

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Clinical and radiological evaluation of cherubism: A rare case report

Ali Fuat Tekin, MD^{a,*}, Ömer Faruk Ünal, MD^b, Sevede Göksel, MD^c, İlknur Özcan, MD^c

^a Department of Radiology, Konya Training and Research Hospital, Konya, Turkey

^b Department of Radiology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey

^c Department of Oral and Maxillofacial Radiology, Istanbul University Faculty of Dentistry, Istanbul, Turkey

ARTICLE INFO

Article history:

Received 22 December 2019

Revised 7 January 2020

Accepted 7 January 2020

Keywords:

Cherubism

Multilocular radiolucency

Jaw expansion

Imaging

Computed tomography

ABSTRACT

Cherubism is a rare, non-neoplastic, genetic disorder, characterized by painless bilateral swelling of the jaws. A 5-year-old girl presented with a painless, bilateral symmetrical swelling of both mandible and maxilla. Intraoral examination revealed malocclusion with displacement of teeth and expansion of the alveolar ridges. There was a bilateral expansion of the jaws. In conclusion, cherubism is a genetic disorder that has non-neoplastic bone lesions that affect the jaws. If there is a functional or esthetic problem, it should be treated surgically. The surgical treatment is usually delayed until after puberty.

© 2020 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license.

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

Cherubism is an autosomal dominant familial fibro-osseous disease that causes painless bilateral expansion of the mandible, maxilla or both. In 1933, Jones described this disease as “familial multilocular cystic disease of jaws”. However, the name “cherubism” was given later on, because it gave the children the weird look of a cherub with “rounded cheeks and eyes looking upward”. Cherubism often represents toddler or a baby angel, that is described in European Renaissance art, with plump cheeks and upward eyes [1]. The disease is char-

acterized by progressive cystic proliferation in mandible and maxilla, followed by self-dissolution and bone reformation in puberty [2]. Cherubism diagnosis is based on radiographic and histological findings. Clinical findings are as follows: Familial occurrence, bilateral involvement of the jaws in early childhood period, high arched palate, deficiency in second and third molars, indolent lymph node swelling, the spontaneous halt or regression in clinical status after puberty and no involvement in the temporomandibular joint [3]. The involved bones together with the lower bounds radiographically show a multilocular radiolucency with thin and expanded cortexes. Condyle and condylar neck seem normal. Drifting of the teeth

Funding: There is no financial support in this report.

Declaration of Competing Interest: There is no conflict of interest between the authors Ali Fuat TEKİN, Ömer Faruk ÜNAL, Sevede GÖKSEL, İlknur ÖZCAN to be disclosed.

* Corresponding author.

E-mail address: Md_aliftekin@yahoo.com (A.F. Tekin).

<https://doi.org/10.1016/j.radcr.2020.01.003>

1930-0433/© 2020 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license. (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)



Fig. 1 – A) B) Facial view of the cherubism C) Lateral view of the cherubism.

is not seen, rather the dislocation of the teeth is common. The cases both radiographically and clinically report asymmetrical involvement. Computed Tomography (CT) displays comb-like lesions of mandibular cortical bone. The blockage of the maxillary sinus in the maxilla and sometimes the elevation of orbital floor affect tuberosity region [4]. In this case study, we present the radiological findings of a familial cherubism case of a 5-year-old who had been going through painless swelling in both mandibles for 1 year.

Case report

A 5-year-old girl presented with a painless, bilateral symmetrical swelling of both mandible and maxilla. Her parents had noticed her round face, full of cheeks, which later became more pronounced. Intraoral examination showed malocclusion with displacement of teeth and swelling of the alveolar bone. The patient had oral caries on her upper anterior teeth and her oral hygiene was poor. Some deciduous teeth were missing and wide edentulous interdental spaces were detected on intraoral examination. Physical and mental development were normal. In family history, we learned that the patient's parents were second-degree relative and the patient's father and brother also had cherubism. Extraoral examination revealed symmetrical expansion of jaws. (Fig. 1) No lymphadenopathy was noted. Laboratory tests which included serum calcium, phosphorus, and alkaline phosphatase were normal. No abnormality was found on clinical examination of the chest, abdomen, cardiovascular, or central nervous system [1–12].

The panoramic radiograph showed the multiple soap foam-like multilocular radiolucent lesions including both maxilla and mandible except mandibular condyles. There was a bilateral expansion of the jaws and the tooth germs (white arrows) (Fig. 2).

