

EDITOR'S
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CASE REPORT

Cherubism with multiple dental abnormalities: a rare presentation

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Accepted 17 September 2014

SUMMARY

Cherubism is a progressive, hereditary fibro-osseous lesion exclusively affecting the jaw bones. It is caused by the abnormal functioning of osteoblasts and osteoclasts, leading to replacement of normal bone by cellular fibrous tissue and immature bone, which produces painless progressive growth of the jaw, with a round facial appearance. It was first described in 1933 by Jones as 'familial multilocular cystic disease of the jaws'. The term 'cherubism' was later coined to describe the rounded facial appearance resulting from jaw hypertrophy that was reminiscent of cherubs depicted throughout Renaissance art. The bony lesions generally occur at an early age, affect one or both jaws symmetrically, and grow progressively until puberty. Spontaneous regression is seen in most cases, although surgical re-contouring may be required for others for aesthetic reasons.

BACKGROUND

Cherubism is characterised by bilateral symmetrical swelling of the mandible and/or maxilla in infants, which increases progressively until puberty, when regression and bone remodelling occurs. Depending on the clinical and radiological features, cherubic lesions are classified as quiescent, non-aggressive or aggressive. Although the disease is self-limiting, aggressive lesions may cause cortical thinning and perforation, root resorption and displacement of teeth. The present case is unusual because in addition to bilateral asymptomatic swelling in the mandibular rami, a plethora of dental abnormalities such as impacted teeth, dens invaginatus, taurodontism, dilacerations, talons cusp and complex composite odontome are seen. We report this rare case of cherubism associated with multiple dental anomalies.

CASE PRESENTATION

A 14-year-old patient reported to the dental hospital with a 6-year history of swelling in the lower jaws.

History revealed that the patient had noticed a mild swelling in his lower jaw which over time had gradually increased in size. No discomfort or toothache was associated with the swelling over the previous 6 years. Medical, surgical, dental, personal and family histories were non-contributory.

On examination, bilaterally diffuse swellings were seen in the posterior mandible with ill-defined margins, extending antero-posteriorly from the angle to the parasymphysis region of the mandible on both sides and measuring 3×2 cm without any

secondary changes such as ulceration or discharge (figure 1). On palpation, the swellings were firm in consistency, non-tender and fixed to the underlying bone. Two discrete, enlarged, non-tender, submandibular lymph nodes were palpable bilaterally. The patient had a characteristic cherubic appearance.

Intra-orally, the buccal vestibule was slightly obliterated bilaterally in the posterior mandible with unerupted second molars in both the jaws. There was focal swelling in the periapical region of 45, which was soft and fluctuant in consistency with slight tenderness on palpation. Talon cusps were seen in both 11 and 21 palatally, with 15 palatally displaced.

In light of the history and clinical findings, the condition was provisionally diagnosed as cherubism.

INVESTIGATIONS

Biochemical investigations

Peripheral blood was sent for determination of serum alkaline phosphatase, calcium, procalcitonin and parathyroid hormone assay. All investigations revealed normal values.

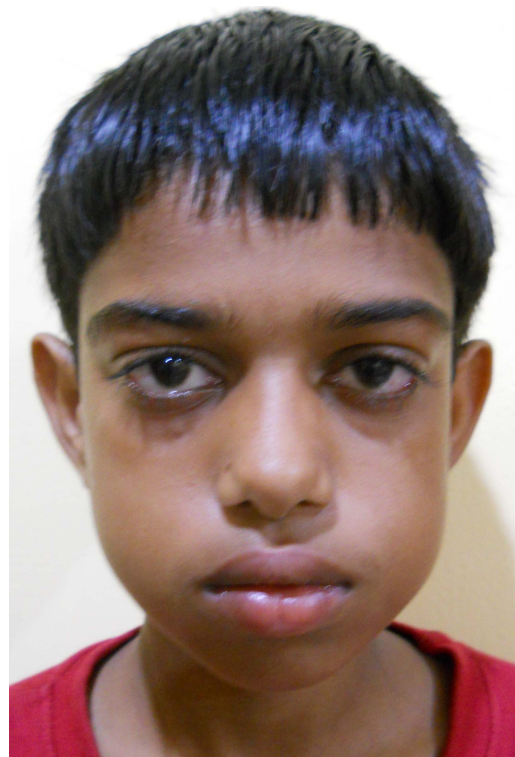


Figure 1 Frontal photograph of the 14-year-old child with diffuse, bilateral facial swelling with a cherubic appearance.



