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# DIAGNOSIS AND MANAGEMENT OF CHERUBISM: A review of literature

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**Abstract:**

Cherubism is a rare benign (non-neoplastic) hereditary condition of childhood, which is inherited as an autosomal dominant trait and is characterized by bilateral expansion of the mandible, maxilla or both. Giving them a characteristic cherubic appearance. The treatment of cherubism is still controversial and is said that the disease regresses itself and after regressing if any asymmetry is left then the bony deformity can be corrected by decortications of bone and osseous shaving. This article reviews the recent development in the literature of cherubism.

**Key words:** Cherubism, benign, non-neoplastic, bilateral.

Introduction:

Cherubism is a non-neoplastic progressive hereditary disease affecting the jaw bones. It occurs bilaterally and symmetrical. Cherubism is a genetic disorder of the Jaw characterized by bilateral, symmetrical enlargement of the mandible or maxilla resulting from rapid bone degradation followed by extensive bone remodelling with multilocular benign cysts. Skin over the swelling is stretched, pulling the lower eyelids down and exposing a line of sclera, giving the eyes a typical appearance named *"rapid heaven ward"*.

The facial appearance of the upwardly turning eyes and swollen cheeks have been described as resembling the faces of cherubs found in Renaissance art. [1,2] The variable Cherubism

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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, then the swelling spontaneously stabilizes and then regresses. Radiographic change can last up to the fourth decade. [3] This disease is usually manifests in facial region only rarely it may affect ribs and other bones of the body. Yet a lot of study is to be done to know the actual genetic treatment for this genetically mediated disease.

**Diagnosis:**

Cherubism is diagnosed on histopathological examination. Other differential diagnosis can be hyperparathyroidism, giant cell tumor, peripheral, and central giant cell lesions of the jaw. Normal level of serum calcium, phosphorus, and alkaline phosphatase rules out hyperparathyroidism. Giant cell tumor commonly involves epiphyses of long bones. Peripheral giant cell lesion is usually related to local factor of gingiva or periosteum. Central giant cell lesions develop in anterior mandible in young females. [4] Cherubism synonymous with familial or hereditary fibrous dysplasia, bilateral giant cell tumor and familial multilocular disease is a rare benign condition with autosomal dominance inheritance. It is one of the very few genetically determined osteoclastic lesions in the human body. [5] It has 100 and 50-70% in males and females, respectively. However, there is a great variation in clinical expression. Cases with no family history or unilateral disease have been described. These cases may be secondary to newer mutation or incomplete penetrance. [5] The locus for cherubism gene is chromosome 4p16. [5] Tiziani concluded locus to be located on the telomeric side of D4S1582. [6] Ueki detected point mutation at SH3 binding protein SH3BP2. [7] Cherubism can be associated with Noonan's syndrome, [8] neurofibromatosis, [9] lesion in

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humerus, gingival fibromatosis, psychomotor retardation, orbital involvement and obstructed sleep apnea syndrome. Cherubism manifests at around 14 months to 3 years of age. Earlier the appearance, more rapid is the progression. Disease progress usually slows down at around 5 years of age and stops by 12 to 15 years. Jaw remodelling continues till 3rd decade and then condition may be subtle. At times it may attain grotesquely deforming jaw overgrowth causing respiratory obstruction and difficulty in vision and hearing.

