
ORIGINAL ARTICLE

Cherubism as a Rare Cause of Bilateral Expansion of the Mandible: Radiological Manifestations

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ABSTRACT

Objective: To describe the radiological findings of the rare osseous disorder cherubism.

Methods: Five patients with cherubism underwent clinical, radiological, and histopathological evaluation. The patients' sex, age, and physical characteristics were recorded. Bilaterality, location (mandible, maxilla, and orbit), extent of involvement, presence or absence of cortical thinning, degree of expansion, presence or absence of periosteal reaction, and trabeculation measurements were included in the radiological findings.

Results: Three boys and 2 girls were included in the study. The age of the patients ranged from 6 to 20 years. Panoramic radiography and computed tomography were performed for all patients. Additionally, 3-dimensional images were reformatted from the axial computed tomography sections. Two patients underwent magnetic resonance imaging. Radiological investigation revealed bilateral mandibular involvement with preservation of the mandibular condyles, and progressive expansion of the mandible in all patients. Two patients had involvement of the maxilla and the orbit. All of the involved bones demonstrated expansion and cortical thinning. There was no periosteal reaction.

Conclusions: Cherubism should be considered in the differential diagnosis for young patients who present with bilateral mandibular swelling. Comprehensive clinical, radiological, and histopathological evaluation can facilitate the diagnosis of cherubism.

Key Words: Cherubism, Magnetic resonance imaging, Mandible, Radiography, panoramic, Tomography, X-ray computed

INTRODUCTION

Cherubism, or familial intraosseous fibrous expansion of the mandible, is a disease characterised by the presence of giant cells and fibrous tissue proliferation. Cherubism was first described in 1933 and was referred to as familial multilocular cystic disease of the mandible.^{1,2} The condition is usually observed in patients aged 2 to 5 years. The word 'cherubism' refers to the spherical facial appearance of angels painted in the Renaissance era. The characteristic spherical and symmetrical chubby facial appearance observed in cherubism is diagnostic of the condition.¹⁻⁴ This study aimed to describe the radiological findings of 5 patients with cherubism.

METHODS

Panoramic radiography, computed tomography (CT) scans, and magnetic resonance images (MRIs) of 5 patients diagnosed with cherubism between June 2002 and February 2007 at the Department of Radiology, Cumhuriyet University School of Medicine, Sivas, Turkey, were retrospectively reviewed. The study was approved by the institutional review board.

Five patients diagnosed with cherubism according to the combination of histopathological characteristics, lesion distribution, and age were evaluated with regard to their clinical, radiological, and histopathological features. There were 3 boys and 2 girls. At the time of the radiological evaluation, the mean age of the patients was 10.5 years (SD, 5.28 years; range, 6 to 20 years). The patients underwent panoramic radiography and non-enhanced CT scan. CT scan was performed with the Picker PQS (Picker International, Cleveland, USA) model spiral CT scanner and the Philips Brilliance 16 (Philips Medical Systems, Amsterdam, The Netherlands) model multislice CT scanner.

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Additionally, 3-dimensional (3D) volume-rendered images were obtained from axial images at a separate workstation to display vascular and osseous structures. MRI was performed on a 1.5 Tesla MR unit (Excelart, Toshiba, Tokyo, Japan), and T1-weighted (T1W) spin echo (SE), T2-weighted (T2W) fast spin echo (FSE), and fat-suppressed T2W FSE and T1W SE sequences were performed before and after administration of gadolinium chelate (Gd-diethylenetriaminepentaacetic acid). Bilaterality, location (mandible, maxilla, and orbit), extent of involvement, presence or absence of cortical thinning, degree of expansion, presence or absence of periosteal reaction, and trabeculation measurements were included in the radiological evaluation. By comparison with the neighbouring muscle tissue, fatty tissue, and basic fluid, MRIs were evaluated with regard to signal character, signal homogeneity, and localisation of the lesions.

RESULTS

There was progressive expansion of the mandible in all patients and dental disarrangement in 3 patients (60%). Three patients had positive family history of cherubism. The remaining 2 patients had sporadic disease. Apart from the signs of cherubism, physical and mental development was normal for all patients. None of the patients demonstrated lymphadenopathy, and routine laboratory examination, including serum calcium, phosphorus, and alkaline phosphatase levels were within normal limits. Thoracic, abdominal, cardiovascular, and central nervous system examinations of all patients were normal. All patients (100%) had bilateral mandibular involvement, and 2 (40%) had additional maxillary and orbital involvement. The 2 patients with orbital involvement demonstrated severe ocular disturbances of proptosis and superior globe displacement. All of the lesions resulted in reformatting and cortical thinning of the involved bones, and were radiolucent in panoramic radiographs (Figure 1). CT images revealed symmetrical multiloculated cystic lesions of rough trabecular pattern and fibro-osseous matrices. The cystic lesions involved the external cortex of the diseased bones. The cystic structures were filled with a material of soft tissue density. The mandibular condyles had been spared in all patients, and there was no periosteal reaction or soft tissue density accompanying the osseous lesions (Figure 2). Additionally, 3D CT scans provided information on bilateral osseous involvement and expansile reformatting of the osseous tissue (Figures 3a and b).

