UDK: 616.716.1/.4-007-056.7-053.2

CHERUBISM- A CASE REPORT
УПОТРЕБА НА CARRIERE MOTION III АППАРАТ

Bolis-Gjurikj T.[1], Bogdanovska B.[2], Dimovska R.[3], Bajram M.[4]

[1]Private Dental Office „Luka dent"- Skopje, [2]Faculty of dental medicine, University „St. Cyril and Methodius"-Skopje, [3]Private Dental Polyclinic „Kruna MS"-Skopje, [4]Private Dental Office „Dental Designe"

Abstract

Introduction: Cherubism is a rare hereditary benign fibro-osseous disorder characterized by bilateral enlargement of the mandible and/or the maxilla, with varying degrees of involvement and a tendency for spontaneous remission. On radiographs, cherubic lesions appear as cystic multilocular radiolucencies that limited to the jaw bones. **Case report:** A 4-year-old girl came to our dental office with deformations of the lower and middle section of her face and missing teeth. After taking her history, a panoramic radiograph and a computed tomography revealed missing teeth and caries in her remaining teeth. Based on the cystic formations and overall appearance, the patient was suspected of having Cherubism and was referred to the University Clinic for Face, Jaws and Neck Surgery - Maxillofacial surgery Clinic in Skopje for a confirmatory diagnosis. **Conclusions:** The radiologic features of cherubism are not pathognomonic, but the bilateral, relatively symmetrical jaw involvement limited to the jaw bones, combined with clinical and histopathological findings, strongly suggest the diagnosis. It should be noted that genotypic characterization confirms the diagnosis. **Key words:** cherubism, clinical signs, diagnosis, hereditary syndrome.

Апстракт

Цел: Черубизмот е невообичаено наследно бенигно фибро-коскено нарушување кое се карактеризира со билатерално проширување на мандибулата и максилата што се манифестира со различни степени на зафатеност и склоност кон спонтана ремисија. На ртг, черубичните лезии се појавуваат како цистична мултилокуларна радиолуценција ограничена на коските на вилицата. **Приказ на случај:** 4-годишно девојче прв пат дојде во ЛУКА ДЕНТ поради деформација на долниот и средниот дел на лицето и отсуство на заби. Панорамската снимка и компјутерската томографија откри отсуство на заби и кариес лезии на постојаните заби. Поради формирањето на цисти и целокупниот изглед, пациентката беше суспектна на черубизам, и беше препратена на Универзитетската клиника за максилофацијална клиника во Скопје каде е потврдена дијагнозата черубизам. **Заклучок:** Радиолошките карактеристики на черубизмот не се патогномонични, но дијагнозата е силно сугерирана со билатерално релативно симетрично зафаќање на вилицата што е ограничено на коските на вилицата и, заедно со клиничките и хистопатолошките наоди, го потврдува черубизам. Генотипската карактеристика ја потврдува дијагнозата. **Клучни зборови:** Черубизам, фибро-коскено нарушување, вилици.

Introduction

Cherubism is a skeletal dysplasia characterized by the development of bilateral symmetrical fibro-osseous lesions on the mandible and/or maxilla. It is described for the first time in 1933 by William A. Jones[7-11].

The name of cherubism is correlated with the specific facial appearance of the patients: rounder cheeks and upper eyelids, giving them so-called „angelic appearance"[2,3]. It is one of the rarest disorders in medicine with approximately 350 documented instances worldwide. Due to the rarity of this condition, it is difficult to determine the frequency (incidence) of this disorder. From an epidemiological standpoint, the female and male populations of all races and ethnicities are equally affected by it.

Cherubism is a genetic disorder with an autosomal dominant type of inheritance, and the cause of its appearance is a mutation of the SH3BP2 gene[4].

The radiological definition of this disorder is a symmetrical expansive radiolucent lesion of the mandible and/or maxilla. Children are born with a normal appearance, and the maxilla and mandible usually swell between the ages of 2 and 7, until adolescence. The lesion then begins to spontaneously resolve and bone remodeling continues until the age of 30[5]. As cherubism is a syndrome with a brief duration, surgical intervention is not necessary, unless patients or their parents seek it for cosmetic reasons.

