NON-FAMILIAL CHERUBISM IN AN ADULT FEMALE: A CASE REPORT

A Case Report

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ABSTRACT

Cherubism is a congenital childhood disease of autosomal dominant inheritance. This disease is characterized by painless bilateral enlargement of the jaws, in which bone is replaced with fibrous tissue. The condition has sui generis clinical, radiographic and histological features, of which the clinician should be aware for a better differential diagnosis in the presence of a fibro-osseous lesion affecting the bones of the maxillomandibular complex.

INTRODUCTION:

Cherubism is a rare disease of autosomal dominant inheritance and is characterized by painless, frequently symmetrical, enlargement of the jaws as a result of the replacement of bone with fibrous tissue 1-6. The disease is also known as familial fibrous dysplasia of the jaws, but it has been has shownto be a separate entity at the molecular levelby recent genetic investigations7. Furthermore, Lannon et al.8 mentioned necessity to distinguish cherubism from central giant cell granuloma and giant cell tumour of the jaws, with which it holds a false synonymity.

A molecular pathogenesis of cherubism has been proposed, with the detection of a mutation in the gene encoding SH3 - binding protein 2 (SH3BP2)6,9,10 and possible degradation of the Msx-1 gene which is involved in the regulation of mesenchymal interaction during craniofacial morphogenesis11. It is believed that the different clinical manifestations of cherubismare due to the changes secondary to mutations or incomplete penetrance 9

Clinically, cherubismis characterized by bilateral enlargement of the mandible and/or maxilla, causing a rounded face and swollen cheeks accompanied by upward-looking eyes. This condition gives the patient the appearance of cherubs depicted in baroque artwork1-4 hence, the name of the disease introduced by Jones 12, who published the first four cases affecting the same family.

CASE REPORT:

A 27-year-old female patient suffering from cherubism reported to the department of OMFS with the chief complain of swelling in lower left jaw back region since one and a half months. History revealed that the patient had symmetrical and bilateral swelling of the face since the age of 2 years. This enlargement had continued in gradually progressive fashion throughout the subsequent years. No familial history of similar swelling was seen. At the age of 7, she had visited the Government hospital where she was diagnosed with cherubism and had undergone corrective surgical procedures for the same. She was relativelyasymptomatic for the next few years. However, at the age of 11, she noticed a recurrence of the swelling of the jaws which again gradually increased over a period of time but she did not seek any medical intervention for the same. Since the last one and a half months, she noticed loosening of teeth in the offending region which gradually exfoliated. 10 days later she noticed bleeding and swelling in that region. She went to a local dental clinic forthat from where she was referred to ADCH for further treatment.

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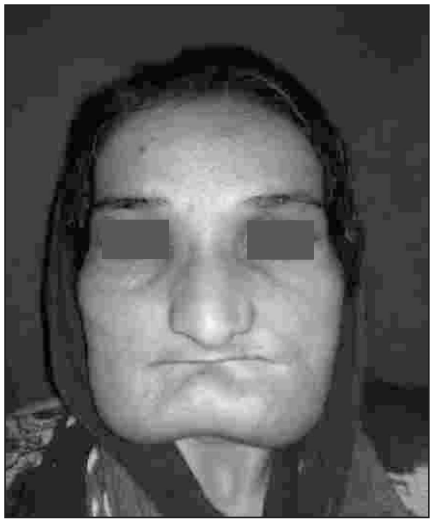


Fig 1: Front profile of the patient

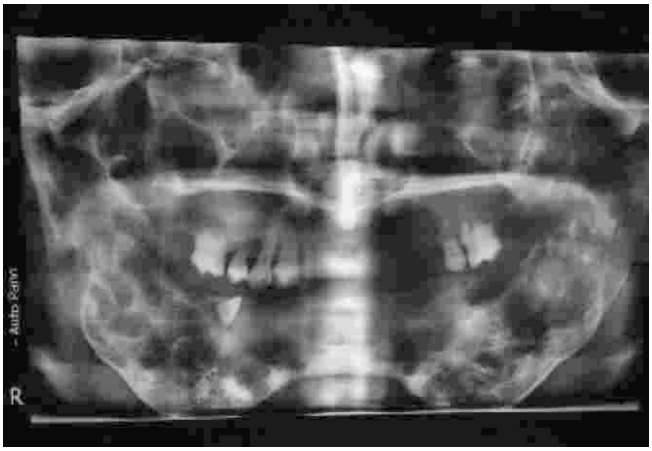


Fig 2: Orthopantomogram

Upon extra-oral examination and palpation, a single, round swelling was present on the right and left side of the face extending antero-posteriorly from corner of the mouth to 3cm posteriorly and supero-inferiorly from 2 cmbelow the Ala-tragus line to lower border of mandible with size of 3 cm in diameter with involving sub mandibular region on both sides with ill-defined borders. It was non-tender, firm, bony hard consistency and non-mobile upon palpation. Margins of the swelling were well-defined and the swelling was attached to the underlying tissue. Bilateral submandibular lymph nodes were palpable, firm and mobile. There was no sign of bleeding and pus discharge. Mouth opening was reduced to 20 mm. The face appeared square shaped with non-prominent chin.

