Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology 34 (2022) 195–199

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

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

Case Report

Non-Familial Cherubism: A rare case report with long-term clinical and radiological follow-up

Sodaba Ghawsi [a,*], Kristoffer Schwartz [a], Niels Korsgaard [b], Jens J. Thorn [a]

[a] Department of Oral and Maxillofacial Surgery, University Hospital of Southern Denmark, Esbjerg, Denmark
[b] Clinical Diagnostic Center, University Hospital of Southern Denmark, Esbjerg, Denmark

ARTICLE INFO

Article history:
Received 16 April 2021
Received in revised form
13 September 2021
Accepted 27 September 2021
Available online 1 November 2021

Keywords:
Cherubism
Diagnosis
Mandibular disease
Pathology
Surgery

ABSTRACT

Cherubism is a rare autosomal-dominant genetic defect that primarily affects the mandible or occasionally the mandible and the maxilla. It evolves and progresses in childhood to resolve spontaneously to a certain degree in adulthood. Clinical characteristics is a symmetrical expansion of the bone which in case of maxillary involvement may give a scleral show with the resemblance of a cherub.

Increased volume can affect the patient psychologically and esthetically as well as give clinical symptoms as tooth loss, missing eruption of teeth, phonetic challenges and malocclusion. Surgical approaches depend on the degree of affection.

A 15-year old male with an atypical asymmetrical growth pattern due to cherubism is presented. This patient is not among previous described Danish genealogies of cherubism. In spite of the unusual asymmetry, other characteristic features of cherubism left no doubt of the diagnosis. The patient's esthetic dissatisfaction was solved by surgical correction. Recall at 18 year follow-up showed the characteristic features associated with regression of the disease.

1. Introduction

Cherubism is a rare non neoplastic fibro-osseous disease characterized by bilateral increase of jaw volume primarily in the mandible and maxilla due to replacement of bone with multilocular cysts filled with stromal and osteoclast-like cells. The condition was first described by William A. Jones in 1933 [1].

Sporadic as well as familial cases have been reported with a predominance of the latter. The genome for cherubism was detected in 2001 on the 4p16.3 chromosome and named SH3BP2 [2]. In Denmark the condition have been registered in 7 different genealogies [3].

Approximately 300 cases have been reported in the litterature. The genome expression in males is 100 % compared to 50–70 % in females [4]. There is, in contrary to common believe, an equal frequency among males and female regardless of ethnicity [5]. Diagnostic timeline depends on the degree of affection. In severe cases the condition is diagnosed at birth or ages 2–5 years and in mild cases typically at 10–12 years. Clinical changes progress at different rates until the patient reaches puberty where the condition spontaneously regresses. Characteristically cherub like facial structures are seen with a round shape and chubby angelic structures which later in life become less pronounced [6].

Despite the condition being painless, increase of bone volume affects the patients psychosocially and esthetically with occasional clinical symptoms as loss of teeth, drooling, dry mouth, impacted teeth, phonetic problems and malocclusion [4]. In rare cases sight and hearing loss as well as compromised airways and an increased risk of obstructive sleep apnea have been registered [7].

In the current case a 15-year old male is presented with non-familial cherubism that has caused atypical asymmetric features. The patient was treated by surgical correction with an 18 year follow-up.

2. Case report

A 15-year old male was referred to the Department of Oral and Maxillofacial Surgery for treatment of cherubism. The diagnosis was verified with an incisional biopsy in the Children's Oral Health Clinic in relation to removal of wisdom teeth 4 years prior. The patient's main complaint was esthetic dissatisfaction due to an asymmetrical increase of volume on his right side during a 2- year period. No prior familial history was reported.