Cherubism lesions can be classified according to their severity: grade I, bilateral involvement of the ascending ramus of mandible; grade II, bilateral involvement of the ascending ramus of mandible and maxillary tuberosity; grade III, complete involvement of the maxilla and mandible compromising the coronoid processes and condyles[6].

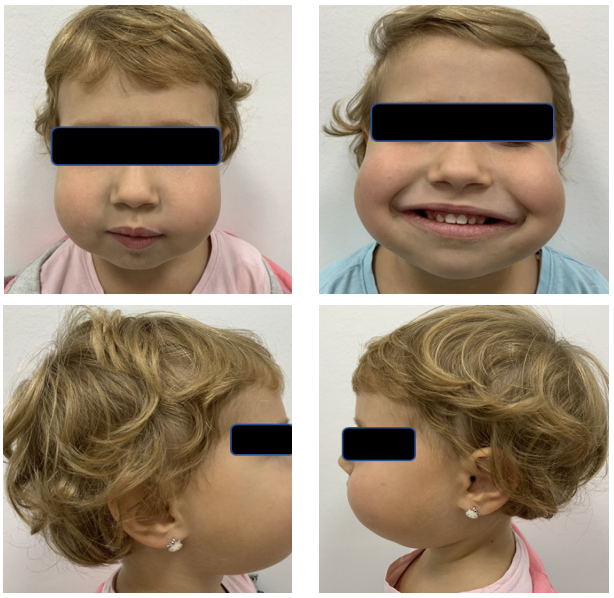
Albert Durer, a German painter, printmaker, and theorist of the German Renaissance who lived from 1471 to

Picture 1. *Head of weeping cherub*

1528, kept the look of cherubs in his paintings. This is an interesting fact. Head of Weeping cherub is the name of the picture (Picture 1)

Case report

Four-year old female patient came to our dental office for the first time for clinical examination in August 2021



Picture 2. *Extraoral status (Status localis extraoralis)*

with a specific appearance. During the extraoral examination, swollen cheeks were observed bilaterally, submandibular and sublingual glands were enlarged, mobile and painless on palpation. The face was asymmetrical with a strong swelling in the area of the cheeks (Picture 2).

Swelling was discovered during the intraoral examination in the area of the tuberosity of maxilla and in the area of the ramus of the mandible (ramus mandibulae). The local tissue enlargements were painless on palpation. Carious lesions were also observed in the area of deciduous molars. Polypomatous formation (pulpitis chronica

