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Cherubism: A Case Report

KEYWORDS: Cherubism ,posterior mandible,giant cells, stroma, biopsy

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ABSTRACT *Cherubism is a rare disease of autosomal dominant inherited fibro-osseous bone disease affecting mainly mandible and maxilla causing prominence in the lower portion of face. A 10 yr old male child with a swelling of lower jaw since 3 year had bilateral multilocular radiolucencies in posterior mandible in both X-ray and CT scan. Histopathologic examination revealed proliferating fibrous connective tissue containing numerous multinucleated giant cells .Correlating with clinical, radiological, cytological and biopsy findings it was confirmed to be a case of cherubism. Since it is a self regressingcondition after puberty no treatment was done, with a follow up every 3 months. We reported this case because of its extreme rarity.*

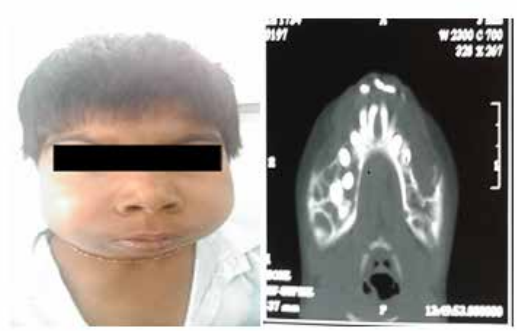
Introduction

Cherubism is a rare disease of autosomal dominant inherited fibro-osseous bone disease affecting the jaws(Penarrocha et al., 2006). Bilateral enlargement of mandible produces rounded face and swollen cheeks accompanied by upward-looking eyes. This condition gives the patient the appearance of cherubs depicted inbaroque artwork hence, the name of the disease.It was first described as familial multilocular cysticdisease of jaw by Jones in 1933. The affected mandible and sometimes the maxilla begin to swell in earlychildhood at 13 month to 2 year age and this gradually increases until puberty(Kaugars et al., 1992). Boys are more affected than girls at the proportion of 2:1 (Caballero et al., 1998)."The variable Cherubism phenotype can range from absence of any clinical features to severe mandibular and maxillary over growth causing respiratory , vision , speech and swallowing concerns". Typical age of onset is 2 to 5 years, with the jaw lesions progressing gradually until puberty –whenthe swelling spontaneously stabilizes and then regresses. Radiographic change can last up to the fourth decade.Although the condition is known to regress spontaneously at puberty, surgical management is sometimes required for cosmetic reasons (Hamner et al., 1969; Kaugars et al.,1992). We present this non-hereditary case of cherubism due to its extreme rarity in the present investigation.

Clinical case

A 10 year old male visited outpatient department of paediatric with complaint of swelling over b/l cheeks since 3 years and b/l submandibular swellingsince 1 year .Swelling was gradually increasing in size . His family history did not include any evidence suggestive of similar complaints.

Physical examination revealed diffuse, symmetrical enlargement of both the jaws, with ill defined margins, extending anteroposteriorly from the angle to parasymphysis region of the mandible on both sides roughly measuring 5x4 cm in size . There were no secondary changes like ulcer or sinus and no discharge. The swellings were firm inconsistency, nontender and there was no pressure effect Skin over the swelling was pinchable and swelling were immobile.The sub-mandibular lymphnode palpable,nontender mobile of size 2 x2cm.High arch palate with right sided palatal thicking and dental malocclusion present.Eye movement normal . Computed topography (CT) scan of the mandible showed well defined, bilateral, multilocular expansile hypodenselesions with moderate enhancement of the soft tissues within it, displacing first mandibular molar anteriorly All available laboratory data were within normal limits including complete blood count , blood urea ,serum creatinine , alkaline phosphate ,HBsAg. Biopsy under general anesthesia wasperformed and a fragment from the lesion wasremoved. Histological examination revealed afibrous tissue with a large number ofmultinucleated giant cells irregularly distributedand ovoid to spindleshaped fibroblasts in a collagenous well vascularized stroma. The diagnosis of cherubism was confirmed from the histology correlating with the history, clinical, radiographic and cytological findings. Since it is a self regressing condition repeated follow up every 3 months was advised.



Discussion

Cherubism is a rare hereditary fibro-osseous childhood disease characterized by bone degradation and fibrous tissue replacement at the angle of mandible and tuberosities of maxilla leading to the prominence of lower face (Gomes et al., 2005). According to WHO classification, cherubism belongs to the non-neoplastic bone lesion group involving mandible. The disease can also be referred as familial or hereditary fibrous dysplasia, bilateral giant cell tumor or familial multiloculated disease (Ozkan et al., 2003).

Natural history :-

a) Classically normal at birth.