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To cite: Misra SR, Mishra L, Mohanty N, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-206721

Karyotyping

Karyotyping was performed to rule out genetic mutations, and a normal human male karyotype was obtained. However, molecular analysis to detect specific genetic mutation in the SH3BP2 gene was not carried out as a suitable facility was not available locally and because of the financial constraints of the patient.

Periapical radiography

Periapical radiographs revealed numerous dental abnormalities: all second molars were impacted, and there was taurodontism in all first molars, dilacerated roots in 12 and 22, talon cusps in 11 and 21, dens invaginatus in 24, root resorption in 25 and 45 with periapical rarefaction, and a complex odontome lingual to 47.

Mandibular occlusal radiographs

Bicortical expansion of the mandible was seen posterior to the second molars (figure 2A, B).

Posterior–anterior view of the mandible

Bicortical expansion of the mandibular ramus seen bilaterally (figure 3A).

Panoramic radiograph

A panoramic radiogram revealed multilocular irregular radiolucency in the rami sparing the condyle and coronoid, with numerous dental abnormalities: impacted second molars, taurodont first molars, dilacerated 12 and 22, talon cusps in 11 and 21, dens invaginatus in 24, root resorption in 25 and 45 with periapical rarefaction, and a complex odontome lingual to 47 (figure 3B).

CT scan

A CT scan of the mandible in the axial (figure 4A), coronal (figure 4B) and sagittal (figure 4C) planes showed well-defined, bilateral multilocular, expansile, heterodense lesions in the ramus and body, with moderate soft tissue enhancement within them and anterior displacement of the mandibular molars. Three-dimensional CT images revealed perforation of the buccal cortical plate (figure 5A–C).

Figure 2 (A, B) Mandibular lateral occlusal radiographs showing bicortical expansion.



Fine needle aspiration cytology

Fine needle aspiration cytology (FNAC) was performed and a scanty aspirate obtained. A cytosmear showed oval to spindle stromal cells in small clusters with large numbers of multinucleated osteoclastic giant cells (figure 6A).

Biopsy

Incisional biopsy was performed and the H&E-stained section showed multinucleated osteoclast-type giant cells separated by loosely arranged fibro-vascular stroma (figure 6B).

DIFFERENTIAL DIAGNOSIS

Clinical differential diagnosis

The clinical differential diagnosis included:

- ▶ Craniofacial fibrous dysplasia
- ▶ Masseteric hypertrophy
- ▶ Familial gigantiform cementoma
- ▶ Central giant cell granuloma
- ▶ Brown tumour of hyperparathyroidism.

Craniofacial fibrous dysplasia occurs in children but is generally unilateral. Masseteric hypertrophy is rarely seen in children, and although bilateral, does not involve the bones. Familial gigantiform cementoma occurs in adult females but manifests as focal rather than diffuse swellings. Central giant cell granuloma is also common in females and is seen anterior to the first molar. Brown tumour of hyperparathyroidism is unilateral and accompanied by systemic manifestations of hypocalcaemia/renal failure.

Radiological differential diagnosis

The radiological differential diagnosis included:

- ▶ Ameloblastoma
- ▶ Odontogenic myxoma
- ▶ Aneurysmal bone cyst
- ▶ Craniofacial fibrous dysplasia
- ▶ Central giant cell granuloma
- ▶ Brown tumour of hyperparathyroidism.

Ameloblastoma, odontogenic myxoma and aneurysmal bone cyst manifest as multilocular radiolucency in the mandibular ramus region but are uncommon in children and definitely not bilateral. Craniofacial fibrous dysplasia occurs unilaterally and is not seen as multilocular radiolucency. Central giant cell granuloma is seen as unilateral multilocular radiolucency and is



Figure 3 (A) Posterior–anterior view of the skull showing bicortical expansion. (B) Panoramic radiograph with multilocular irregular radiolucency in the rami sparing the condyle and coronoid, with numerous dental abnormalities: impacted second molars, taurodont first molars, dilacerated 12 and 22, talon cusps in 11 and 21, dens invaginatus in 24, root resorption in 25 and 45 with periapical rarefaction, and a complex odontome lingual to 47.

anterior to the first molar. Brown tumour of hyperparathyroidism is unilateral and all bones are osteopaenic.

TREATMENT

Since cherubism is a developmental condition which can regress after puberty, no treatment was initiated for the patient, but regular follow-up every 6 months was advised.

OUTCOME AND FOLLOW-UP

The patient has been attending for follow-up twice annually and there has been a slight increase in the size of the facial swelling over the past year.