Radiologically cherubism is characterized by bilateral multilocular cystic expansion of jaws commonly involving ramus and body of mandible. Condyles are always spared [5] as in our case. Temporal bone may also be involved. Extracranial involvement is rare. [10] Maxillary lesions may easily escape early detection because of overlapping with sinuses and nasal cavity. [5] Destruction of alveolar cavity may displace the teeth producing radiological appearance of "floating teeth syndrome". In adulthood cystic areas become remodeled giving irregular sclerosed appearance. [5] Histopathology reveals numerous multinucleate giant cells which are tartarate resistant acid phosphatase positive (characteristic of osteoclast). These cells are scattered in between mononuclear spindle cells. Eosinophilic cuffing of vessels is specific for cherubism. [7] However its absence doesn't rule out the disease. Older resolving lesions show abundance of fibrous tissue with decrease in giant cells and formation of new bone.Treatment of cherubism is based on the natural history of the disease and clinical behavior in individual case. Most of the cases require no treatment. Surgery should be reserved for the cases presenting with ugly features or with functional abnormality. [11] Curettage is surgery of choice. However simple countering of the lesion has also produced equally good cosmetic appearance. [5] Liposuction has also been used to achieve good contour. [12] Surgery gave good immediate results, arrested active growth of remnant cherubic

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lesions and even stimulated bone regeneration. [13] Radiotherapy is contraindicated because of fear of retardation of jaw growth, radio osteonecrosis and chances of malignant degeneration. Medical therapy like calcitonin is theoretically appropriate but without proven results. Recent advancement in understanding genetic based pathogenesis of cherubism may bring us closer to genetic therapy.

Cherubism has been classified according to the severity grades with a supplement in from the Seward and Hankey system. [14]

- Grade I: Involvement of bilateral mandibular molar region and ascending rami, mandible body or mentis.
- Grade II: Involvement of bilateral maxillary tuberosities as well as the lesion of grade I, diffused whole mandible.
- Grade III: Massive involvement of the entire maxilla and mandible except the condyles.
- Grade IV: Involvement of both jaws with condyles.

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In general, the treatment of cherubism is to biopsy the lesion, extract any ectopic and impacted teeth and correct it surgically when appropriate. Some surgeons wait and approach to observe the condition because it is assumed that the lesion resolves automatically on its own in the third decade of the life. The cherubic appearance in a young patient may be highly traumatic to the psychosocial element of one's personality, so surgical reconstruction and correction of the deformity as an option cannot be ruled out. In patients with aggressive signs and symptoms, surgical curettage is not an effective therapy.(15)

**Discussion:**

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The current knowledge about the clinical behaviour of cherubism is based on the study by Joneson a few series of cases and some single case reports. However, most reports did not follow the patients for a sufficient period of time to confirm spontaneous regression. In some cases, patient's adult appearance has been found to be normal but documentation of previous facial swelling or radiographs are missing.

The clinical presentation of the disease in our patients was similar to the findings in other follow up studies. Radiographically the lesions appeared as multilocular cystic radiolucencies involving jaws. The disease manifested itself in childhood but did not regress even after puberty in both these cases.

Recommended therapy ranges from radical surgical reconstruction to an attitude of wait and see, the latter being preferred today. Radical surgery is absolute when disease occurs in all four quadrants. Poor results have been reported for curettage but only in early childhood where a tendency to relapse has been reported by such an early intervention due to its high growth potential and lack of complete removal of pathological tissue. A remodelling osteotomy as in fibrous dysplasia is not indicated as bone repair process is disrupted. Attempts to control this disease with radiotherapy should be rejected for risk of developing an osteosarcoma in the irradiated area. Conservative treatment is appropriate until functional or emotional disturbances demand surgical intervention. Medical therapy in the form of calcitonin is theoretically appropriate but clinical evidence is lacking so as to endorse its application though calcitonin has been shown to cause inhibition of bone resorption in cherubic tissue in vitro. However curettage in the beginning of resorption phase has been successful with or without bone graft. [16,17]

## Conclusion

Cherubism is a rare benign bone disease with autosomal dominant inheritance. The signs and symptoms depend on the severity of condition and range from no clinically or radiographically detectable features to grotesquely deforming mandible or maxilla with respiratory embarrassment, impaired vision and hearing. Because of the genetically determined course of cherubism any surgical removal should be exclusively restricted to specific indications. Deterioration of visual acuity otherwise an attitude of wait and see should be preferred.

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