

Non-familial cherubism

Jain V, Gamanagatti S R, Gadodia A, Kataria P, Bhatti S S

ABSTRACT

Cherubism is a disease that usually affects the jaws in the paediatric population, mostly below five years of age. Radiologically, it closely resembles fibrous dysplasia and other giant cell lesions of the mandible. Computed tomography (CT) is helpful in defining the true extent of cherubic lesions, which is often not possible on radiographs due to the overlapping facial bones. We describe the radiographical and CT features of cherubism in a 12-year-old boy and highlight the ability of multidetector CT and various post-processing techniques to accurately depict the anatomical extent of the cherubic lesions.

Keywords: cherubism, computed tomography, giant cell lesions, mandible, multidetector computed tomography

Singapore Med J 2007;48(9):e253–e257

INTRODUCTION

Cherubism is a benign disease with a characteristic symmetrical involvement of the maxilla and mandible. It was first described by Jones in 1933 as a “familial multilocular disease of the jaws” in three siblings who appeared as though they were “looking towards heaven”. This inspired him to call the condition “cherubism”, to describe the round appearance of the cheeks, typical of cherubs, resulting from jaw hypertrophy.⁽¹⁾ Affected children usually present before five years of age with painless progressive swelling of the cheeks, frequently associated with dental malformations. It progresses until puberty, and shows partial or complete spontaneous involution in adulthood; therefore, management is mostly conservative. The condition was initially characterised as familial, particularly as a form of craniofacial fibrous dysplasia.⁽²⁻⁶⁾ Now, both hereditary and sporadic cases have been reported and recent genetic studies have shown it to be a separate entity at the molecular level.^(7,8)

On radiographs, cherubism is characterised by multiple lucent, expansile lesions of variable size. The mandible is bilaterally involved; with only one case reported with unilateral involvement.⁽⁹⁾ Maxillary involvement is variable, and always accompanies



Fig. 1 Orthopantomogram shows variably expansile, multiloculated osteolytic lesions involving the body and rami of mandible with sparing of condyles (black arrows) and loss of lower incisor teeth. Similar lesions are also seen in the maxilla bilaterally (white arrows).

mandibular involvement. Histologically, the lesions show numerous giant cells in a fibrovascular stroma containing spindle-shaped cells.⁽¹⁰⁾ We describe radiographical and computed tomography (CT) appearances of a boy with non-familial cherubism, and highlight the ability of multidetector CT (MDCT) to accurately depict the extent of lesions.

CASE REPORT

A 12-year-old male child of non-consanguineous parents, youngest of three siblings, presented with painless progressive swelling of bilateral cheeks with two years duration. There was no history of similar disease in any of the siblings or the parents of the affected child. The swelling was most marked in the midline in the lower jaw and accompanied with loss of multiple lower teeth. On clinical examination, the child had mild swelling of bilateral cheeks, more prominent on the left side. There was a prominent bulge in the chin area with loss of lower incisor teeth. Orthopantomogram (OPT) revealed variably expansile, multiloculated osteolytic lesions involving the entire body as well as the rami of mandible, with sparing of condyles. The midline lesion was associated with marked expansion, cortical thinning and loss of lower incisor teeth. Similar lesions were also seen involving the maxilla bilaterally (left more than right); however, the upper row of teeth was normal (Fig. 1). The lateral view of his skull showed ill-defined haziness in the region of maxillary antra in addition to the mandibular lesions (Fig. 2).

