Cherubism

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Oral Pathology 2021

Section OL43 - Monday

Overview

Cherubism is a rare autosomal-dominant inherited bone disease caused by a mutation in the *SH3BP2* gene. The condition was first reported in 1933 and it is named by the resemblance of patients to cherubs from renaissance paintings; round face and upward gaze. It is generalized characterized by an asymptomatic symmetrical expansion of the jaws where bone is replaced with soft tissue abundant in fibroblasts and multinucleated giant cells. "The bone lesions and fibrous tissue expansions in cherubism increase before puberty and regress thereafter, with the lesions becoming filled in by woven bone later in life." (Chrcanovic et al 43) Signs and symptoms of the disease vary significantly depending on the severity of the condition, ranging from asymptomatic bilateral swelling of maxilla and mandible to life-threatening lesions.

Etiology

"The disease is caused by a point mutation in the SH3BP2 gene (chromosome 4pl6.3), which leads to dysrégulation of the Msx-1 gene; this gene is involved in regulating mesenchymal interaction in craniofacial morphogenesis." (Thompson 22) The mutation of this gene has so far been described as affecting only the face. On the other hand, the author Chrcanovic states that case reports suggest that the patient's genotype is not a determinant of the phenotype and that the rarity of the disease can be a challenge to analyze possible genotype-phenotype correlation (44).

Clinical presentation

The most common clinical presentation is a bilateral symmetrical hard swelling of maxilla or mandible. When the disease involves the infraorbital portion in the maxilla it can affect the inferior rim of the sclera and create the classic “eyes to heaven” appearance that patients with cherubism have. Hypertelorism, prognathism, oligodontia, malocclusion and tooth displacement are also seen on clinical examinations. The next figure shows an illustration of the general clinical appearance of patients with cherubism.

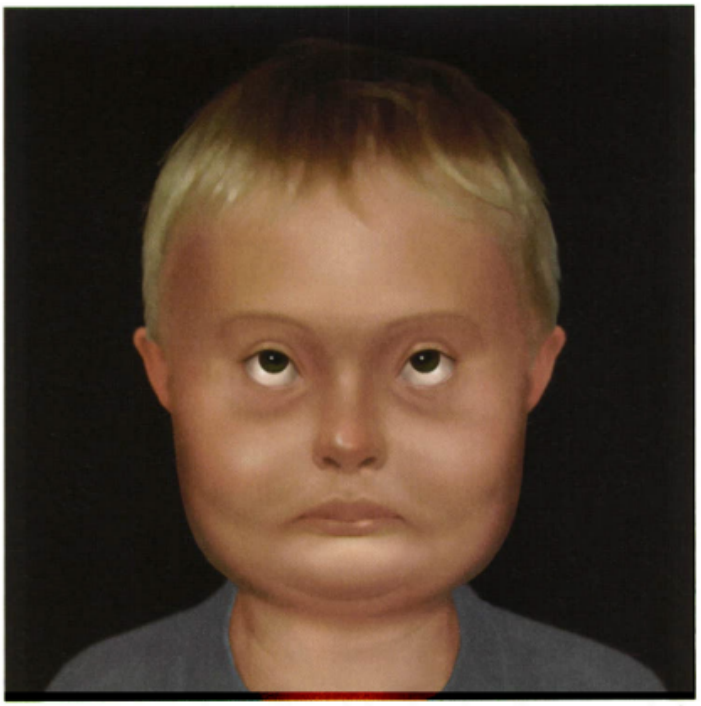

Figure 1. Illustration of a young boy with cherubism shows the prominent cheeks and upwardly gazing eyes. Reprinted with permission from Gannon FH, Thompson LD. Cherubism. In: Thompson LD, Wenig BM (eds). Diagnostic Pathology: Head and Neck. Altona, Manitoba, Canada: Lippincott Williams & Wilkinson; 2011:6/5.)

Demographics

The disease predominantly affects males more than females by twices as many cases. It follows a natural course of expansion that is usually identified within the first 2 years of life, and nearly always by the time the patient is 5 years old. Moreover, as a result of being an

autosomal dominant genetic condition, first and second degree relatives of the patient are also affected. Studies do not specify a race predilection.

Biopsy / Histology / Radiographs

To confirm the condition an incisional biopsy is taken and histopathologically examined. The histological features are fibrous connective tissue stroma with agglomerations of multinucleated giant cells. Eosinophilic cuff-like perivascular deposits can also be seen in most cases. "With time, bone remodeling can be seen, and there is no true bone formation. Polarization will show woven bone." (Thompson 24) Figure 2 shows the histological characteristics. Radiographically most of the cases show multilocular well-defined radiolucent lesions that affect all 4 quadrants of the maxilla and mandible creating a soap bubble appearance. One distinct characteristic is that radiolucencies can be seen in the body, ramus and angle of the mandible except condylar region. Moreover the radiographs can also show tooth displacement, tooth agenesis, root resorption and destruction of cortical bone. Figure 3 shows an 11 years old girl's panoramic radiograph. Without knowing the clinical and radiographic features, the histologic appearance is not diagnostic, so clinicopathologic correlation is required to make a clear diagnosis.

