Cherubism

Description

Cherubism is a disorder characterized by abnormal bone tissue in the jaw. Beginning in early childhood, both the lower jaw (the mandible) and the upper jaw (the maxilla) become enlarged as bone is replaced with painless, cyst-like growths. These growths give the cheeks a swollen, rounded appearance and often interfere with normal tooth development. In some people the condition is so mild that it may not be noticeable, while other cases are severe enough to cause problems with vision, breathing, speech, and swallowing. Enlargement of the jaw usually continues throughout childhood and stabilizes during puberty. The abnormal growths are gradually replaced with normal bone in early adulthood. As a result, many affected adults have a normal facial appearance.

Most people with cherubism have few, if any, signs and symptoms affecting other parts of the body. Rarely, however, this condition occurs as part of another genetic disorder. For example, abnormal jaw growth, like that in cherubism, can occur in Ramon syndrome, which also involves short stature, intellectual disability, and overgrowth of the gums (gingival fibrosis). Additionally, cherubism-like growths have been reported in rare cases of Noonan syndrome (a developmental disorder characterized by unusual facial characteristics, short stature, and heart defects), fragile X syndrome (a condition primarily affecting males that causes learning disabilities and cognitive impairment), and neurofibromatosis type 1 (a condition primarily characterized by multiple skin tumors).

Frequency

The incidence of cherubism is unknown. Nearly 350 cases have been reported worldwide.

Causes

Mutations in the *SH3BP2* gene have been identified in about 80 percent of people with cherubism. In most of the remaining cases, the genetic cause of the condition is unknown.

The *SH3BP2* gene provides instructions for making a protein that plays a role in relaying chemical signals within cells. the SH3BP2 protein is particularly important for the function of cells involved in the replacement of old bone tissue with new bone (bone

remodeling) and certain immune system cells.

Mutations in the *SH3BP2* gene lead to production of an abnormal protein that does not get broken down when it is no longer needed. Too much SH3BP2 protein likely increases signaling in certain cells, causing an immune reaction (inflammation) in the jaw bones and also triggering the production of osteoclasts, which are cells that break down bone tissue during bone remodeling. An excess of these bone-destroying cells contributes to the destruction of bone in the upper and lower jaws. A combination of bone loss and inflammation likely underlies the cyst-like growths characteristic of cherubism.

When cyst-like growths in the jaw, like those in cherubism, occur as a feature of a genetic syndrome, they are caused by the genetic alteration involved in the syndrome rather than by an *SH3BP2* alteration.

Learn more about the gene associated with Cherubism

- SH3BP2

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- Familial benign giant-cell tumor of the jaw
- Familial fibrous dysplasia of jaw
- Familial multilocular cystic disease of the jaws

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Fibrous dysplasia of jaw (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0008029/)

Genetic and Rare Diseases Information Center

- Cherubism (https://rarediseases.info.nih.gov/diseases/6036/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Cherubism%22)

Catalog of Genes and Diseases from OMIM

- CHERUBISM (https://omim.org/entry/118400)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Cherubism%5BMAJR%5D%29+AND+%28cherubism%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