Department of
Radiodiagnosis,
All India Institute of
Medical Sciences,
Delhi 110029,
India

Jain V, MD, DNB
Senior Resident

Gamanagatti SR, MD
Assistant Professor

Gadodia A, MBBS
Junior Resident

Department of
Pathology

Bhatti SS, MD
Senior Resident

Department of
Otorhinolaryngology,
Maulana Azad
Medical College,
Lok Nayak Jai
Prakash Hospital,
Bahadur Shah
Zafar Marg,
Delhi 110002,
India

Kataria P, MS
Senior Resident

Correspondence to:
Dr Vaibhav Jain
C-28, Rohit Kunj,
Pitam Pura,
Delhi 110034,
India
Tel: (91)112 735 3946
Fax: (91)112 658 8663
Email: drjain_vaibhav
@yahoo.com



Fig. 2 Lateral skull radiograph shows soft tissue haziness in the region of maxillary antra (asterisk) in addition to the mandibular lesions.

MDCT with thin section axial acquisition and overlapping reconstruction was performed. Multiplanar images were constructed and three-dimensional (3D) images obtained using shaded-surface display (SSD) software. CT confirmed the presence of multiloculated cystic lesions affecting the body and rami of mandible. Similar lesions were also seen in the maxilla (left side was affected more than the right), indenting the maxillary sinuses with associated maxillary sinusitis. The lesions caused marked expansion of the bones, with a multifocal cortical breakthrough. They contained a soft tissue density material when viewed on standard soft tissue window settings (Fig. 3). The midline mandibular lesion particularly showed marked loss of cortical integrity with loss of lower incisors (Fig. 4). Multiplanar reconstructions (MPR) clearly delineated the lack of involvement