* Corresponding author at: Finsensgade 35, 6700, Esbjerg, Denmark.
E-mail address: sodaba.ghawsi@rsyd.dk (S. Ghawsi).

https://doi.org/10.1016/j.ajoms.2021.09.006

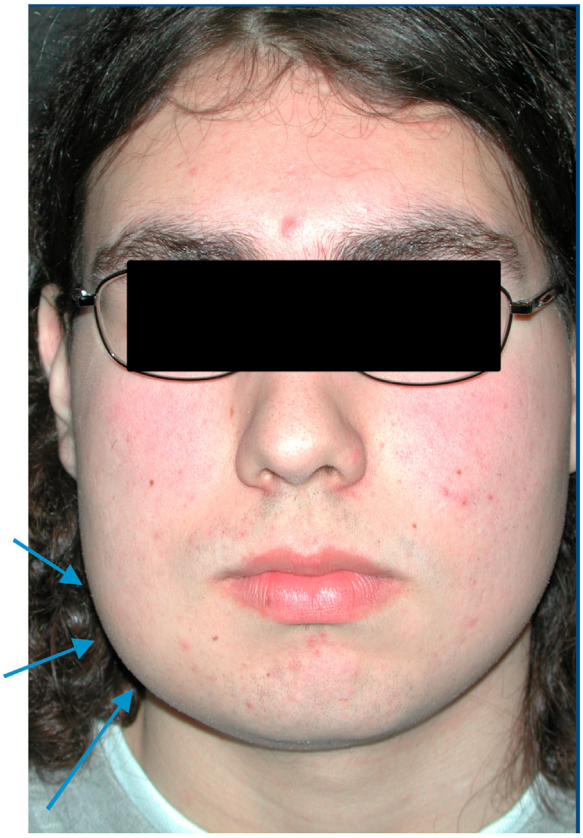


Fig. 1. Soft tissue volume increase on the patient's right side (blue arrow).

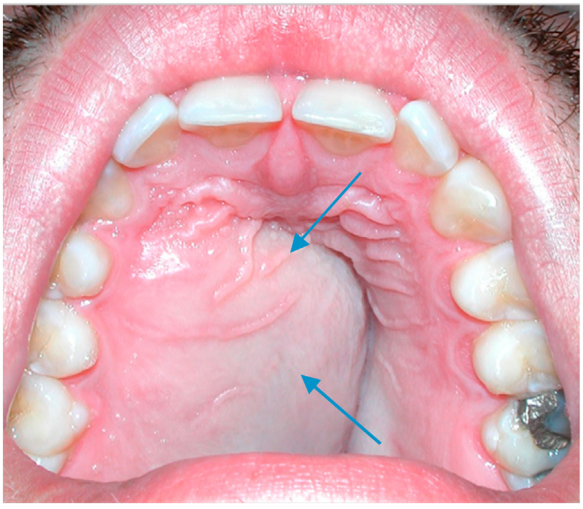


Fig. 2. An asymptomatic 25 × 35 mm expansion covered with normal mucosa was observed in the right side of the palate (blue arrow).

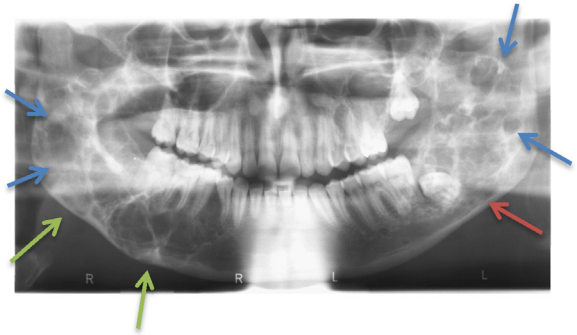


Fig. 3. Multilocular radiolucencies in ramus mandibula bilaterally (blue arrow). Basis mandibula unaffected posteriorly on the left side (red arrow) but thinned from 45 and posteriorly on the right side (green arrow).

2.1. Objective examination

Extra oral: A mandibular transversal broadening as well as an increased volume anteriorly at the right side of the body of the mandible was observed revealing an evident asymmetry (Fig. 1). On palpation a bulky volume expansion was detected in the regions 46 to 43 on the right side of the mandible. On the left side an expansion could be palpated on the proximal segment without an anterior element. An unaffected mouth opening as well as normal sensibility in the lower lip and chin was observed.