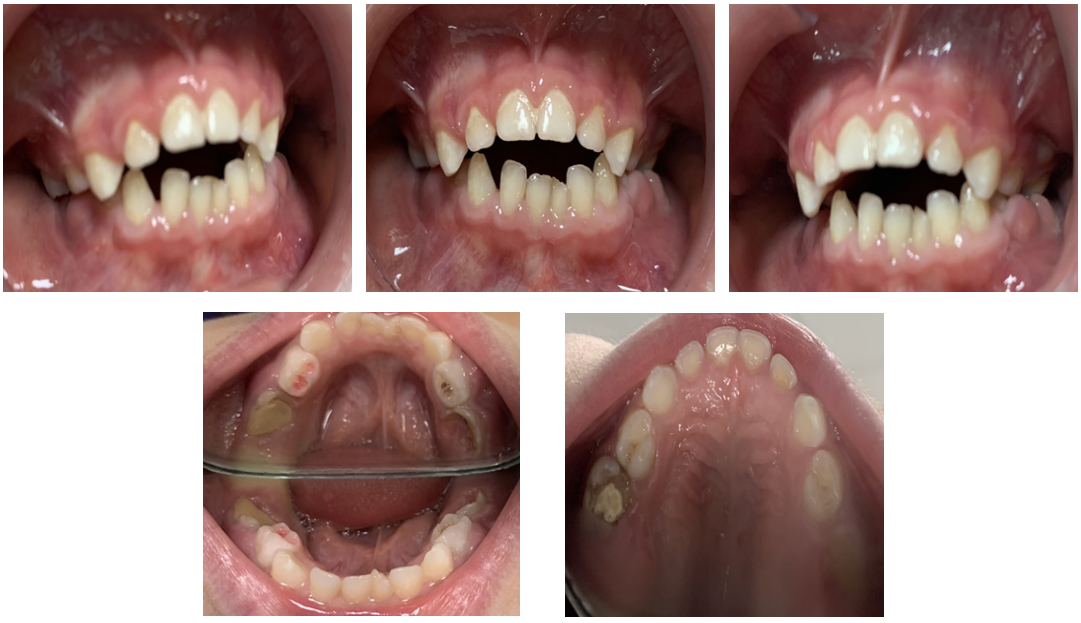


Figure 3. *Intraoral status (status localis intraoralis)*

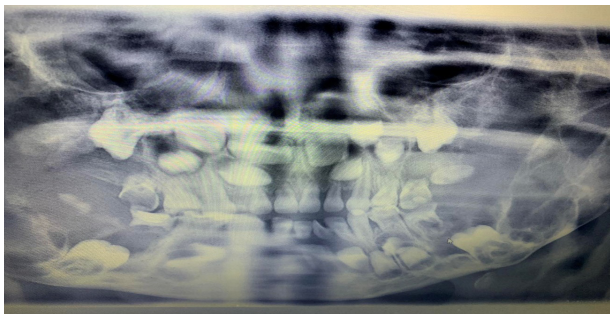
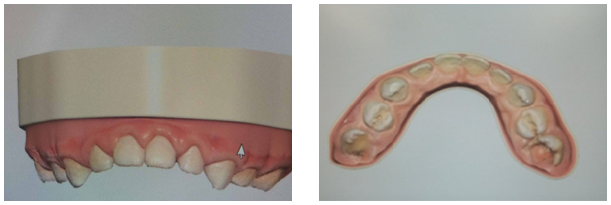
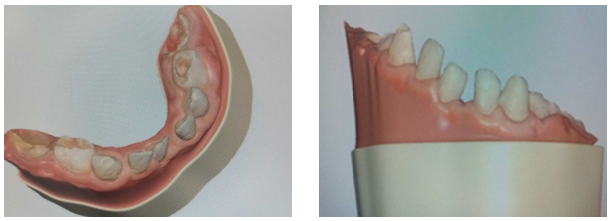


Figure 4. *Panoramic x-ray*



Picture 5. *Scans from upper jaw*



Picture 6. *Scans from lower jaw*

Центар за имуни, молекуларни и генетски истражувања (ЦИМГИ),
Институт за имунобиологија и хумана генетика,
Медицински факултет,
Универзитет "Св. Кирил и Методиј";
1109 Скопје, П.Фах, Република Македонија
Тел.: +389-2-3110-556 E-mail: ilbhg@medf.ukim.edu.mk

Center for Immuno, Molecular and Genetic Investigations (CIMGI),
Institute of Immunobiology and Human Genetics, Faculty of Medicine,
University "St. Kiril & Metodij",
1109 Skopje, PO Box 60, Republic of Macedonia

ИЗВЕШТАЈ ОД ГЕНЕТСКО ИСПИТУВАЊЕ

Презиме и име: [redacted] Датум на раѓање Лаб. Бр. 11995	Испратен од: Др Тереза Болис-Ѓурик Амбул. бр: ГенС 033/2022 Мат. Бр:
Примен примерок: ДНК од плунка	Упатна клиничка дијагноза:
Примерокот е земен на: 05.04.2022	Тест: Анализа на генот *SH3BP2*
Клинички податоци: Черубизам, со позитивна семејна историја	

РЕЗУЛТАТ:

- ***Позитивен резултат***
  Во испитуваниот примерок е откриена патогена варијанта во генот ***SH3BP2*** асоциран со автозомно доминантен черубизам.

Ген	Варијанта	Генотип	Класификација
SH3BP2	c.1258G>A (p.Gly420Arg)	Хетерозигот[1]	Патогена