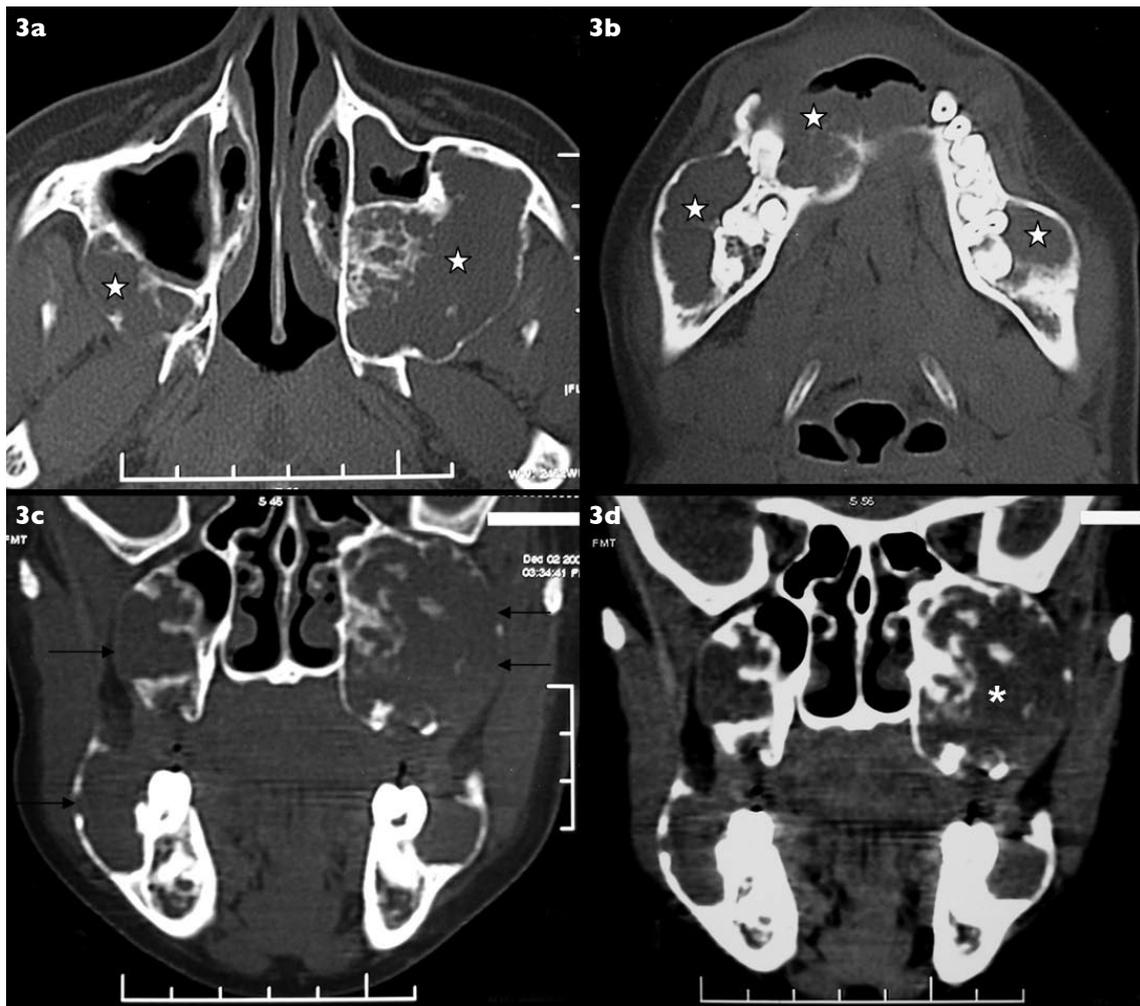


Fig. 3 Axial CT images taken at the level of the (a) maxilla, (b) mandible, and (c,d) coronal MPR CT images, show expansile, multiloculated lesions involving the mandible and posterior walls of both maxillary sinuses with associated mucosal thickening (stars in a,b). These lesions are causing marked expansion and thinning of the outer bony cortex that appears interrupted at several points (arrows in c). They contain a low attenuation material within when seen on standard soft tissue window settings (asterisk in d).

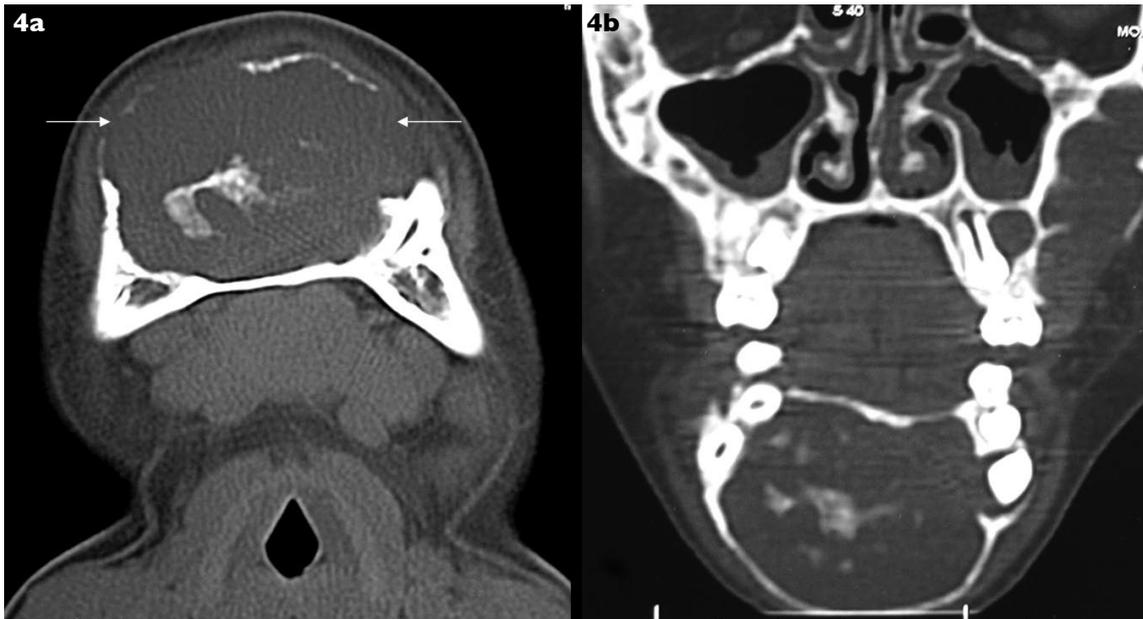


Fig. 4 (a) Axial, and (b) coronal MPR CT images show the extensive thinning, expansion and disruption of the mandibular cortex near the midline (arrows); with loss of lower incisor teeth.