The lesions were isointense on T1W SE MRIs, and showed heterogeneous hyperintensity on T2W FSE



Figure 1. Panoramic mandibular radiograph of an 8-year-old girl demonstrates multiloculated cystic lesions and disarranged dysmorphic teeth central to the lesions in the mandible.

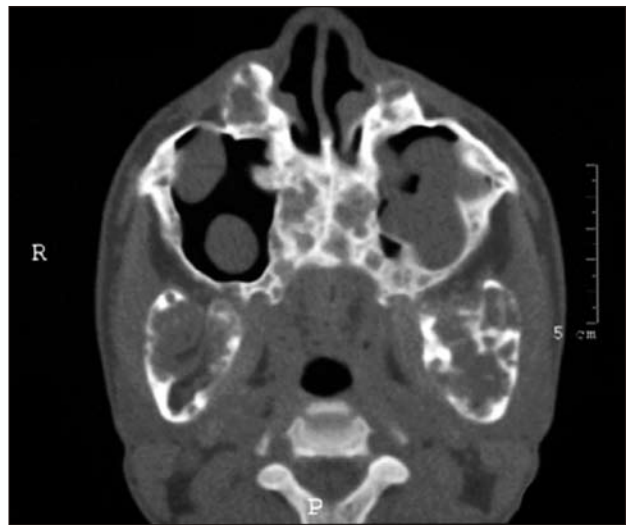


Figure 2. Axial computed tomography image of a 12-year-old boy shows multicystic bone lesions with expansion and erosion in the mandible and the maxillae. The cystic areas contain a low-attenuation material.

MRIs (Figures 4a and b). The lesions were homogeneously enhanced following contrast medium injection on T1W SE sequences (Figure 4c). Two patients underwent exploration under general anaesthesia. The mandibular lesions and accompanying soft tissue components were examined and tissue samples were obtained for histopathological assessment. Microscopic evaluation revealed multinuclear giant cells and hypervascular fibroblastic proliferation. There was no osteoid or chondroid conformation (Figure 5). Due to the extensive maxillary involvement with extension into the orbital cavity, the known expansile nature of the lesion, and potential risk of compressive optic neuropathy, a multidisciplinary team performed surgery to debulk the orbital and maxillary lesions for both patients with orbital involvement. The remaining 3 patients did not

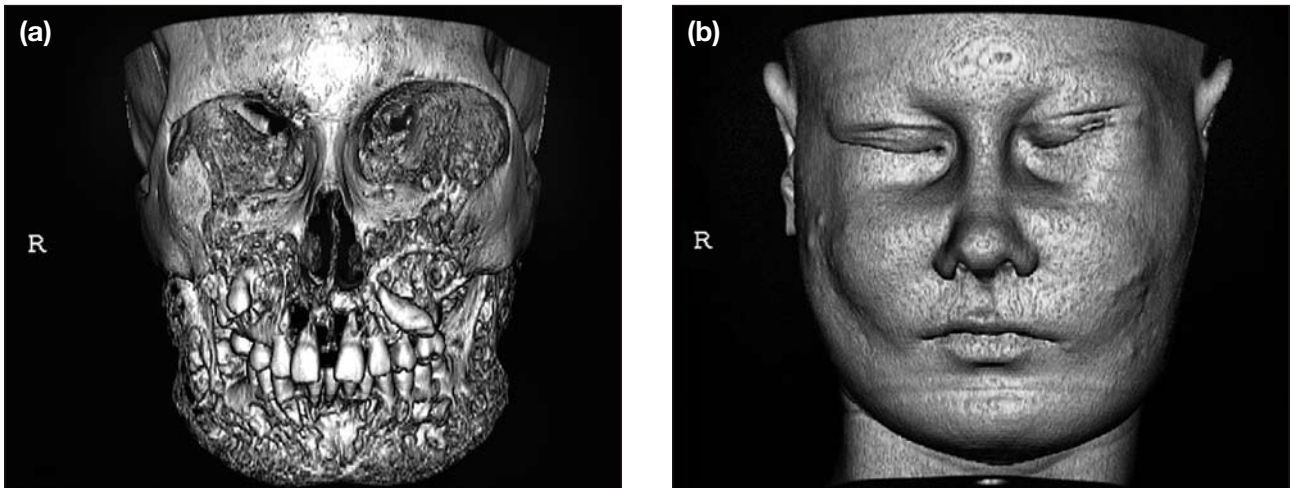


Figure 3. Computed tomography scans of a 12-year-old boy. (a) Anterior view of a 3D image shows the large mandibular body deformity with antero-inferior extension and proliferation of the lesions involving the whole maxilla to the deep regions of the face; and (b) 3D volume rendering image shows expansile osseous remodelling of the jaws.