[1] Се наследува на автозомно доминантен начин

Интерпретација:
Во испитуваниот примерок е откриена **патогена** варијанта **c.1258G>A (p.Gly420Arg)**, во генот ***SH3BP2***. Генот *SH3BP2* е асоциран со автозомно доминантен черубизам (MedGen UID: 40219). Черубизмот се карактеризира со прогресивно, билатерално зголемување на максилата и мандибулата предизвикан од брза коскена деградација со формирање на мултилокуларни цисти (PMID: 12907058, 11381256, 11113824). Овие цисти се безболни, но доведуваат до карактеристично лицево отекување и често влијаат врз нормалниот развој на забите. Дентиналните абнормалности вклучуваат конгенитален недостаток на заби, прематурна ексфолијација на децидуалните (млечни) заби, и поместување на трајните заби. Лезиите на вилиците обично започнуваат во раното детство и напредуваат полека до пубертетот. По пубертетот цистите постепено се заменуваат со нормална коска, а абнормалностите на лицето честопати се повлекуваат т.е не се забележуваат до возраст од 30 години. Многу ретко се зафатени и другите коски. Тежината на клиничката слика е варијабилна, од субклинички манифестации (PMID: 21045962) до сериозни промени кои го афектираат дишењето, видот, говорот и голтањето (PMID: 10716121, 10740181).
Откриената варијанта c.1258G>A во генот *SH3BP2* доведува до замена на глицин со аргинин во кодонот 420 од протеинот SH3BP2 (p.Gly420Arg). Оваа варијанта не е присутна во популациските бази на податоци (нема фреквенција во gnomAD). Оваа генска промена е забележана кај индивидуи со черубизам (PMID: 12900899, 23296820). Откриената варијанта е присутна во ClinVar базата на податоци (Variation ID: 372503). Алгоритмите за предвидување на ефектот на промената врз протеинската структура и функција се со контрадикторни резултати (SIFT: "Deleterious"; PolyPhen-2: "Probably Damaging"; Align-GVGD: "Class C15"). Експерименталните студии покажуваат дека варијантата c.1258G>A во генот SH3BP2 ја засегнува функцијата на SH3BP2 протеинот (PMID: 22153076). Поради наведените причини, откриената варијанта е класифицирана како патогена.

Препорака:
Се препорачува генетско советување.

Забелешка:
Листата на гени и региони вклучени во анализата, како и дополнителни информации поврзани со резултатот се наведени во приложеният оригинален резултат.

Асист. д-р Горјан Милановски
Генетски советник

Проф. д-р Тодор Арсов
Раководител на ЦИМГИ
Скопје
04.05.2022

Проф. д-р Александар Петличковски
специјалист по клиничка генетика
738464

Picture 7. *Results from the genetic examination*

aperta hyperplastica) and luxation of the teeth were observed on all four second deciduous molars (Picture 3).

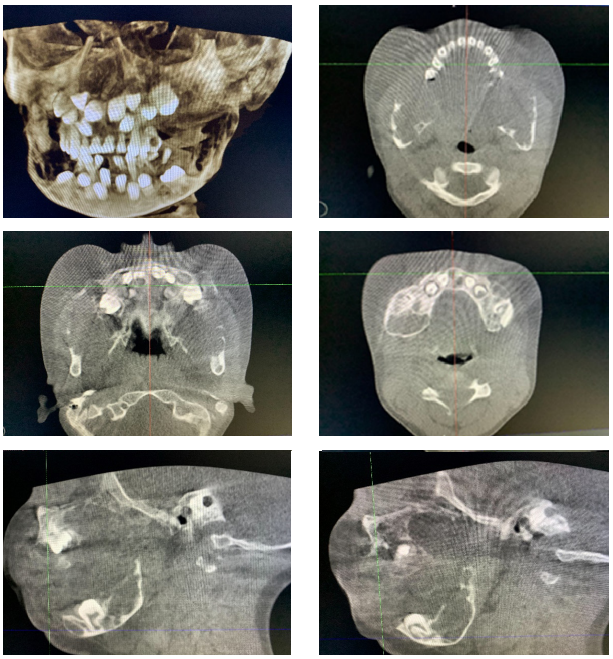
From the orthodontic point of view, the patient has a High arched palate (Gothic palate), displaced middle, an open bite and crowding in the mandible.

Family history for cherubism was positive. The father and several cousins from his family have already been diagnosed with this disorder.

Based on thorough medical and dental history and an extensive physical examination, we suspected cherubism and referred the patient to the University Clinic for Face, Jaws and Neck Surgery - Maxillofacial Surgery for further study and confirmation of the diagnosis (Picture 4)

Meanwhile, all carious lesions were cured. Due to the luxation of the lower left incisor, it was extracted.

