tender and hard on palpation. Submandibular lymph nodes were bilaterally palpable, non tender and mobile. Intraoral evaluation was normal. On the basis of clinical findings, our provisional diagnosis was cherubism, giant cell granuloma, and brown tumour of hyperparathyroidism.

In the view of these finding we decided to perform panoramic radiograph and head CT scan in order to guide the diagnosis. Radiographs showed several multilocular cysts involving bilateral posterior body of mandible, angle and rami extending towards coronoid process sparing condyle. CT examination revealed expansileosteolytic lesion involving body and ramus of the mandible on both sides. There was marked thinning of cortex on both sides. Extension of lesion was also seen in maxilla. Anterior walls of maxillary sinus appeared more affected than posterior, mainly on right side. Visualized portion of base of the skull appeared normal

Laboratory investigations showed a haemoglobin level of11.2 gm/dl (normal 13 to 18 gm/dl), haematocrit value of 37.5% (normal, 40 to 52%), each being slightly low, and an elevated alkaline phosphatase value of 629 IU/L (normal,85 to 270 IU). Parathyroid hormone level and other lab investigations were within normal limits. No significant alteration was observed with biochemical analysis of calcium metabolism.

The history revealed that the patient had been born as a full-term normal delivery to a healthy mother with a low birth weight 1.5 kg thorough he was admitted to natal intensive care unit and

Table: 1

Grade I: Lesions of the mandible without signs of root resorption	Class 1 solitary lesion of the mandibular body Class 2 multiple lesions of the mandibular body Class 3 solitary lesion of the ramus Class 4 multiple lesions of the rami Class 5 lesions involving the mandibular body and rami
Grade II: Lesions involving the mandible and maxilla without signs of root resorption	Class 1 lesions involving the mandible and maxillary tuberosities Class 2 lesions Involving the mandible and anterior maxilla Class 3 lesions involving the mandible and entire maxilla
Grade III: Aggressive lesions of the mandible with signs of root resorption	Class 1 solitary lesion of the mandibular body Class 2 multiple lesions of the mandibular body Class 3 solitary lesion of the ramus Class 4 multiple lesions of the mandibular rami Class 5 lesions involving the mandibular body and rami
Grade IV: Lesions involving the mandible and maxilla and showing signs of root resorption	Class 1 lesions involving the mandible and maxillary tuberosity Class 2 Lesions involving the mandible and anterior maxilla Class 3 lesions involving the mandible and entire maxilla
Grade V: The rare, massively growing, aggressive, and extensively deforming juvenile cases involving the maxilla and mandible, and may include the coronoid and condyles	
Grade VI: The rare, massively growing, aggressive, and extensively deforming juvenile lesions involving the maxilla, mandible and orbits	