2.2. Intra oral

Clinical inspection revealed a healthy dentition without cavities and periodontal disease and normal mucosa. On palpation a bulky expansion was detected on his right ramus and body of the mandible. In the palate a 25 × 35 mm expansion covered with normal mucosa filled the right side transversing the midline to include one third of the left side of the palate. This expansion, although large, was not uncomfortable to the patient (Fig. 2).

2.3. Radiological examination

Orthopantomography (OTP) showed multilocular radiolucencies in the ramus of the mandible bilaterally. The base of the mandible was unaffected posteriorly on the left side but was thinned from 45 and posteriorly on the right side. Both condyles were unaffected. No resorption of roots was observed. (Fig. 3). On the anterior-posterior (AP) projection locular radiolucencies could be observed from the bottom of the maxillary sinus on the left side, however involvements where more uncertain on the right side. Furthermore, an increased growth laterally was seen on the right side of the mandible (Fig. 4).

2.4. Treatment

A bilateral surgical approach with resection and contouring of the affected tissue was performed as well as surgical removal of 38. Denudation of 27 with the application of a chain was preformed.

In general anesthesia a marginal incision was made from 47 to 37 with a releasing incision in the midline and posteriorly. Periosteal elevation, which was complicated on the right side due to adhesion, revealed a thin cortex that was elevated and almost separated from the underlying tissue (Fig. 5). An uneven partly osseous fibrous tissue had expanded significantly bilaterally in the mandible. The inferior alveolar nerve was localized and protected. Pathological tissue was removed on the right side respective of the mandibular canal, which was displaced lingually. The lateral aspect of the corpus and ramus of the mandible was shaved and contoured to normal size and open caverns where emptied of soft tissue. On the left size the canal contents where seen in a lateral position. The inferior alveolar nerve was preserved but with lacerated perineurium (Fig. 6). The nerve was lateralized as the tissue was chiseled to normal mandible form. The caverns here where also emptied of fibrous tissue. Surgical removal of 38 and denudation of 27 was completed without complications.

2.5. Histological examination

The sample showed a tumor like material consisting of fibrillary tent pole cells in random patterns. Areas with multiple giant

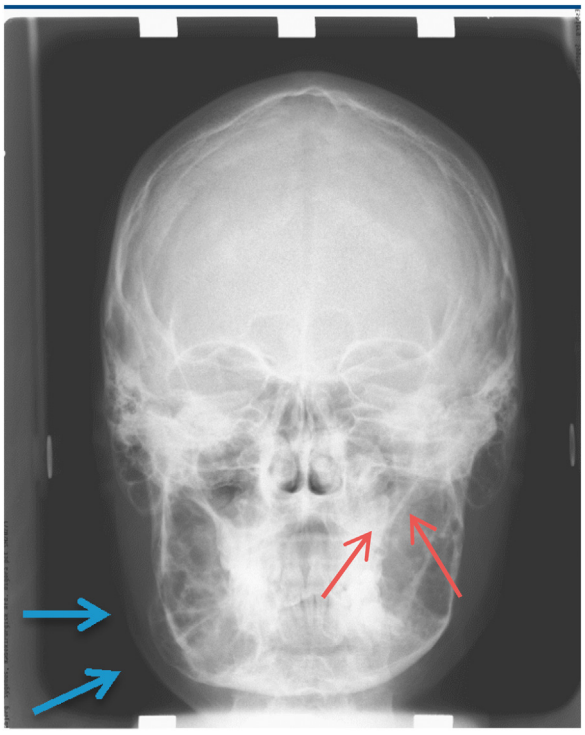


Fig. 4. Increased growth was seen on the right side of the mandible (blue arrow). On the left side of the maxilla a locular radiolucency could be observed from the bottom of sinus maxillaris (red arrow).