A digital impression of the upper and lower jaws was obtained at the private polyclinic KRUNA MS – Skopje, without a bite determination because of the severity of the case and the patient's age. The scanning was per-



Picture 8. *CBCT scans*

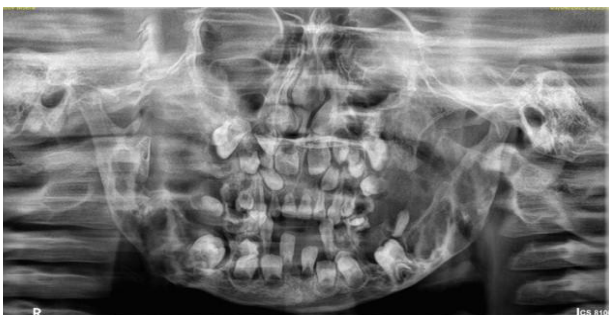


Figure 9. *Panoramic x-ray after 8 months*

formed on a MEDIT brand scanner I 1500 owned by the above private polyclinic (Picture 5, 6).

At the same time, a karyotype genetic examination was conducted. The diagnosis of cherubism was confirmed with this genetic examination. Presented is the result of the genetic test (Picture 7).

CBCT scan was performed six months later. (Picture 8)

New panoramic X-ray was performed eight months following the first one. (Picture 9).

Discussion

In addition to the presented clinical case, the following section of the article describes the diagnostic, clinical, and therapeutic aspects of this unusual condition.

• *Clinical description*

In the majority of instances, there is a symmetrical expansive lesion affecting the mandible and/or maxilla, accompanied by enlargement of the submandibular and cervical lymph nodes. The severity of the disease phenotype is highly variable even within a family, with one member having a mild form of the disease and another member having a more severe form of the disease.

The first changes seen on X-ray are usually presented in the angle of the mandible (angulus mandibulae). These lesions are asymptomatic, although they may influence the development or eruption of the first permanent molars.

Cherubism is usually limited to both jaws, and very rarely the condyle of mandibule and the zygomatic arch are affected[7-11]. Due to the fenestration in the cortical bone, a more aggressive variety can lead to the creation of fibrous tissue ,and if located in the orbit, can cause eye problems[12]. Less frequently, respiratory changes might lead to obstruction of the upper airways. If they occur, they can cause mouth breathing, snoring, chronic nasal infection and obstructive sleep apnea[13].

Cherubism can have an impact on the development of deciduous and permanent teeth. Eruption of permanent dentition can result in missing teeth (usually the first molars), rudimentary, abnormally shaped and ectopically erupted teeth[14-16].

According to contemporary scientific data, radiographic manifestations of Cherubism typically include multilocular, bilateral radiolucent areas within the mandible, mostly located at the angles and rami. The coronoid processes are most commonly involved, whereas the condyles are rarely affected. Lesions on the mandible are symmetric, whereas maxillary lesions may be asymmetric. Radiographic images typically reveal expansive remodeling of the involved alveolar bones, thinning of the cortices, and multilocular radiolucencies with a coarse trabecular pattern.

• *Biochemical markers*

In patients with cherubism, the serum levels of calcium, parathyroid hormone, calcitonin and alkaline phosphatase are normal. The urine markers for bone remodeling, pyridinium and deoxypyridinium hydroxyproline and calcium-creatinine, are elevated. The serum value of alkaline phosphatase in active phase increases[16-18].

• *Histological characteristics*

A considerable number of multinucleated giant cells resembling osteoclasts are observed in all patients. Three different phases are distinguished in the lesions of cherubism[19]. In the first osteolytic phase, round, fusiform and multinucleated giant cells resembling osteoclasts are observed. The tissue is extensively vascularized, and hemosiderin, a breakdown product of hemoglobin can be observed as a sign of hemorrhage[20]. The second phase is characterized by the proliferation of spindle-shaped cells that are associated with a reparative phase. The third phase is the formation of bone with cells that are positive for alkaline phophatase (probably osteoblasts) and a high level of ATP associated with a presence of mineralizing matrix.

• *Diagnose*

The diagnosis is based on the family history, age of the patient, the clinical examination, X-ray investigations, CBCT, genetic and biochemical examinations, biopsy and FNAC (fine needle aspiration cytology).

Family history is usually positive for this disease.

Clinically, cherubism should be distinguished from

1. Craniofacial fibrous dysplasia - this disease is usually unilateral
2. Masseteric hypertrophy-rarely observed in children and bone structures are not affected.
3. Gigantoform cementoma - is more prevalent in adults and manifests as a widespread swelling.
4. Gigantocellular granuloma-swelling in the area of the first molar
5. Brown tumor- is presented unilaterally and accompanied by systemic manifestations.