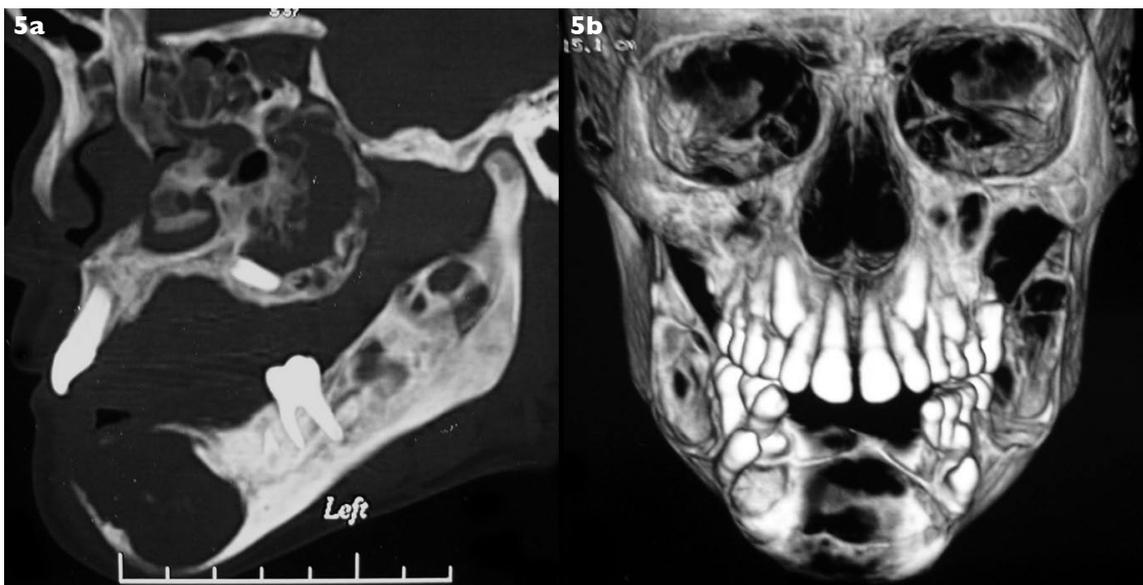


Fig. 5 (a) Oblique MPR CT image shows the multiloculated cystic mandibular and maxillary lesions with sparing of mandibular condyle. (b) SSD 3D CT image gives an excellent overview of the extent of the disease.

of the mandibular condyles and the SSD images provided an excellent anatomic overview of the involved bones (Fig. 5).

Due to lack of family history of similar disease and slightly later age of presentation, a biopsy was obtained from the midline mandibular lesion. Histopathological examination revealed the presence of a lesion containing multiple benign multinucleated giant cells and cellular spindle cell stroma without mitotic activity. Therefore, a diagnosis of cherubism

was made, based on the characteristic radiological findings, along with compatible histopathological features. Due to the expected tendency of these lesions to regress spontaneously, no surgical intervention was undertaken and the patient was kept on follow-up.

DISCUSSION

Cherubism is a disease of childhood that usually presents before the age of five, most often between 12 and 36 months, with males affected more commonly

than females.⁽¹¹⁾ The age of presentation was slightly higher than usual in this patient, who presented at 12 years of age. Many other authors have also reported a higher age of presentation, ranging from one to 19 years of age.^(3,5,6,9,10,12,13) Early studies reported cherubism to be a familial disease with autosomal dominant inheritance and a variable degree of penetrance and expressivity.⁽¹⁻⁶⁾ There was no history of a similar disease in any of the family members of our patient, thus adding to the list of non-familial cases that have now been reported in literature.^(11,13,14) Cherubism has been described as a subtype of the craniofacial variety of fibrous dysplasia, because of the close radiological resemblance of the two conditions.^(2,4-6) However, the gene responsible for cherubism was recently mapped to the chromosome, 4p16.3.⁽⁷⁾ Further studies concluded that cherubism results from a different mutation – those in SH3-binding protein SH3BP2 (MIM 602104) on chromosome 4p16.3;⁽⁸⁾ as compared to the craniofacial fibrous dysplasia, and hence, the two are distinct entities at the molecular level.