Upon intra oral examination and palpation, it was observed that the mouth opening was reduced to 20 mm. Blanching was present on both buccal mucosae, retromolar area, soft palate. Tongue & soft palate movements were found to be restricted. De-pappilation of tongue was also present. No signs of bleeding and ulceration were present. A single, ovoid shaped growth was present on lower left alveolar region extending antero-posteriorly from,1cm away from the midline to 2 cm posteriorly and supero-inferiorly from the upper occlusal line to depth of vestibule. On the superior surface of the growth there was pinching of the maxillary left canine tooth. Size of the growth was 2.5 cm in diameter approx. which was extending bucco-lingually from buccal aspect to lingually floor of the mouth. The lesion was found to be well-defined, sessile, hyperplastic, exophytic growth and was normal in colour with bluish red tinge on the entire surface of the lesion. Upon palpation, it was non-tender and soft in consistency.Excisional

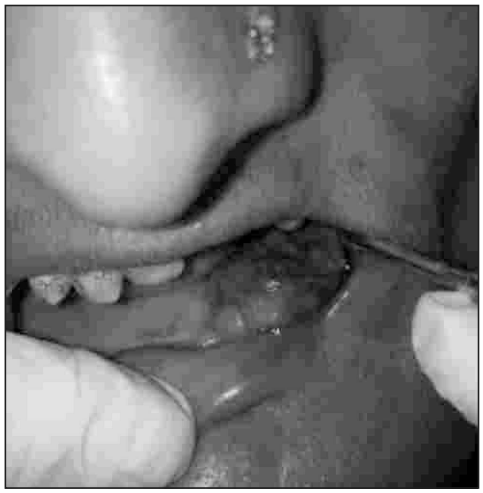
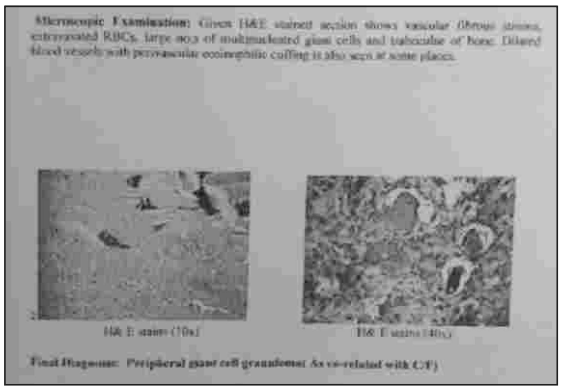
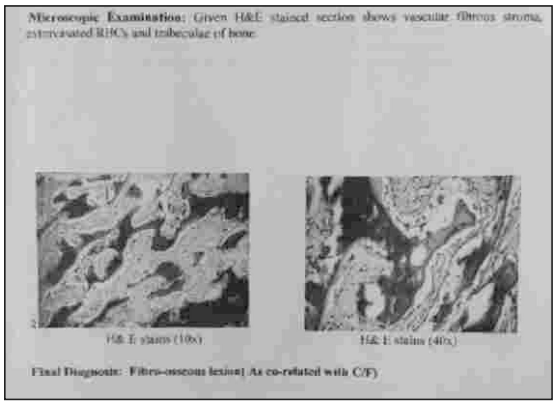


Figure 3: Intra-oral site

Figure 4: Excised tissue

biopsy for the lesion was planned to rule out the differential diagnosis. The tissue was excised to full length from the involved region with help of BP blade No.15.Heamostasis was obtained using a pressure pack. The area was examined properly for the presence of local irritating factors and extraction of second pre molar and first molar was done. Primary closure was done with 3-0 silk sutures. The patient was prescribed analgesics and antibiotics for five days and chlorhexidine mouthwash for two weeks. The specimen was sent for histopathological examination. Sutures were removed after 1 week. The patient was followed up after 6 months and the surgical area showed uneventful healing. The biopsy report obtained showed the presence of vascular fibrous stoma, extravasated RBCs, aggregates of multinucleated giant cells and trabeculae of bone.Dilated blood vessels with perivascular eosinophilic cuffing were also seen at some places. A diagnosis of peripheral giant cell granuloma was reported.





1. Discussion:

Cherubism is a rare hereditary autosomal dominant benign lesion of childhood[13].

According to the World Health Organization, cherubism belongs to a group of nonneoplastic bone lesions that affect only the jaws. It is also considered a member of the family of fibrous-osseous diseases and some authors refer to this disorder as familial fibrous dysplasia.[13]

Cherubism or multilocular cystic disease of jaws was first recognized as a separate entity in 1933 by William A. Jones in a family with several affected members. He designated the descriptive name "cherubism" because "the full round cheeks and the upward cast of the eyes give the children a peculiarly cherubic appearance." As this name so accurately captured the clinical features of the disease, it became the standard nomenclature.