With the help of roentgenography, this disease should be separated from

1. Ameloblastoma
2. Odontogenic myxoma
3. Aneurysmic bone cyst
4. Craniofacial fibrous dysplasia
5. Gigantocellular granuloma
6. Brown tumor

- ***Age***

The typical clinical presentation for this disease is characterized by bilateral cheek enlargement, enlarged lymph nodes, high "gothic" palate and early loss of primary teeth in children aged 2 to 7 years. There is a possibility of tongue enlargement, which can cause problems with breathing, speech, mastication and swallowing. Fastest progression of the disease is between 2-4 years until 7-8 years, when it begins to spontaneously withdraw until the puberty. At the age of 20, new bone tissue is already being formed, and at the age of 41, the bone structures of the affected parts have returned to normal. In the mandible, the ramus mandiblae, angulus mandiblae and procesus coronoideus mandibulae are more frequently affected than the condyles.

Genetic testing is required to prove SH3BP2 mutation (21)

Sequence analysis of SH3BP2 detects small intragenic deletions, insertions and missense, nonsense and splice site variants. Typically, exon or whole-gene deletions or duplications are not detected. If pathogenic genetic variant cannot be identified, gene-targeted deletion and duplication analysis could be considered; however, because cherubism occurs through a gain-of-function mechanism and large intragenic deletion or duplication have not been reported, testing for intragenic deletions or duplication is unlikely to identify a disease-causing variant.

As previously stated, to confirm the cherubism, a panoramic image and a CBCT (cone-beam computed tomography) image are required. FNAC (fine needle aspiration cytology) aspiration to demonstrate the presence of abnormal cells. If the soft tissues are also involved, an MRI (magnetic resonance imaging) should also be performed.

Complications of cherubism

Many complications are associated with cherubism. First, severe malformation of the jaws may influence the physical functions such as chewing and swallowing, and may affect the social and psychological well-being of the individual, thereby necessitating surgical intervention. However, it should be noted that the recurrence of the jaw lesions after surgery is possible. Although the cherubic appearance of patients is expected to be reduced due to involution of the bubble-like distensions of the jaws in early adulthood, this may not be the case for all patients. The facial disfigurement associated with cherubism can affect an individual's sense of self-worth and lead to bullying. A recent Scandinavian study, however, reported that persons with cherubism were psychosocially well adapted and enjoyed a good quality of life[22]. Difficulties with pronunciation have not been reported as a significant problem, although they exist in a smaller number of cases of cherubism.

Patients with cherubism frequently complain of oral pain and discomfort when consuming food. The most affected persons have misplaced, unerupted, unformed, or absent, teeth or teeth that may appear to float in cyst like spaces. Malocclusion, premature exfoliation of deciduous teeth and root resorption may be the most common occurrences.

Some of the patients suffer from respiratory problems. These can include obstructive sleep apnea and upper airway obstruction caused by backward displacement of the tongue.

Prior reports of patients with maxillary involvement leading to orbital mass effect have varied in their ophthalmic sequelae and age of occurrence, with occurrence ranging from age 7 to 27 years[23,24].

Treatment

Due to the rarity of cherubism, treatment protocols for its complications are not well established and are evolving as a result of recent advances in our understanding of the autoinflammatory nature of this bone disease. Given that cherubism is considered to be a self-limited condition that improves over time, treatment should be tailored to the individual's presentation and the evolution of the disease. Depending on the severity, surgery may be needed for functional and esthetic concerns.

Children with cherubism should be referred to a maxillofacial clinic with pediatric experience for ongoing management. A craniofacial clinic associated with a major pediatric medical center usually includes a surgical team, general dentists, orthodontic specialists, ophthalmologists and child psychologist or social worker.

Surgical interventions in these patients include curettage with or without bone grafting. Liposuction has also been used successfully to re-contour the jaws. Surgical interventions are likely to occur between ages 5 and 15 years in individuals with disfiguring enlargement of jaws or locally aggressive lesions associated with complications such as impaired swallowing, respiratory issues, nasal airway obstruction, or tongue displacement. Surgical therapy needs to be individually tailored and not create unrealistic expectations since recurrence of the lesions is possible and surgery may not halt disease progression.

