

# Cherubism

Subjects: Genetics & Heredity

Contributor: Nicole Yin

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.

Keywords: genetic conditions

---

## 1. Introduction

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, cherubism can occur with Ramon syndrome, which also involves short stature, intellectual disability, and overgrowth of the gums (gingival fibrosis). Additionally, cherubism has been reported in rare cases of Noonan syndrome (a developmental disorder characterized by unusual facial characteristics, short stature, and heart defects) and fragile X syndrome (a condition primarily affecting males that causes learning disabilities and cognitive impairment).

## 2. Frequency

The incidence of cherubism is unknown. At least 250 cases have been reported worldwide.

## 3. 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 transmitting 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 cherubism occurs as a feature of a genetic syndrome, it is caused by the same genetic alteration that causes the syndrome.

### 3.1. The Gene Associated with Cherubism

- SH3BP2

## 4. 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.

## 5. 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

---

## References

1. Carvalho Silva E, Carvalho Silva GC, Vieira TC. Cherubism: clinicoradiographic features, treatment, and long-term follow-up of 8 cases. *J Oral Maxillofac Surg*. 2007 Mar;65(3):517-22.
2. de Lange J, van Maarle MC, van den Akker HP, Redeker EJ. A new mutation in the SH3BP2 gene showing reduced penetrance in a family affected with cherubism. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007 Mar;103(3):378-81.
3. Guettler S, LaRose J, Petsalaki E, Gish G, Scotter A, Pawson T, Rottapel R, Sicheri F. Structural basis and sequence rules for substrate recognition by Tankyrase explain the basis for cherubism disease. *Cell*. 2011 Dec 9;147(6):1340-54. doi: 10.1016/j.cell.2011.10.046. Erratum in: *Cell*. 2012 Jan 20;148(1-2):376.
4. Kannu P, Baskin B, Bowdin S. Cherubism. 2007 Feb 26 [updated 2018 Nov 21]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1137/>
5. 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 the underlying pathogenic mechanism of cherubism. *Cell*. 2011 Dec 9;147(6):1324-39. doi: 10.1016/j.cell.2011.10.045.
6. Lo B, Faiyaz-Ul-Haque M, Kennedy S, Aviv R, Tsui LC, Teebi AS. Novel mutation in the gene encoding c-Abl-binding protein SH3BP2 causes cherubism. *Am J Med Genet A*. 2003 Aug 15;121A(1):37-40.
7. Novack DV, Faccio R. Jawing about TNF: new hope for cherubism. *Cell*. 2007 Jan 12;128(1):15-7.
8. Ozkan Y, Varol A, Turker N, Aksakalli N, Basa S. Clinical and radiologic evaluation of cherubism: a sporadic case report and review of the literature. *Int J Pediatr Otorhinolaryngol*. 2003 Sep;67(9):1005-12. Review.
9. Peñarrocha M, Bonet J, Mínguez JM, Bagán JV, Vera F, Mínguez I. Cherubism: a clinical, radiographic, and histopathologic comparison of 7 cases. *J Oral Maxillofac Surg*. 2006 Jun;64(6):924-30.
10. 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 to M-CSF and RANKL cause bone loss and inflammation in SH3BP2 "cherubism" mice. *Cell*. 2007 Jan 12;128(1):71-83.
11. Ueki Y, Tiziani V, Santanna C, Fukai N, Maulik C, Garfinkle J, Ninomiya C, do Amaral 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 SH3BP2 cause cherubism. *Nat Genet*. 2001 Jun;28(2):125-6.
12. 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 Dec;90(6):765-72. Review.