DISCUSSION

Cherubism is a familial disorder of the jaws first described by Jones in 1933; however, sporadic cases are not uncommon.¹ The term ‘cherubism’ is derived from the characteristic cherubic appearance of patients. The characteristic spherical and symmetrical chubby facial appearance observed in cherubism is diagnostic of the condition. Since the condition typically affects only the jaw bones, which bear teeth, there may be an odontogenic origin.

Neurofibromatosis type 1, Noonan-like/multiple giant cell lesion syndrome, Ramon syndrome and Jaffe-Campanacci syndrome have all been reported to be associated with cherubism.¹

The exact aetiology of cherubism is unknown. It is an autosomal dominant disease, and mutations in exon 9 of the

SH3BP2 gene have been mapped to chromosome region 4q16.3.5.²

Cherubism rarely manifests at birth and is usually seen between 14 months and 5 years of age as bilaterally symmetrical diffuse facial swellings progressing until puberty after which it regresses.³ The mandible is more commonly affected than the maxilla. The swelling of the mandible and the cheeks results in the typical cherubic appearance. When the maxillae are affected, the floor of the orbits is swollen and the lower eyelids are retracted by the skin stretched over the cheeks. Hence a thin rim of sclera is exposed giving the appearance of heavenly gaze in cherubic patients.⁴

Premature exfoliation of the deciduous teeth, delayed eruption of permanent teeth, crowding or impaction of permanent teeth, and agenesis of the first and second permanent molars have been reported.⁵ Another unusual finding is enlarged cervical lymph nodes that are discrete, non-tender on palpation and mobile, which are otherwise unrelated to this bone disorder, suggesting an immune-mediated pathogenesis of the disease.⁶

The radiological appearance, although not pathognomonic, is characteristic, with bilateral, well-defined, multilocular radiolucencies and thinned cortex with bicortical expansion seen in both the maxilla and the mandible, or more frequently only the mandible.⁷ The epicentre is always in the posterior aspect of the jaws, in the ramus of the mandible or the maxillary tuberosity. Periosteal bone reaction is not usually seen. The entire ramus

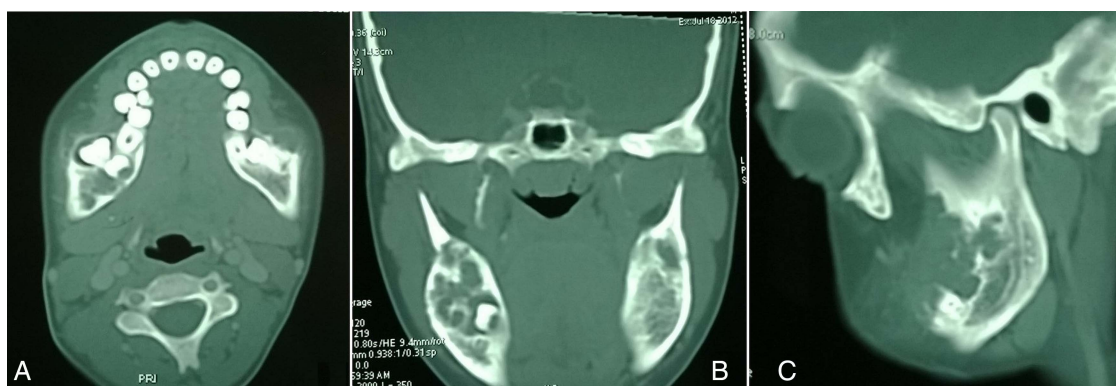


Figure 4 (A) Axial, (B) coronal and (C) sagittal CT images of the mandible exhibiting well-defined, bilateral, multilocular expansile, hypodense lesions with moderate enhancement of the soft tissues within them.