Some individuals with orbital manifestations such as lower lid retraction, ptosis, diplopia, eyeball displacement and visual loss caused by optic atrophy may require ophthalmologic treatment.

Speech and language therapy may be necessary in rare cases where physical obstruction to the production of speech or swallowing is present.

And perhaps the most significant is orthodontic treatment. It is commonly required because the jaw distortion

leads to permanent dental abnormalities including a malocclusive bite, premature loss of deciduous teeth and widely spaced, misplaced, unerupted or absent permanent teeth.

Further approach in treatment

Current contemporary researches on a mouse model indicate a high level of tumor necrosis factor[25,26]. The presence of TNF in the circulatory system contributes to the regression of the disease. This holds true for a number of autoimmune-inflammatory diseases. It leads to a decrease in pro-inflammatory production of cytokines and a reduced effect of osteoclasts.

Additionally, mechanisms that will act on the SH3BP2 gene are being investigated. However, this type of therapy still requires proper development.

Forecast

In most cases, the lesions spontaneously regress by the age of 12. The X-ray examination reveals filling of the lesions with normal bone tissue. In some cases, the lesions may be filled with sclerotic bone and in more severe cases, they may remain unfilled with bone. However, it should be noted that spontaneous fractures are not observed[27].

Conclusion

Cherubism is a rare disease that has a significant impact on children and their families. In this particular case, the girl inherited from her father. Surgery is usually not required as the lesions resolve spontaneously by the age of 12. This autonomous disease is caused by a genetic change of the SH3BP2 gene in the chromosomal part 4q16.3.5 which codes for the protein. When the coding gene is mutated, the protein changes and cannot perform the function or performs it inadequately.

Mild forms of cherubism without facial deformities do not need to be treated. It is sufficient to monitor the patients with annual panoramic images and after regression of the disease, the images should be taken every 2 to 5 years. Surgical intervention is required if there are functional or aesthetic problems. Lytic changes occur in the bone with resorption of the roots and a floating appearance of the teeth, the girl already loose teeth 81,71 and 75. It leads to the premature loss of deciduous teeth and the more difficult eruption of permanent teeth. In this situation, a possible solution would be to install space brackets. As a choice of therapy, calcitonin is administered, in the form of tablets or nasal spray, with a note that if there are rapidly growing lesions, its use is contraindicated[8,27].

Interferon is still in experimental use.