The radiographical appearance of cherubic lesions is characteristic, with bilaterally symmetrical, well-defined, multilocular radiolucencies in the mandible that extend from the region of the molar teeth towards the midline. However, unilateral involvement of the disease has also been documented.^(3,9) Sparing of mandibular condyles was earlier considered a hallmark of this condition;^(1-6,11,13) however, condylar involvement has also been described.^(12,14,15) Maxillary involvement is less frequent, usually less extensive, and always accompanies mandibular involvement. The lesions manifest as a soft tissue density in the postero-inferior part of the maxillary antrum with forward displacement or absence of dental follicles in that region. Dental anomalies in the form of incomplete or non-development of teeth, root resorption, and displacement or loss of teeth are frequently present. Our case showed similar, classical radiographical appearances of cherubism, and the mandibular condyles were not involved.

CT provides a clear delineation of the disease extent in cherubism, which is often not possible on plain films due to overlapping of facial bones. MPRs are particularly helpful in this regard.^(12,14-16) Although the role of MDCT has not been established, we believe that the acquisition of thinner slices with overlapping reconstruction that is possible using MDCT, enables generation of higher quality MPR and 3D images which show the anatomy better. However, it is essential to emphasise that the axial source images should always be carefully reviewed as they provide the maximum diagnostic

information. The CT findings in our patient were in agreement with those reported in the literature,^(12,14-16) with multilocular lesions in the mandible and maxilla with marked expansion and loss of continuity of the outer cortex. The lesion contents were of low attenuation when viewed on standard soft-tissue window settings.

The main differential diagnoses of cherubism include craniofacial variety of fibrous dysplasia, central giant cell reparative granuloma, brown tumours, true giant cell tumour, infantile hyperostosis, and familial gigantiform cementoma.^(3,4,10,15,17,18) Patients with fibrous dysplasia present at a later age, usually between 15 and 30 years of age, and lack the typical “cherubic” look. Also, the lesions do not have a tendency to regress after puberty. On imaging, the multiloculated, ground glass lesions of fibrous dysplasia closely resemble cherubic lesions; however, they are rarely ever bilaterally symmetrical. Central giant cell reparative granuloma is a close mimic of cherubism. Histologically, lesions of central reparative granuloma are indistinguishable from those of cherubism;⁽¹⁰⁾ however, radiologically, these lesions have a predilection to involve the anterior mandible. They are rarely bilateral or symmetrical, and it is unusual for them to involve the maxilla, unlike the distribution in cherubism. The age of presentation is also later, usually between ten and 30 years of age.

Brown tumours of hyperparathyroidism are rare in the jaw region. Multiloculated radiolucent lesions may be seen with cortical bone thinning, but an appearance similar to the symmetrical bilateral pattern of cherubism is not likely. In addition, concomitant characteristic radiographical signs of hyperparathyroidism, along with characteristic biochemical anomalies, make the distinction between the two easy. True giant cell tumours occur in the older age group, 20–40 years of age, and most commonly occur as a solitary lesion located at the metaphyses of long bones, particularly the knee. They are extremely rare in jaw bones, and more rarely, in bilaterally symmetrical distribution. Infantile cortical hyperostosis may affect siblings and present with bilateral jaw enlargement. It occurs at a younger age than cherubism and radiographs show bilaterally symmetric cortical thickening caused by marked periosteal new bone formation, without any loculation or lucent lesions. Familial gigantiform cementoma is a rare disorder involving the mandible and maxilla, characterised by the production of cementum in the lesions. These lesions are focal in distribution, predominate in the maxilla, and frequently extend to involve the orbits and nasal septum. These latter locations usually exclude the diagnosis of cherubism.