In the Non-Contrast Maxillofacial Computed Tomography (Tree axial (A,B,C) and one coronal (D) image) of the patient, expansile lytic lesions in mandible and maxilla were observed. There was a foamy hypodense expansion which caused a significant expansion and thinning in mandibular and maxillary



Fig. 2 – Panoramic roentgenogram, radiolucent multilocular lesions are present on both sides of the maxillary and mandibular bone. Maxillary and mandibular tooth alignment is disrupted due to mass.

bone (white arrows). Both of the mandibular bone condyles were preserved (A,B,C axial noncontrast maxillofacial CT, D coronal noncontrast maxillofacial image) (Fig. 3).

This case was diagnosed with cherubism as a result of the clinical and radiological examination. The patient in this case report is clinically and radiologically classified as 4th Degree, Class 3. No treatment was administered and the parents are advised to bring their children for periodical follow-ups for the condition to be observed.

Discussion

Cherubism is a childhood-onset auto-inflammatory bone disease characterized by bilateral and symmetrical proliferative fibro-osseous lesions confined to the mandible and maxilla. Expansion is often symmetrical. Phenotype extends from clinically asymptomatic to severe mandibular and maxillary overgrowth with respiratory, ocular, speech and swallowing problems. The course and duration of active bone destruction process vary among affected individuals; at the beginning, it is often observed in early childhood and typically, new lesions may emerge until puberty. Regression of the symptoms is a result of the ossification and reformation of the lesion during the second and third decades of life [5]. According to the

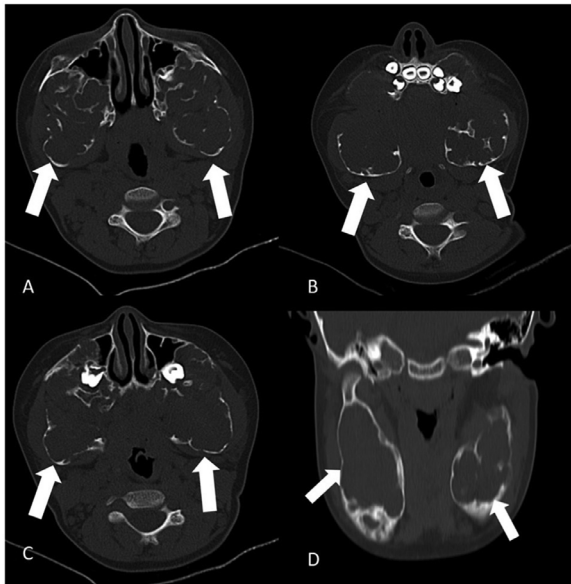


Fig. 3 – A) B) C) Noncontrast axial maxillofacial CT of cherubism bilateral expansile multiloculated cystic masses with symmetric involvement of mandible and maxilla (white arrows) D) Coronal maxillofacial CT with expansile radiolucent mass in mandible, bilateral condyle is preserved (white arrows).

classification of the World Health Organization, cherubism is a group of non-neoplastic bone lesions that only effects jaws [6]. It is a rare, benign condition that arises with autosomal dominant inheritance. Various names have been used to describe this condition such as familial or hereditary fibrous dysplasia, bilateral giant cell tumor, and familial multilocular disease [7]. The pathophysiology of cherubism results from mutations in the gene encoding SH3 binding protein SH3BP2 on chromosome 4p16.3. Overactive SH3BP2 protein triggers the production of osteoclasts in the jaws causing bone resorption and fibrous tissue replacement. The family of the patient did not give consent to further genetic study so no genetic study was conducted at the time of this report.

Mineral metabolism was reported normal in cherubism patients. Serum calcium, parathyroid hormone, calcitonin, and alkaline phosphatase levels are within normal limits. However, some reports have revealed an increase in TNF- α serum levels in cherubism patients [8].

Cherubism is radiographically characterized by bilateral multiloculated cystic expansion of the jaws. Early lesions occur at the posterior body of mandible and ramus. Teeth appear to be dislocated, impacted and floating in cyst-like spaces.

Wide lytic lesions and soft tissue masses in the mandible are more clearly seen in the CT scan [9]. Our patient's CT showed expansions in soft tissue density in the mandibular and maxillary bone and mandibular condyles seem preserved.

Differential diagnosis includes fibrous dysplasia, bilateral parotid swelling, giant cell recurrent granuloma, giant cell tumor, bilateral odontogenic cysts, histiocytosis X (Hand-Schuller-Christian), odontogenic keratocysts (including nevoid basal tumor syndrome), Brown tumor (hyperparathy-

roidism), infantile cortical hyperostosis, fibro-osteoma, ossified fibroma, ameloblastoma, odontogenic fibroma, myxoma and aneurysmal cysts [10].