Reference

1. Jones WA. Familial multilocular cystic disease of the jaws. The American Journal of Cancer. 1933 Apr; 17(4):946-50.
2. Jones WA. Further observations regarding familial multilocular cystic disease of the jaws. The British Journal of Radiology. 1938 Apr; 11(124):227-41.
3. Jones WA, Gerrie J, Pritchard J. Cherubism—a familial fibrous dysplasia of the jaws. Oral Surgery, Oral Medicine, Oral Pathology. 1952 Mar 1; 5(3):292-305.
4. Preda L, Dinca O, Bucur A, Dragomir C, Severin E. Identical mutation in SH3BP2 gene causes clinical phenotypes with different severity in mother and daughter–case report. Molecular Syndromology. 2010; 1(2):87-90.
5. Wagel J, Luczak K, Hendrich B, Guziński M, Sąsiadek M. Clinical and radiological features of nonfamiliar cherubism: A case report. Pol J Radiol. 2012; 77(3):53-57. doi:10.12659/pjr.8833756
6. Lima Gde M, Almeida JD, Cabral LA. Cherubism: clinicoradiographic features and treatment. J Oral Maxillofac Res. 2010; 1(2):e2. Published 2010 Jul 1. doi:10.5037/jomr.2010.1202
7. Motamedi MH. Treatment of cherubism with locally aggressive behavior presenting in adulthood: report of four cases and a proposed new grading system. Journal of oral and maxillofacial surgery. 1998 Nov 1; 56(11):1336-42.
8. Raposo-Amaral CE, de Campos Guidi M, Warren SM, Almeida AB, Amstalden EM, Tiziane V, Raposo-Amaral CM. Two-stage surgical treatment of severe cherubism. Annals of plastic surgery. 2007 Jun 1; 58(6):645-51.
9. Anderson DE. Cherubism: hereditary fibrous dysplasia of the jaws. 1 Genetic considerations. Oral Surg.. 1962;15(2):5.
10. Reichenberger EJ, Levine MA, Olsen BR, Papadaki ME, Lietman SA. The role of SH3BP2 in the pathophysiology of cherubism. Orphanet Journal of Rare Diseases. 2012 Jun;7(1):1-2.
11. Thompson N. Cherubism: familial fibrous dysplasia of the jaws. British Journal of Plastic Surgery. 1959 Jan 1;12:89-103.
12. Timoşca GC, Găleşanu RM, Cotutiu C, Grigoraş M. Aggressive form of cherubism: report of a case. Journal of oral and maxillofacial surgery. 2000 Mar 1;58(3):336-44.
13. Battaglia A, Merati AL, Magit A. Cherubism and upper airway obstruction. Otolaryngology—Head and Neck Surgery. 2000 Apr;122(4):573-4.
14. Faircloth Jr WJ, Edwards RC, Farhood VW. Cherubism involving a mother and daughter: case reports and review of the literature. Journal of oral and maxillofacial surgery. 1991 May 1;49(5):535-42.
15. Pontes FS, Ferreira AC, Kato AM, Pontes HA, Almeida DS, Rodini CO, Pinto Jr DS. Aggressive case of cherubism: 17-year follow-up. International journal of pediatric otorhinolaryngology. 2007 May 1;71(5):831-5.
16. Ireland AJ, Eveson JW. Cherubism: a report of a case with an unusual post-extraction complication. British Dental Journal. 1988 Feb 20;164(4):116-7.
17. 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. International journal of pediatric otorhinolaryngology. 2003 Sep 1;67(9):1005-12.
18. Shah N, Handa KK, Sharma MC. Malignant mesenchymal tumor arising from cherubism: a case report. Journal of oral and maxillofacial surgery. 2004 Jun 1;62(6):744-9.
19. Roginsky VV, Ivanov AL, Ovtchinnikov IA, Khonsari RH. Familial cherubism: the experience of the Moscow central Institute for Stomatology and Maxillo-Facial Surgery. International journal of oral and maxillofacial surgery. 2009 Mar 1;38(3):218-23.
20. Chomette G, Auriol M, Guilbert F, Vaillant JM. Cherubism: Histoenzymological and ultrastructural study. International journal of oral and maxillofacial surgery. 1988 Aug 1;17(4):219-23.
21. Ueki Y, Tiziani V, Santanna C, Fukai N, Maulik C, Garfinkle J, Ninomiya C, doAmaral C, Peters H, Habal M, Rhee-Morris L. Mutations in the gene encoding c-Abl-binding protein SH3BP2

cause cherubism. Nature genetics. 2001 Jun;28(2):125-6.
22. Prescott T, Redfors M, Rustad CF, Eiklid KL, Geirdal AØ, Storhaug K, Jensen JL. Characterization of a Norwegian cherubism cohort; molecular genetic findings, oral manifestations and quality of life. Eur J Med Genet. 2013;56:131–7.
23. Colombo F, Cursiefen C, Neukam FW, Holbach LM. Orbital involvement in cherubism. Ophthalmology. 2001;108:1884–8.
24. Ahmadi AJ, Pirinjian GE, Sires BS. Optic neuropathy and macular chorioretinal folds caused by orbital cherubism. Arch Ophthalmol. 2003;121:570–3.
25. Peñarrocha M, Bonet J, Mínguez JM, Bagán JV, Vera F, Mínguez I. Cherubism: a clinical, radiographic, and histopathologic comparison of 7 cases. Journal of oral and maxillofacial surgery. 2006 Jun 1;64(6):924-30.
26. Ueki Y, Tiziani V, Santanna C, Fukai N, Maulik C, Garfinkle J, Ninomiya C, doAmaral C, Peters H, Habal M, Rhee-Morris L. Mutations in the gene encoding c-Abl-binding protein SH3BP2 cause cherubism. Nature genetics. 2001 Jun;28(2):125-6.
27. Wong M, Ziring D, Korin Y, Desai S, Kim S, Lin J, Gjertson D, Braun J, Reed E, Singh RR. TNFα blockade in human diseases: mechanisms and future directions. Clinical immunology. 2008 Feb 1;126(2):121-36.