To summarise, cherubism is a rare, giant cell-containing lesion of the jaw bones that manifests in the paediatric age group. Imaging plays an important role in diagnosing as well as assessing the extent of the lesions. Although not pathognomonic, the presence of multiloculated, expansile, radiolucent lesions involving the mandible and/or maxilla, and occurring in a bilaterally symmetrical fashion, may allow a prospective diagnosis in an appropriate clinical setting. CT examination, particularly MDCT, helps in accurate delineation of the extent of bony involvement and avoids the overlapping of various facial bones that occurs on standard radiographs.

REFERENCES

1. Jones WA. Familial multilocular cystic disease of the jaws. *Am J Cancer* 1933; 17:946-50.
2. Burland JG. Cherubism: familial bilateral osseous dysplasia of the jaws. *Oral Surg Oral Med Oral Pathol* 1962; 15 suppl 2:43-69.
3. Peters WJN. Cherubism: A study of twenty cases from one family. *Oral Surg Oral Med Oral Pathol* 1979; 47:307-11.
4. Cornelius EA, McClendon JL. Cherubism: hereditary fibrous dysplasia of the jaws - roentgenographic features. *Am J Roentgenol Radium Ther Nucl Med* 1969; 106:136-43.
5. Mock D, White GC. Cherubism: report of case. *J Oral Surg* 1974; 32:57-9.
6. Dukart RC, Kolodny SC, Polte HW, Hooker SP. Cherubism: report of case. *J Oral Surg* 1974; 32:782-5.
7. Mangion J, Rahman N, Edkins S, et al. The gene for cherubism maps to chromosome 4p16.3. *Am J Hum Genet* 1999; 65:151-7.
8. 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.
9. Reade PC, McKellar GM, Radden BG. Unilateral mandibular cherubism: brief review and case report. *Br J Oral Maxillofac Surg* 1984; 22:189-94.
10. Kaugars GE, Niamtu J, Svirsky JA. Cherubism: diagnosis, treatment, and comparison with central giant cell granulomas and giant cell tumors. *Oral Surg Oral Med Oral Pathol* 1992; 73:369-74.
11. Zachariades N, Papanicolaou S, Xypolyta A, Constantinidis I. Cherubism. *Int J Oral Surg* 1985; 14:138-45.
12. Beaman FD, Bancroft LW, Peterson JJ, et al. Imaging characteristics of cherubism. *Am J Roentgenol* 2004; 182:1051-4.
13. Grünebaum M, Tiqva P. Non familial cherubism: report of two cases. *J Oral Surg* 1973; 31:632-5.
14. Bianchi SD, Boccardi A, Mela F, Romagnoli R. The computed tomographic appearances of cherubism. *Skeletal Radiol* 1987; 16:6-10.
15. Jain V, Sharma R. Radiographic, CT and MRI features of cherubism. *Pediatr Radiol* 2006; 36:1099-104.
16. Lupescu I, Hermier M, Georgescu SA, Froment JC. [Helical CT and diagnostic evaluation of cranio-facial fibrous dysplasia]. *J Radiol* 2001; 82:145-9. French.
17. Bernaerts A, Vanhoenacker FM, Hintjens J, et al. Tumors and tumor-like lesions of the jaw mixed and radiopaque lesions. *JBR-BTR* 2006; 89:91-9.
18. Mafee MF, Yang G, Tseng A, Keiler L, Andrus K. Fibro-osseous and giant cell lesions, including brown tumor of the mandible, maxilla, and other craniofacial bones. *Neuroimaging Clin N Am* 2003; 13:525-40.