Treatment protocols for cherubism are not well established and are developing due to a better understanding of the auto-inflammatory nature of this bone disease. Given that cherubism is a self-limiting condition that improves over time, treatment should be administered according to the individual's condition and the development of the disease. Depending on the severity, functional and aesthetic concerns may require surgery [5].

Children with cherubism should be referred to a craniofacial clinic with pediatric experience for ongoing treatment. A craniofacial clinic associated with a large pediatric medical center usually includes a surgical team, a dentist, an orthodontist, an ophthalmologist, and a pediatrician or a social worker. Among surgical interventions, there is curettage with or without bone grafting. Liposuction is also used to rearrange the jaw contour. Surgical interventions are performed between 5 and 15 years of age in individuals who have jaw expansion or local aggressive lesions associated with complications such as deteriorated swallowing and respiratory functions, nasal airway obstruction or tongue displacement [11].

In Cherubism, orthodontic treatment is commonly required because of jaw distortion, a malignant bite, premature loss of primary teeth, and permanent tooth abnormalities including wide-spaced, improperly located, impacted or non-existent permanent teeth [12].

Ophthalmologic treatment is required in rare individuals with orbital findings such as lower eyelid retraction, proptosis, diplopia, dislocation of bulbous and visual loss caused by optical atrophy [12].

As medical treatment, Ricalde et al. treated 3 cases of cherubism with TNF-alpha inhibitor imatinib and achieved positive results. Although there is no clinical evidence on the use of calcitonin in the treatment of cherubism, Papadaki et al. and Chen et al. have come up with promising results in inhibiting bone resorption in multinucleated giant cells while other investigations and in vitro experiments together with other researches are also needed.

Conclusion

Although rare, cherubism has a significant impact on patients and their families by causing facial deformation and functional problems. Since most cases are self-limited, surgical treatment should be performed for lesions that are aggressively growing and for patient's aesthetic concern.

Author contributions

Study concept and design: TEKİN, ÜNAL.

Analysis and interpretation of data: TEKİN, ÜNAL.

Drafting of the manuscript: TEKİN.

Critical revision of the manuscript for important intellectual content: GÖKSEL, ÖZCAN.

REFERENCES

-
- [1] Jones WA. Further observations regarding familial multilocular cystic disease of the jaws. *Br J Radiol* 1938;11(124):227–41.
- [2] Batsakis JG, Regezi JA, Rice DH. The pathology of head and neck tumors: fibro adipose tissue and skeletal muscle, part 8. *Head Neck Surg* 1980;3(2):145–68.
- [3] Hyckel P, Berndt A, Schleier P, Clement JH, Beensen V, Peters H, et al. Cherubism—new hypotheses on pathogenesis and therapeutic consequences. *J Cranio-Maxillofac Surg* 2005;33(1):61–8.
- [4] Silva EC, Silva GCC, Vieira TC. Cherubism: clinicoradiographic features, treatment, and long-term follow-up of 8 cases. *J Oral Maxillofac Surg* 2007; 65(3):517–22.
- [5] Kannu P, Baskin B. FACMG, 2 and Sarah Bowdin, BM, MSc, MRCPCH 3. 1993.
- [6] Ongole R, Pillai RS, Pai KM. Cherubism in siblings: a case report. *J Can Dent Assoc* 2003;69(3):150–4.
- [7] Ayoub AF, El-Mofty SS. Cherubism: report of an aggressive case and review of the literature. *J Oral Maxillofac Surg* 1993;51(6):702–5.
- [8] Papadaki ME, Lietman SA, Levine MA, Olsen BR, Kaban LB, Reichenberger EJ. Cherubism: best clinical practice.. In: Orphanet Journal of Rare Diseases. BioMed Central; 2012. p. S6.
- [9] Atalar MH, Arslan M, Aker H, Müslehiddinoğlu A. Cherubism: an unusual cause of bilateral mandibular swellings. *Eur J Radiol Extra* 2004;49(1):11–15.
- [10] Özkan Y, Varol A, Turker N, Aksakalli N, Basa S. Clinical and radiological evaluation of cherubism: a sporadic case report and review of the literature. *Int J Pediatr Otorhinolaryngol* 2003;67(9):1005–12.
- [11] Ricalde P, Ahson I, Schaefer ST. A Paradigm Shift in the Management of Cherubism? A Preliminary Report Using Imatinib. *J Oral Maxillofac Surg* 2019.
- [12] Chen G, Dimitriou ID, La Rose J, Ilangumaran S, Yeh W-C, Doody G, et al. The 3BP2 adapter protein is required for optimal B-cell activation and thymus-independent type 2 humoral response. *Mol Cell Biol* 2007;27(8):3109–22.