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b) Onset between 14 months and 5 years.
However the severe cases are evident at birth. Progresses until puberty. Usually progressive stops after puberty. Regression of bone lesions. (Resolution of the disease without treatment in somecases). Rapidly growing lesions of the maxilla and the mandible including the Coronoids and Condyles – in severely affected individuals

Eyes – raised to heaven Cherubic appearance Fullness of the lower half of the face (Checks and Jaw).

Retraction of the lower lids by the stretched skin-over the checks – pulling down the lower eyelids. Consequently a thin line of sclera is exposed beneath – and the eyes appear to be raised to heaven.

Painless – enlargement of Jaws

Exclusively affecting maxilla and mandible Mandible usually involved. Involvement of the maxilla in 60% of cases. Bilateral enlargement with loss of bone in the jaws and its replacement with large amount of fibrous tissue.Premature loss of deciduous teeth and Displacement of permanent dentitions .Swelling usually – third decade whereas radiographic changes commonly persist until fourth decade. Lower lid retraition , proptosis , diplopia,Globe displacement , Visual loss due to optic nerve atrophy. Rarely the lesion may extend upto the orbit.Displaced tongue affecting speech, mastication swallowing and respiration.

Extremely rare extrafacial skeletal involvement involving the upper humerus,anterior ribs, Upper femoral necks.Rarely associated syndromes – Noonan syndrome (Addane-1995).

Functional impairment – Leading to mastication problems, speech difficulty, and altered tooth. All the above physical and clinical alterations can lead to psychological impairment. When the patient reaches puberty, the osseous lesion of cherubism regress spontaneously. But, the underlying cause of this regression is unknown (Beaman et al., 2004). The widely accepted theory for the pathogenesis of cherubism is the perivascular fibrosis leading to the mesenchymal disorder and decreased oxygenation. A molecular pathogenesis has been proposed, with detection of a mutation in the gene encoding SH3-binding green fluorescent protein 2 (SH3BP2) (Li and Yu,2006).Mineral metabolism is normal in patients with cherubism,and serum levels of calcium, parathyroid hormone (PTH),parathyroid hormone related peptide (PTHrP), calcitoninand alkaline phosphatase (ALP) are typically within normal range (Southgate et al., 1998). Serum levels for alkaline phosphate may be increased during the active stages of cherubism (Ozkan et al., 2003). Serum phosphate may also be increased. Biopsy and histopathologic examination are not required in most cases to establish the diagnosis of cherubism .However, when performed, numerous osteoclast like multinucleated giant cells in a moderately loose fibrous stroma are present. Perivascular eosinophilic cuffing appears to be specific to cherubism. However, these deposits are not present in many cases, and their absence does not exclude the diagnosis of cherubism as seen in our case (Lannonet al., 2001). The differential diagnosis of cherubism includes fibrous dysplasia and giant cell granuloma of mandible. Fibrous dysplasia can present with similar radiographic features to cherubism, however it does not show the swollen cheeks or upward turning of eyes which is the characteristic of cherubism (Pierce et al.,1996). The biopsy of the fibrous dysplasia shows fibroblastic proliferation with scattered multinucleated giant cells and bone trabeculae without osteoblast rimming in addition (Valiathan and Prasanth, 1997). Giant cell granuloma is usually unilatearal and involves patients aged 20 to 40 years. It is not inherited, does not regress in adulthood and has a predilection for the anterior mandible. Its biopsy shows dispersed giant cells in hypervascular fibroblasts and presence of foci of haemorrhage associated with hemosiderine deposition(Valiathan and Prasanth, 1997). In cherubism,eosinophilic collagen cuffing can be observed around small blood vessels. Such perivascular hyalunosis is considered pathognomic of cherubism (Davis et al.,1983). The limited and symmetrical distribution of the cherubism lesions can often facilitate distinction of cherubism from these other conditions, and of course mutation analysis of SH3BP2 can confirm the diagnosis. Mild forms of cherubism without facial dysmorphology, dental and ocular involvement may not require treatment as cherubism is expected to regress spontaneously after puberty. Surgical intervention is indicated 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 (Papadaki et al.,2005). Surgical procedures should be performed after puberty when the lesions are quiescent. Experimental use of calcitonin for the treatment of cherubism has been suggested (Southgate et al., 1998). In our case, the patient showed improvement in a regular follow up in every 3 months interval.

Conclusion

Although rare, cherubism has a significant impact on affected children and their families. This is especially true in those cases where aggressive growth leads to facial deformity and functional problems. Therefore, knowledge of the clinical and radiographic alterations observed in patients with cherubism is extremely important.Counselling by a medical geneticist or genetic counselor is recommended if family members are concerned that they may have cherubism.

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