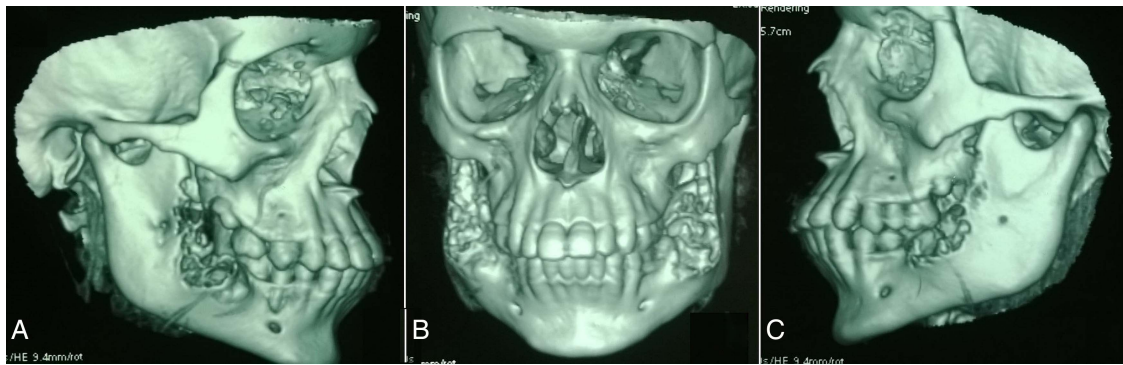


Figure 5 (A) Right profile, (B) frontal and (C) left profile three-dimensional CT scan of the mandible showing bicortical expansion with perforation of the buccal cortex.

and coronoid process may be affected, but the condyles are spared in the mandible, another typical feature of cherubism.⁸

The lesion grows in an anterior direction and in severe cases can extend almost up to the midline. The borders are well defined and sometimes corticated with the internal structure, having fine, granular bone and wispy, irregular trabeculae. The maxillae and mandible are enlarged, although severity varies. Maxillary lesions expand into the antrum and encroach on the orbital floor. When the teeth are present in the radiolucent area without any supporting bone, they are referred to as ‘floating teeth’, which may also be seen in eosinophilic granuloma and gingival carcinoma. The teeth are displaced anteriorly or may be impacted/unerupted, and dental anomalies such as enamel hypoplasia have been reported.^{1 5 7} Rarely, tooth buds are destroyed by the lesion. However, this is the first case of cherubism associated with multiple dental abnormalities to be reported in the English literature.

Panoramic radiography is usually sufficient for diagnosis, but the extent of the lesion is clearly seen only on CT scan. In certain cases, MRI may be performed when soft tissue structures such as optic nerves are impinged on by the cherubic lesion.¹

Grading of cherubism based on the radiographic features has been proposed by many authors. The latest grading system proposed by Raposo-Amaral in 2007⁹ does not account for the numerous dental anomalies seen. Hence, we propose a modification to the classification with the addition of a grade VII which encompasses other abnormalities or syndromes associated with cherubism, including the present case, as follows:

- ▶ Grade I: Bilateral involvement of the mandibular rami without signs of root resorption.
- ▶ Grade II: Involvement of both mandibular rami and maxillary tuberosities without signs of root resorption.
- ▶ Grade III: Aggressive lesions of the mandible with root resorption.
- ▶ Grade IV: Lesions involving both the mandible and maxilla with signs of root resorption.
- ▶ Grade V: Rare, massively growing, aggressive and extensively deforming juvenile lesions involving the maxilla and mandible.
- ▶ Grade VI: Rare, massively growing, aggressive and extensively deforming juvenile lesions involving the maxilla, mandible and orbits.
- ▶ Grade VII: Bilateral involvement of the mandible and/or maxilla associated with other abnormalities/syndromes.

Histologically, multinucleated giant cells and vascular spaces randomly present in a background of highly cellular spindled connective tissue stroma. Focal hemosiderin deposits may be seen in the stroma with perivascular eosinophilic collagen cuffing, and are a pathognomonic feature of cherubism although not observed in all cases.¹⁰ FNAC can also show spindled stroma and the presence of giant cells,¹¹ but the gold standard of diagnosis is molecular analysis of the SH3BP2 gene when the clinical, radiographic or histological features do not correlate. *De novo* mutations detected from genomic DNA sequencing obtained from blood/tissue samples can substantiate the clinical and radiological features, especially in patients without a family

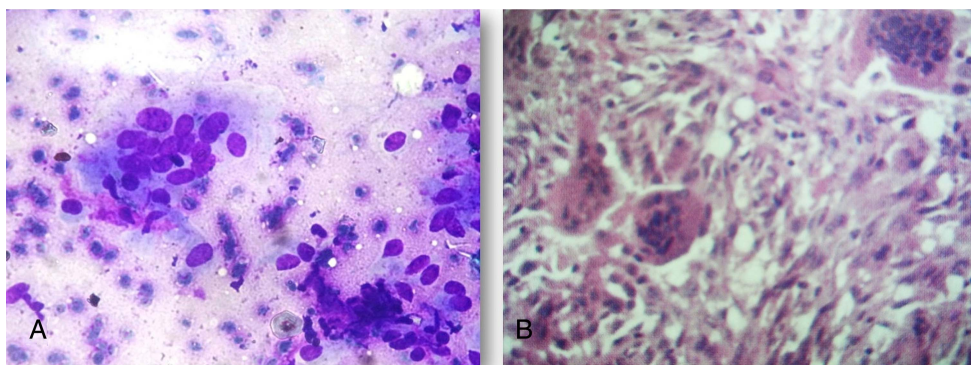


Figure 6 (A) Cytosmear showing oval to spindle stromal cells in small clusters with large numbers of multinucleated osteoclastic giant cells. (B) H&E-stained section (40×) showing multinucleated osteoclast-type giant cells separated by loosely arranged fibro-vascular stroma.