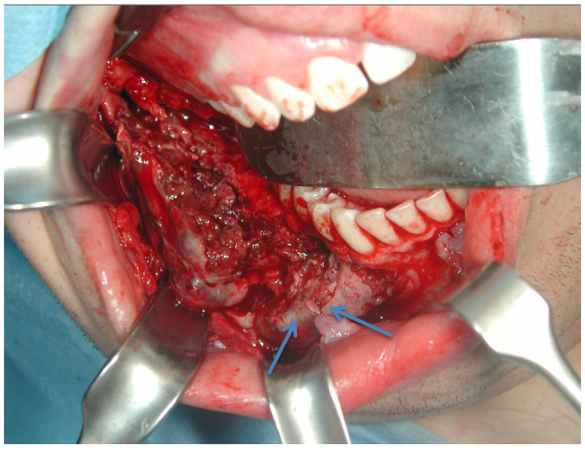


Fig. 5. A thin cortex (blue arrow) was elevated and almost separated away from the peripheral tissue.

cells of osteoclast-like multinucleated giant cells and thin vessels with extravasation of erythrocytes were also seen. At the periphery of the tumor, a more fibrous tissue with larger bony areas was seen. In this area, vessels were observed with spotted pigmentation. An eosinophilic cuffing of collagen was found sporadically around small vessels. No signs of malignancy were noted (Fig. 7).

2.6. Genetic test

Approximately 80 % of cherubism patients have a mutation in the SH3BP2 gene. Genetic testing on the patient was initiated resently in relation to the patient becoming a father.

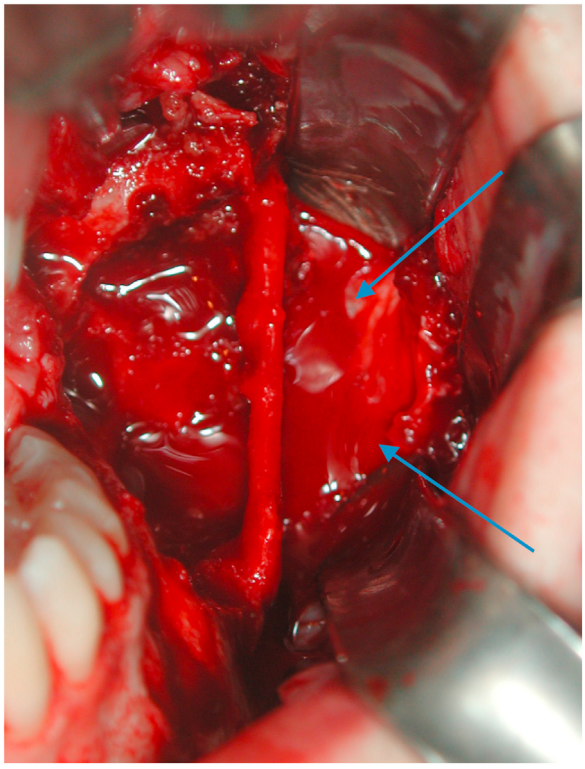


Fig. 6. Illustration of the emptied caverns of fibrous tissue. Laceration at the perineum on the n. alveolaris inferior (blue arrow).

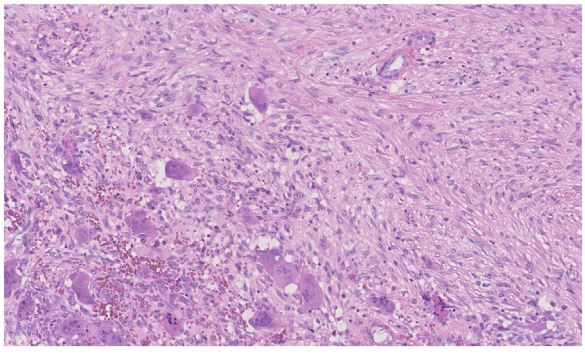


Fig. 7. Histomorphology shows osteoclastic giant cells in a loosely arranged stroma. In the lower left corner extravasated blood is seen and in the upper right corner an eosinophilic, cufflike deposit around a small blood vessel is revealed.