References

- Carvalho Silva E, Carvalho Silva GC, Vieira TC. Cherubism: clinicoradiographicfeatures, treatment, and long-term follow-up of 8 cases. J Oral Maxillofac Surg.2007 Mar;65(3):517-22. doi: 10.1016/j.joms.2006.05.061. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17307601)
- de Lange J, van Maarle MC, van den Akker HP, Redeker EJ. A new mutation in theSH3BP2 gene showing reduced penetrance in a family affected with cherubism. OralSurg Oral Med Oral Pathol Oral Radiol Endod. 2007 Mar;103(3):378-81. doi:10.1016/j.tripleo.2006.05.012. Epub 2006 Sep 26. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17321449)
- Friedrich RE, Zustin J, Luebke AM, Rosenbaum T, Gosau M, Hagel C, KohlruschFK, Wieland I, Zenker M. Neurofibromatosis Type 1 With Cherubism-like Phenotype, Multiple Osteolytic Bone Lesions of Lower Extremities, and Alagille-syndrome:Case Report With Literature Survey. In Vivo. 2021 May-Jun;35(3):1711-1736. doi:10.21873/invivo.12431. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/33910856)
- Guettler S, LaRose J, Petsalaki E, Gish G, Scotter A, Pawson T, Rottapel R,Sicheri F. Structural basis and sequence rules for substrate recognition byTankyrase explain the basis for cherubism disease. Cell. 2011 Dec9;147(6):1340-54. doi: 10.1016/j.cell.2011.10.046. Erratum In: Cell. 2012 Jan20;148(1-2):376. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22153077)
- Kannu P, Baskin B, Bowdin S. Cherubism. 2007 Feb 26 [updated 2018 Nov 21]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, AmemiyaA, editors. GeneReviews(R) [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1137/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301316)
- Levaot N, Voytyuk O, Dimitriou I, Sircoulomb F, Chandrakumar A, Deckert M,

Krzyzanowski PM, Scotter A, Gu S, Janmohamed S, Cong F, Simoncic PD, Ueki Y, LaRose J, Rottapel R. Loss of Tankyrase-mediated destruction of 3BP2 is theunderlying pathogenic mechanism of cherubism. Cell. 2011 Dec 9;147(6):1324-39.doi: 10.1016/j.cell.2011.10.045. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22153076) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3475183/)

- Lo B, Faiyaz-Ul-Haque M, Kennedy S, Aviv R, Tsui LC, Teebi AS. Novel mutationin the gene encoding c-Abl-binding protein SH3BP2 causes cherubism. Am J MedGenet A. 2003 Aug 15;121A(1):37-40. doi: 10.1002/ajmg.a.20226. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12900899)
- Novack DV, Faccio R. Jawing about TNF: new hope for cherubism. Cell. 2007 Jan12;128(1):15-7. doi: 10.1016/j.cell.2006.12.019. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17218248)
- Ozkan Y, Varol A, Turker N, Aksakalli N, Basa S. Clinical and radiologicalevaluation of cherubism: a sporadic case report and review of the literature. IntJ Pediatr Otorhinolaryngol. 2003 Sep;67(9):1005-12. doi:10.1016/s0165-5876(03)00179-4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12907058)
- Penarrocha M, Bonet J, Minguez JM, Bagan JV, Vera F, Minguez I. Cherubism: aclinical, radiographic, and histopathologic comparison of 7 cases. J OralMaxillofac Surg. 2006 Jun;64(6):924-30. doi: 10.1016/j.joms.2006.02.003. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16713807)
- Ueki Y, Lin CY, Senoo M, Ebihara T, Agata N, Onji M, Saheki Y, Kawai T, Mukherjee PM, Reichenberger E, Olsen BR. Increased myeloid cell responses toM-CSF and RANKL cause bone loss and inflammation in SH3BP2 "cherubism" mice.Cell. 2007 Jan 12;128(1):71-83. doi: 10.1016/j.cell.2006.10.047. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17218256)
- Ueki Y, Tiziani V, Santanna C, Fukai N, Maulik C, Garfinkle J, Ninomiya C, doAmaral C, Peters H, Habal M, Rhee-Morris L, Doss JB, Kreiborg S, Olsen BR, Reichenberger E. Mutations in the gene encoding c-Abl-binding protein SH3BP2cause cherubism. Nat Genet. 2001 Jun;28(2):125-6. doi: 10.1038/88832. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11381256)
- Von Wowern N. Cherubism: a 36-year long-term follow-up of 2 generations indifferent families and review of the literature. Oral Surg Oral Med Oral PatholOral Radiol Endod. 2000 Dec;90(6):765-72. doi: 10.1067/moe.2000.108438. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11113824)

Last updated June 1, 2021