Cherubism is defined by the appearance of symmetrical, multilocular expansile, radiolucent lesions of the mandible and/or maxilla that typically appears at the age of 2–7 years. Swelling of the submandibular lymph nodes in the early stages contribute to the fullness of the face as is seen in our case also. As the soft fibrous dysplastic tissue in the lesions expands, the protuberant masses can infiltrate the orbital floor and cause the characteristic upward tilting of the eyes exposing the sclera below the iris. Cherubism lesions are limited to the jaws, and in most cases, the dysplastic expansile masses begin to regress with the onset of puberty[14].

On average, the disease manifests in childhood, is stabilized by the age of 12 years, and begins to regress during puberty. Bone recontouring continues through the third decade of life, and the face alteration gradually disappears. However, it was observed in this case that the lesion showed no signs of regression even though the patient was well past puberty, showcasing a deviation to the usually seen sequelae in the development and progression of this condition

The prevalence in male is 100% when compared with female 50%–70%, i.e., 2:1 ratio[15].Two forms exist: hereditary (familial) and nonhereditary (nonfamilial)[16].

In 1978, Arnott suggested a grading system for the lesions of cherubism. Cherubism is divided into Grades 1, 2, 3 and 4 depending on location and

the severity of involvement of jaws. These classifications are based on the extent of lesion at the time of evaluation. The grade often increases on follow-up examination[17].

On the basis of extent of involvement, Ramon and Engelberg proposed a grading system for cherubism:

Grade 1 - Involvement of both mandibular ascending rami

Grade 2 -Same as Grade 1 plus involvement of both maxillary tuberosities-,

Grade 3 - Massive involvement of whole maxilla and mandible, except the condylar processes

Grade 4 - Same as Grade 3 with the involvement of the floor of the orbits causing orbital compression[18].

Microscopically, the lesions showed numerous multinucleated giant cells and vascular spaces which are randomly distributed against a background of highly cellular connective tissue. Histochemical and immunohistochemical characterization of the multinucleated giant cells reveals that these are osteoclasts since they are positive for tartrate-resistant acid phosphatase and express vitronectin receptor[19].The giant cells are foreign body type with 5–20 nuclei[20].The cellular stroma contains focal deposits of hemosiderin pigments. Eosinophilic collagen perivascular cuffing can be seen in some cases, and this perivascular hyalinosis is considered pathognomonic for cherubism[19].

The diagnosis of cherubism is based on patient age, family history, clinical examination, radiographic findings, biochemical analyses and molecular analysis[14].

Treatment of cherubism has not been standardized. Surgical treatment appears to be unnecessary for Grades 1 and 2 cases, in the absence of secondary disturbances. Curettage appears to be necessary in more aggressive cases (Grade 3), to reduce maxillofacial deformity that occurs after puberty. Dukart et al. found that surgical curettage and recontouring performed during a period of rapid growth of cherubism lesions not only offer a favorable immediate result but also arrests the active growth of remnant lesions while stimulating bone regeneration. Calcitonin therapy seemed to be effective and resulted in remission of the lesion. The administration of calcitonin was done with nasal spray instead of by subcutaneous injections. The rationale of calcitonin administration is that it inhibits the osteoclastic activity of the giant cells. Radiation therapy is ineffective and contraindicated in view of the risk of osteoradionecrosis, interference with dentofacial growth and development and the effect on future surgical procedure[21].

Curettage is the surgery of choice. Simple countering of lesions produces good cosmetic appearance. Liposuction has also been used to achieve good contour. Surgery showed that – good immediate results arrested the active growth of remnant. Cherubic lesions and even stimulated bone regeneration. Radiotherapy is contraindicated because of fear of retardation of jaw growth radio osteonecrosis and chances of malignant degeneration. Medical therapy such as calcitonin is theoretically appropriate but without proven result. The recent advancement in the treatment of cherubism is the genetic therapy[22].

Calcitonin was tried as it inhibits the osteoclastic activity of the giant cells, but with varying results.

Based on the genetic mutations related to the disease, gene therapy is expected to play a role in future treatment[23]. Gene testing for known mutations in SH3BP2 gene is offered by several commercial reference laboratories and testing on a research basis is available.

2. CONCLUSION:

Despite the exceptions, cherubism is a clinically well-characterized disease which confers to the patient the appearance of a baroque cherub; therefore, this derived the name of the disease. In cases of a suspicion of cherubism, radiographic examination is essential since the clinical presentation and the location and distribution of the lesions may define the diagnosis. Histopathological examination is complementary. Nowadays, genetic tests should be used for final diagnosis of cherubism.

Knowledge of the clinical and radiographic alterations observed in patients with cherubism is important since the dentist might be the first professional sought for a diagnosis of this disease.

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