2.7. Follow-up

At the 6-month postoperative control a clinical satisfying healing and normal sensibility of the inferior alveolar nerve was registered. The patient was initially planned for a 1 year follow-up but did not appear to this appointment and was first seen 3 years postoperatively. No clinically signs of recurrence were noted (Fig. 8). The OTP showed remission of the multilocular radiolucencies as well as complete eruption of 27. However, resorptive changes of the roots of 16, 15 and 25 were present (Fig. 9). The patient was seen at frequent appointments until 18 years postoperatively. Here, symmetric extraoral features and unchanged palatal expansion were seen (Fig. 10). Radiographically further remission of the osseous changes in both the mandible and the maxilla was seen, and no further resorption of the involved teeth was observed (Fig. 11). The patient reported persistent satisfaction both functionally and esthetically.

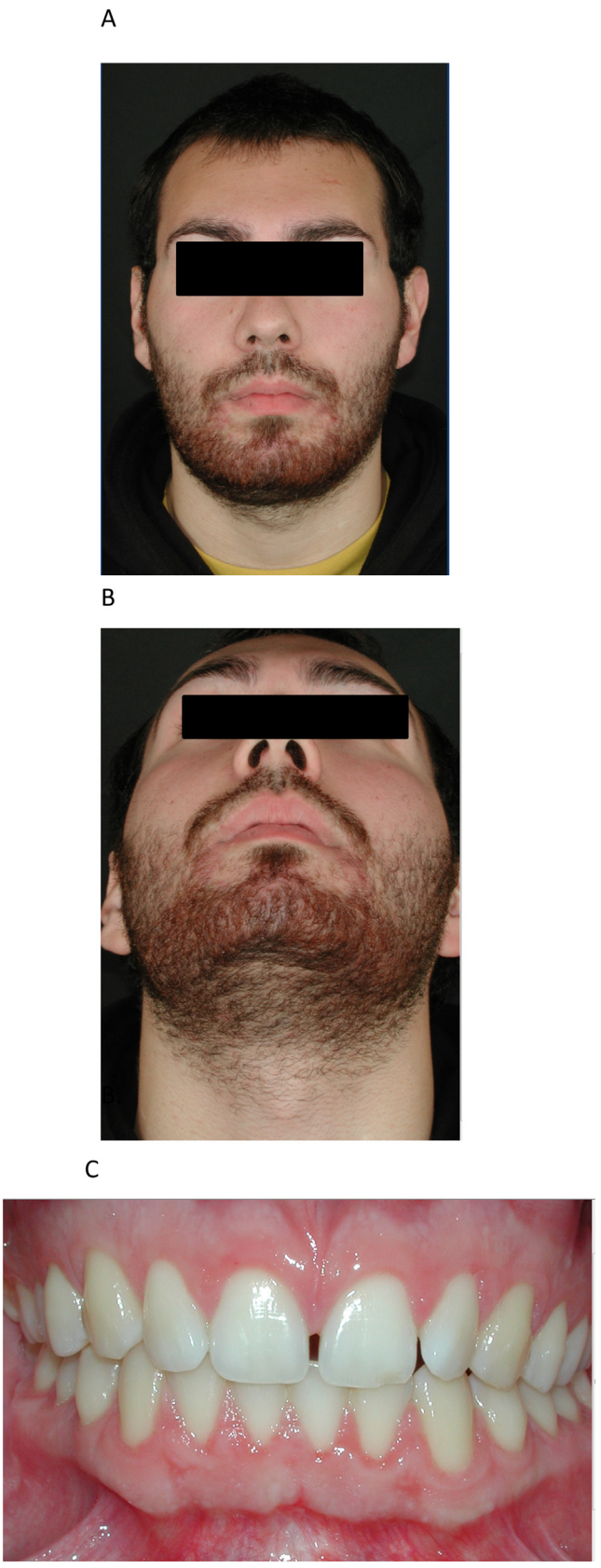


Fig. 8. No clinical signs of recurrence with a persistent facial symmetry and occlusion.