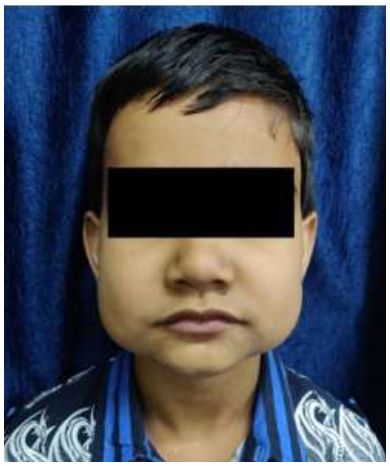

Figure 1: showing the extraoral bilateral symmetrical enlargement of mandible

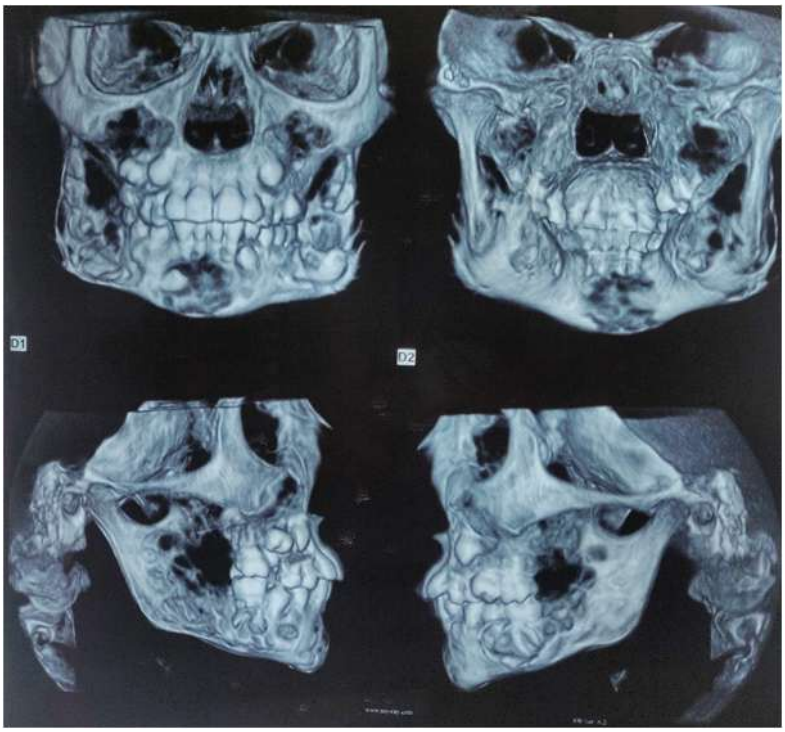

Figure 2: Coronal and sagittal section showing the expansileosteolytic lesion involving body and ramus of the mandible on both sides

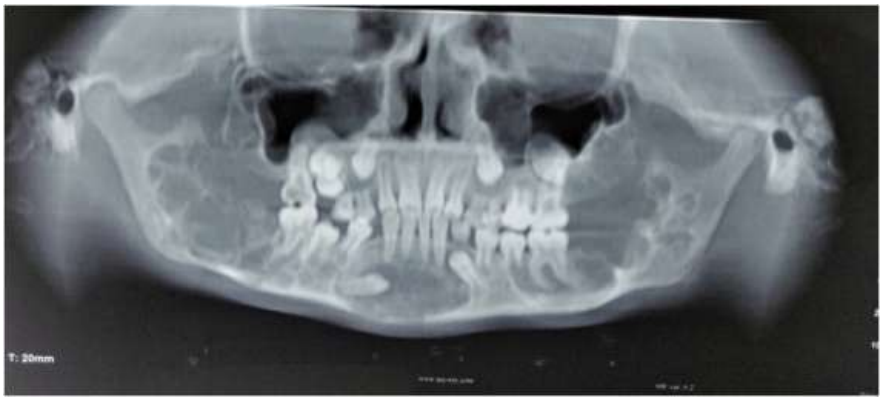

Figure 3: Multilocular cysts involving bilateral posterior body of mandible,

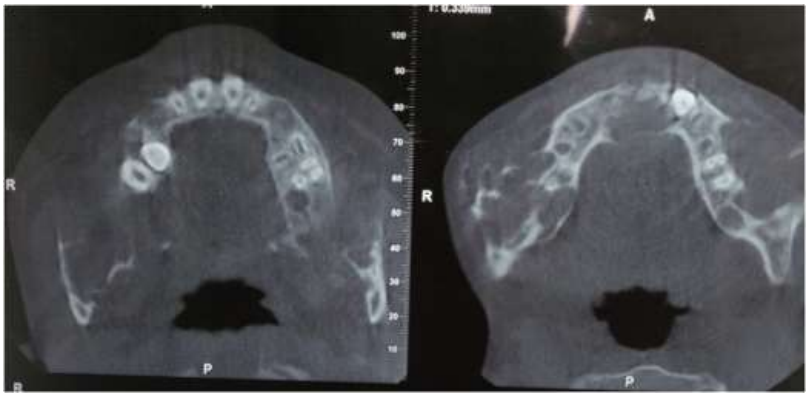

Figure 4: Axial section showing the thinning of cortex.

discharged after two weeks in good condition. The patient showed no abnormalities until the age of 3,his mother noticed a symmetrical bilateral enlargement of the lower face. This enlargement had continued progressive fashion as the patient grows. Family history showed that his father had a similar bilateral fullness of the cheeks and had gone through surgery when he attained 18yr of age. On physical examination it was seen that patient was a 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; there was no evidence of endocrinal disturbance.

The clinical and radiological findings confirmed the diagnosis of cherubism. After doing a detailed clinical review, it was decided that the patient will be kept under observation till he attains the age of puberty. Surgery, if required, will be decided at a later date.

DISCUSSION

The distinctive feature of cherubism is the development of symmetrical multilocular radiolucent expansile lesions in the mandible and/or the maxilla. Cherubism is also called familial fibrous dysplasia of the jaws, but the recent genetic mapping has shown it to be a separate entity at the molecular level.[2] It is more common in males than females. It has a familial inheritance in approximately 80% cases with a variable expressivity in both jaws. Classically the patient is normal at birth; onset generally starts between 14 months to five years of age, however in severe cases it may be seen at the time of birth. It keeps on progressing until puberty but in some cases, it may resolve without any treatment or actively grown in young adults 1, As in our case the patient's father gave the history of persistent of lesion after the puberty.