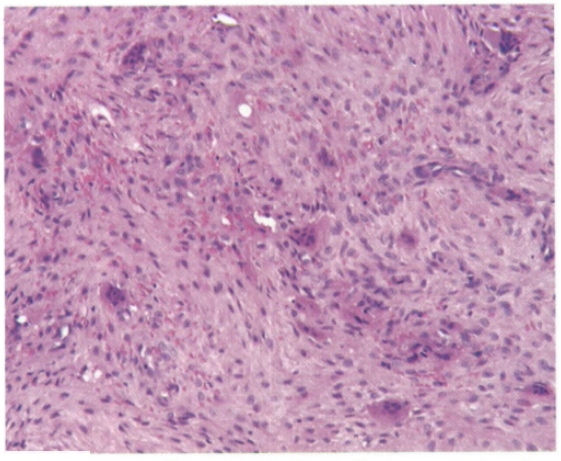

Figure 2 *Giant cells are seen within a fibrous connective tissue stroma with prominent fibroblasts. This finding alone is nonspecific.*

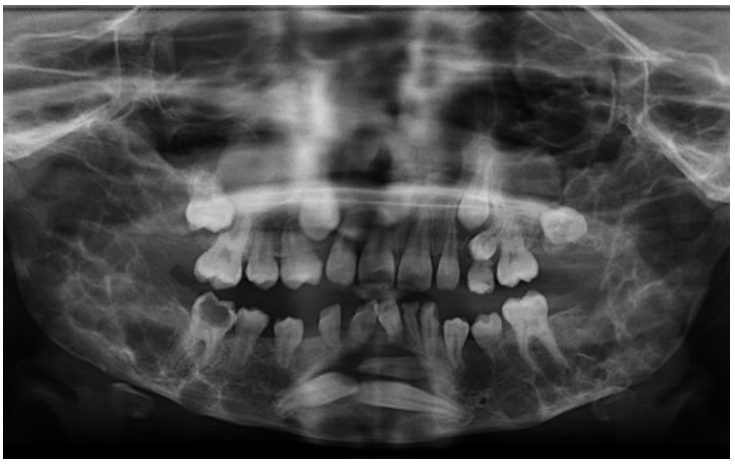

Figure 3

Differential diagnosis

Based on the histological features cherubism could be reasonably mistaken for fibrous dysplasia, brown tumor of hyperparathyroidism, aneurysmal bone cyst, central giant cell granuloma, and infantile cortical hyperostosis. Therefore, definitive diagnosis is made on the basis of radiographic and clinical presentation. The distinctive characteristic between cherubim and the conditions listed above is that these lesions hardly occur in symmetrical-bilateral fashion, do not regress after puberty and do not show the classic cherubic appearance.

Treatment

Watchful waiting is usually encouraged, also known as the 'wait and see' approach specially for the less aggressive cases, because as said before "spontaneous involution, regression, or stabilization can occur during the teenage years." (Thompson 24) Some drug treatments can also be used, like bisphosphonates, denosumab, imatinib, calcitonin, corticosteroids, interferon, and a tumour necrosis factor (TNF) inhibitor. When talking about surgery many studies have shown that early surgery is contraindicated because it can predispose the patient to recurrence. If there are major impediments to speech, chewing, swallowing, vision, or hearing, surgery may aid. Enucleation or curettage may be indicated in more aggressive cases, to reduce the maxillofacial deformity after puberty and to ensure a successful outcome without the risk of progression requiring additional resection. Additionally, radiation therapy is absolutely contraindicated because of the risk of osteoradionecrosis or fibrosarcoma.

Prognosis

As a result of the conditio being benign in most of the cases the it stops progressing when the patient gets to puberty and the lesions can regress and be filled in by woven bone

later in life by the fourth or fifth decade of life. It is a disease that can be managed by a close watch during the developmental years and after that surgery and curettage can be useful for aesthetic purposes or when functional concerns arise. Typical cases of cherubism are non fatal and many times do not need any kind of treatment.

Professional relevance

Cherubism is a relevant disease for dental hygienists because we are doing extraoral and intraoral examinations to many adults and kids that may not know that it is possible they can have a disease. Dental hygienists are often the first line of medical treatment. We can detect suspicious lesions and send referrals to confirm or deny a disease. It is important to know the clinical and radiographic characteristics to identify these lesions. Cherubism also has some intraoral characteristics that need special considerations like malocclusion; the dental hygiene treatment has to be modified for this patient and home care instructions should be given to the parents and also the kids so they can have better oral health.

Citations

Chrcanovic, B. .., et al. “Cherubism: a Systematic Literature Review of Clinical and Molecular Aspects.” International Journal of Oral and Maxillofacial Surgery, vol. 50, no. 1, Elsevier Inc, 2021, pp. 43–53, https://doi.org/10.1016/j.ijom.2020.05.021.

Komerik, Nurgul, et al. “Cherubism.” Head & Neck Pathology (Totowa, N.J.), vol. 8, no. 2, Springer US, 2013, pp. 164–67, https://doi.org/10.1007/s12105-013-0489-1.

Morice, Anne, et al. “Cherubism as a Systemic Skeletal Disease: Evidence from an Aggressive Case.” BMC Musculoskeletal Disorders, vol. 21, no. 1, BioMed Central Ltd, 2020, pp. 564–564, https://doi.org/10.1186/s12891-020-03580-z.

Thompson, Lester D. “Cherubism.” Ear, Nose, & Throat Journal, vol. 94, no. 1, Vendome Group LLC, 2015, pp. 22, 24–E–24, https://doi.org/10.1177/014556131509400107.