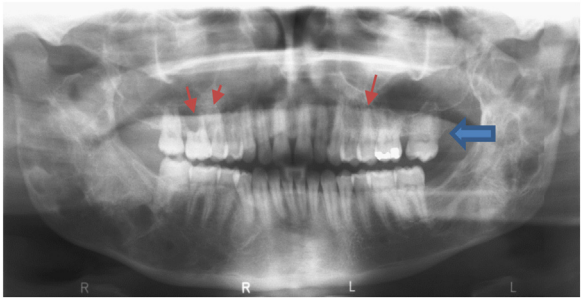


Fig. 9. The 3-year OTP showed complete healing in the boney areas as well as effective down lead of 27 (blue arrow). Resorption at root apex of 16,15 and 25 (red arrow).

3. Discussion

According to the literature cherubism is often genetically related and in one Danish study associated to 7 Danish genealogies [2,3]. The patient did not belong to any of these and had no familiar background for cherubism why a mutation is the most obvious aetiology. The patient has a 2 year old boy, who currently shows no clinical signs of cherubism.

As cherubism is characterized by symmetrical affection, the asymmetrical growth in the present patient is an atypical feature. Radiological differential diagnostic as Langerhans cell histiocytosis and multiple keratocysts should be considered. Additionally Ramon syndrom, Jaffe- Campanacci syndrome and Noonan syndrome could be considered [5,7]. Histologically differential diagnosis of primary hyperparathyroidism should be excluded [4].

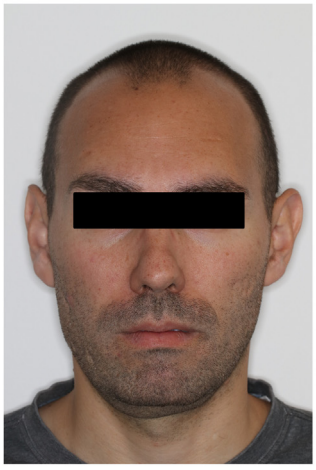
However, the diagnosis is made incontestably by the strict confinement to the jaw bones, the lack of condylar affection together with the characteristic histologic findings.

The expansion of the palatal bone in this case is unusual as well. It had however no functional implications. The root resorptions had taken place between the age of 15–18, and according to the follow-up did not progress any further. This indicates the remission took place after the age of 18 which is in accordance with other reports on root resorption [8].

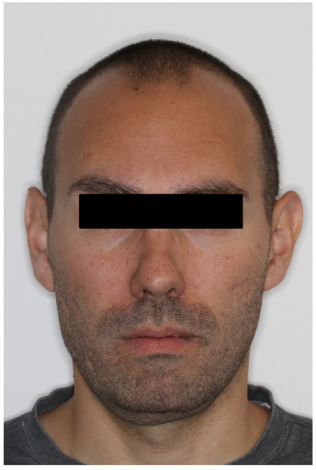
Treatment algorithms are discussed extensively in the literature for both conservative and radical surgical treatment. The conservative medical treatment options with Imatinib [9,10], Tankyrase and Calcineurin are based on empirical ground [11]. Although there are promising results further studies are needed on this topic. With a non-surgical approach the main rational is that natural involution is expected [4]. In the current case no conservative approach was made other than delay of treatment as long as the patient was asymptomatic and not affected psychosocially.

Surgical interventions are based on esthetic and functional considerations. Partial block resection, continuity resection, curettage as well as a combination of these are suggested on an individual basis [12]. The radical surgical approach chosen for the patient case is however inconsistent with certain suggested conservative approaches [4]. Surgical approaches should be made with an aim of symmetrical improvement as well as functional optimization. Currently there is no consensus regarding correct timing of treatment interventions, however a cautious approach is suggested with radical surgical treatment in growing patients [4].