Submandibular and cervical **lymph nodes** are enlarged during the early stages of cherubism during the swelling of lower jaw and maxilla respectively. **Extracranial involvement** is extremely rare and most cases have not been confirmed by genetic testing. Some of the studies has reported the involvement of such lesion in the ribs. The **orbital effects** of cherubism are due to this displacement and not to direct invasion of the globe and surrounding extraocular muscles. Due to retraction of the lower lids by the stretched skin over the cheeks because of which a line of sclera is exposed and the eyes appear to be raised to heaven. In rare cases it may invade the retrobulbar spaces of the orbits and cause displacement of the optic nerves and proptosis.[5]

The impact of cherubism lesions on pattern of **dentition** varies. The arrangement of primary teeth can be disturbed. Disruption of the secondary dentition can include absent teeth (mostly molars), rudimentary development of molars, abnormally shaped teeth, partially resorbed roots or delayed and ectopically erupting teeth. Treatment such as tooth extraction in case of 'floating teeth' or ectopic eruption of teeth and prosthesis requirement if needed.6In the present case the lower premolar tooth bud was absent in orthopantomography.

Mineral metabolism is mostly normal in patients with cherubism, and serum levels of calcium, parathyroid hormone (PTH), parathyroid hormone related peptide (PTHrP), calcitonin and alkaline phosphatase (ALP) are typically within normal range.[7] **Histopathologic features** of the aforementioned lesions are similar to central giant cell granuloma. Thus, Cherubism cannot be diagnosed by histology alone because they are not distinguishable from other giant cell lesions of bone. The histological findings at various stages of this lesion are; present of numerous rounds, fusiform and multinucleated giant-cells at the earliest, then proliferative spindle cells stage associated with a reparative stage, last stage is attributed to bone formation with cells staining positive for alkaline phosphatase.

The familial form of cherubism occurs typically in an autosomal dominant trait with mutations in the SH3-domain binding protein 2 (SH3BP2) on chromosome 4p16.3. Mutations in SH3BP2 result in osteoclasts that lead to increased bone resorption in jaws of cherubism patients. Additionally, cherubism has been reported in rare cases of Noonan syndrome (a developmental disorder characterized by unusual facial characteristics, short stature, and heart defects) and fragile X syndrome (a condition primarily affecting males that causes learning disabilities and cognitive impairment).

Mild forms of cherubism without facial dysmorphology, dental and ocular involvement may not require **treatment** as cherubism is expected to regress spontaneously after puberty, longitudinal observation is mandatory in such cases. However, in some cases the cherubism may still advances in adult. Surgical intervention is indicated in such cases which includes partial resection, contour resection, curettage or a combination of these. That should be done after puberty when the lesions are quiescent. Development of dentition should always be closely monitored. Problem such as early exfoliation of primary teeth, absent of permanent teeth, impacted teeth and also the malocclusion. While such problems require space maintainer for space prevention, extraction of impacted teeth and prosthesis in the later stages.[8]

Radiation therapy has been seen in some of the study but it is having some of the contraindication and potential for long-term adverse consequences such as retardation of jaw growth, osteoradionecrosis and increased incidence of induced malignancy. Favourable results have been obtained with calcitonin administration in the management of CGCG that antagonist the osteoclastic activity.

According to Novack and Faccio[9], hypothesis, cherubism is caused by enhanced cytokine tumour necrosis factor α (TNF-α) production by myeloid cells due to an activating mutation in Sh3bp2 not only represents a major advancement in the understanding of the disease but suggests new potential options for its treatment. Hence, use anti TNF – α would be more advantageous as it is already being used for the treatment of rheumatoid arthritis.

A prosthetic treatment for a cherubism patient was reported by Yilmaz at al.[10] Author presented a case in which some of the mandibular molar has been extracted and the implant would be a big failure in such cases because placement of implant in porous bone might result in lack of osteointegration thus treatment was planned as fixed partial dentures preparation for the maxilla and an overdenture with copings for the mandible.

CONCLUSION

As this case report emphasis, the case of 9-year-old boy showing the clear cherubic look, clinically having no pain or other issue. Radiographic investigation reveals the multilocular cystic lesion which is bilateral involving the jaw. In such cases only regular follow up and timely clinical observation is mandatory any intervention should be delayed until puberty. As the patient parents concern was related to aesthetics, the patient and parents counselling is very much required in such cases. Also, this was the case with familial inheritance. Counselling by a medical geneticist or genetic counsellor is recommended as family members are concerned that they may have cherubism. A gene test may resolve the concern if a mutation has been identified in the proband. Thus, the patient parents were referred to medical consultant.

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