history of the disease.^{1 2} In the present case, although genetic analysis was not performed, a *de novo* mutation in the SH3BP2 gene may be assumed since the clinical, radiological and pathological features are all suggestive of cherubism. It also must be emphasised that rarely genetic mutations may not be detected due to heterogeneity, and then the diagnosis rests on the other criteria mentioned above.¹

Conventionally, cherubism has been treated by surgical re-contouring, curettage and orthodontic treatment for mal-aligned teeth. In the recent past, calcitonin therapy for inhibition of osteoclastic activity has yielded initial favourable results in patients with an aggressive form of cherubism. Recent studies by Yoshitaka *et al*¹² using a knock-in mouse model have suggested anti-TNF- α therapy may be effective in young patients with cherubism provided they are treated before the inflammatory or bone resorption phase. Hero *et al*¹³ treated two cherubic patients with a TNF- α modulator, but the lesions did not regress nor was expansion prevented in either patient. Hence, it may be concluded that early genetic diagnosis with prompt treatment with anti-TNF- α antagonists may be able to prevent or ameliorate cherubism.

Learning points

- ▶ Cherubism is a rare, developmental bone disorder characterised by bilateral asymptomatic facial swelling.
- ▶ It is an autosomal dominant disease which can also arise due to *de novo* mutations in the SH3BP2 gene.
- ▶ It is encountered in children who present with a classic chubby look and bilateral multilocular radiolucent lesions in the jaw bones.
- ▶ The condition is self-limiting and may undergo spontaneous regression at puberty.

Acknowledgements The authors thank Dr Samapika Routray for her valuable suggestions.

Competing interests None.

Patient consent Parental/guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Papadaki ME, Lietman SA, Levine MA, *et al*. Cherubism: best clinical practice. *Orphanet J Rare Dis* 2012;7(Suppl 1):S6.
- 2 Ueki Y, Tiziani V, Santanna C, *et al*. Mutations in the gene encoding c-Abl-binding protein SH3BP2 cause cherubism. *Nat Genet* 2001;28:125–6.
- 3 Meng XM, Yu SF, Yu GY. Clinicopathologic study of 24 cases of cherubism. *Int J Oral Maxillofac Surg* 2005;34:350–6.
- 4 Lima Gde M, Almeida JD, Cabral LA. Cherubism: clinicoradiographic features and treatment. *J Oral Maxillofac Res* 2010;1:e2.
- 5 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;65:517–22.
- 6 Ferguson PJ, El-Shanti HI. Review: autoinflammatory bone disorders. *Curr Opin Rheumatol* 2007;19:492–8.
- 7 Roginsky VV, Ivanov AL, Ovtchinnikov IA, *et al*. Familial cherubism: the experience of the Moscow Central Institute of Stomatology and Maxillo-Facial Surgery. *Int J Oral Maxillofac Surg* 2009;38:218–23.
- 8 Ozkan Y, Varol A, Turker N, *et al*. Clinical and radiological evaluation of cherubism: a sporadic case report and review of the literature. *Int J Pediatr Otorhinolaryngol* 2003;67:1005–12.
- 9 Raposo-Amaral CE, de Campos Guidi M, Warren SM, *et al*. Two-stage surgical treatment of severe cherubism. *Ann Plast Surg* 2007;58:645–51.
- 10 Peñarocha M, Bonet J, Minguez JM, *et al*. Cherubism: a clinical, radiographic, and histopathologic comparison of 7 cases. *J Oral Maxillofac Surg* 2006;64:924–30.
- 11 Jing X, Pu RT. Fine-needle aspiration cytological features of cherubism. *Diagn Cytopathol* 2008;36:188–9.
- 12 Yoshitaka T, Ishida S, Mukai T, *et al*. Etanercept administration to neonatal SH3BP2 knock-in cherubism mice prevents TNF- α -induced inflammation and bone loss. *J Bone Miner Res* 2014;29:1170–82.
- 13 Hero M, Suomalainen A, Hagström J, *et al*. Anti-tumor necrosis factor treatment in cherubism—clinical, radiological and histological findings in two children. *Bone* 2013;52:347–53.

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