A



B



C

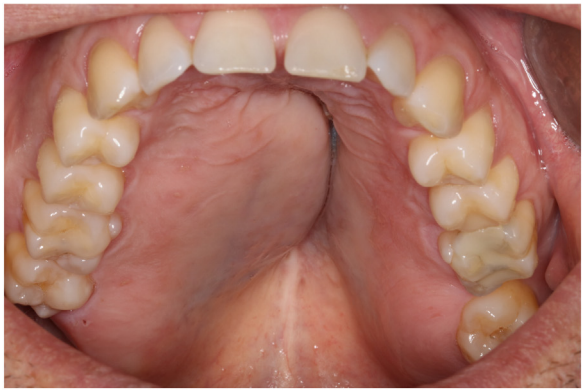


Fig. 10. No signs of recurrence clinically. Palatal expansion was unchanged.

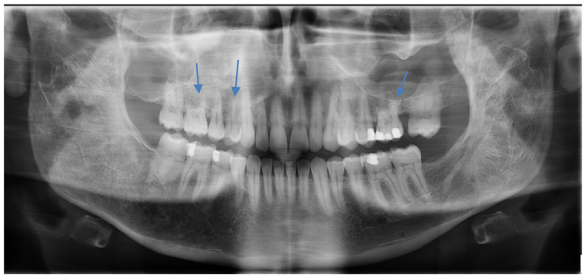


Fig. 11. Continued remission was observed on the OTP without further root resorption on the mentioned teeth.

4. Conclusion

In the current case the patient was dissatisfied with his esthetic look and was offered resection and contouring at the age of 15 years with a successful result (Fig. 11).

Ethical approval

Achieved.

Declaration of Competing Interest

The authors report no declarations of interest.

References

[1] Jones WA, Gerrie J, Pritchard J. Cherubism–familial fibrous dysplasia of the jaws. J Bone Joint Surg Br 1950;32-B:334–47.
[2] Reichenberger EJ, et al. The role of SH3BP2 in the pathophysiology of cherubism. Orphanet J Rare Dis 2012;7(Suppl. 1):S5.
[3] Von Wowern N. Cherubism: A 36-year long-term follow-up of 2 generations in different families and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:765–72.
[4] Marx RE, Stern D. Oral and maxillofacial pathology: a rationale for diagnosis and treatment; 2012. ISBN-10:97808667155129.
[5] Papadaki ME, et al. Cherubism: best clinical practice. Orphanet J Rare Dis 2012;7(Suppl. 1):S6.
[6] Ahmad M, Gaalaas L. Fibro-osseous and other lesions of bone in the jaws. Radiol Clin North Am 2018;56:91–104.
[7] Khirani S, et al. Nocturnal mouthpiece ventilation and medical hypnosis to treat severe obstructive sleep apnea in a child with cherubism. Pediatr Pulmonol 2013;48:927–9.
[8] Kannu P, Baskin B, Bowdin S, et al. Cherubism. In: Adam MP, editor. GeneReviews((R)). 1993. Seattle (WA). URL: https://www.ncbi.nlm.nih.gov/pubmed/20301316.
[9] Ricalde P, Ahson I, Schaefer ST. A paradigm shift in the management of cherubism? A preliminary report using imatinib. J Oral Maxillofac Surg 2019;77, 1278-1278.
[10] Eiden S, Lausch E, Meckel S. Involution von cherubismus im MRT unter therapie mit imatinib. Rofo 2017;189:675–7.
[11] Kadlub N, et al. The calcineurin inhibitor tacrolimus as a new therapy in severe cherubism. J Bone Miner Res 2015;30:878–85.
[12] Papadaki ME, Troulis urname>PapadakiMJ, Kaban LB. Advances in diagnosis and management of fibro-osseous lesions. Oral Maxillofac Surg Clin North Am 2005;17:415–34.