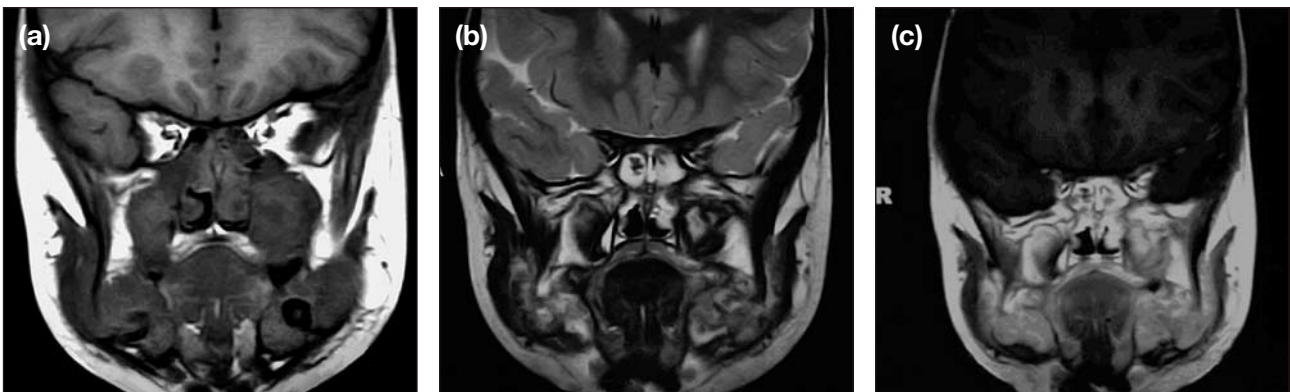


Figure 4. Magnetic resonance images of a 6-year-old boy showing bilateral mandibular involvement. (a) Coronal T1-weighted (TR/TE: 400/15) image demonstrates expansile soft tissue lesions isointense to the neighbouring muscle tissue; (b) coronal T2-weighted (TR/TE: 4500/100) image shows expansile lesions heterogeneously hyperintense to the surrounding soft tissue; and (c) post-contrast coronal T1-weighted image shows expansile mandibular lesions with homogenous contrast enhancement.

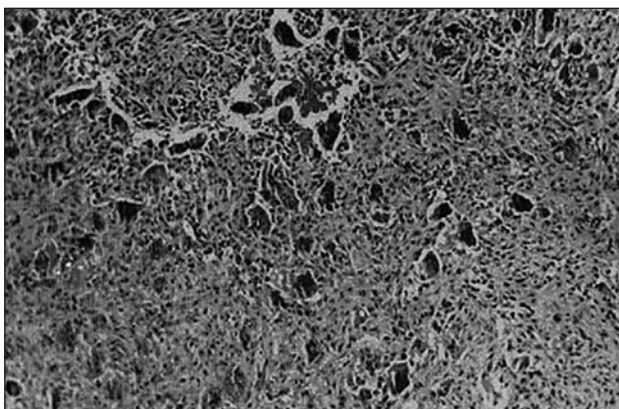


Figure 5. Histopathological evaluation of the samples showing multinuclear giant cells and hypervascular fibroblastic proliferation (haematoxylin and eosin stain; original magnification, x 25).

receive any treatment, but were advised to undergo regular follow-up. Table 1 summarises the radiological features.

DISCUSSION

Cherubism is a rare hereditary fibro-osseous childhood disease characterised by bone degradation and fibrous tissue replacement at the angles of the mandible and the tuberosities of the maxilla that leads to prominence of the lower face.^{1,2} The disorder was first described in 1933 by Jones as a familial fibro-osseous disease involving the maxilla and the mandible.^{1,2} According to the World Health Organization classification, cherubism belongs to the non-neoplastic bone lesions group that involves the mandible.^{4,5} The disease can also be referred to as familial or hereditary fibrous dysplasia, bilateral giant cell tumour, or familial multiloculated disease.³⁻⁶

Perivascular fibrosis leading to mesenchymal disorders and decreased oxygenation is the most widely accepted theory for the underlying pathogenesis of cherubism. When patients reach puberty, the osseous lesions of

Table 1. Radiological features of 5 patients with cherubism.

Patient number	Age (years) /sex	Radiological modality		Grade	Bilaterality	Location	Cortical thinning	Expansion	Periosteum reaction	Trabeculation
		Computed tomography	Magnetic resonance imaging							
1	6/F	+	+	1	+	Mandible	+	+	—	+
2	6/M	+	—	1	+	Mandible	+	+	—	+
3	8/F	+	+	1	+	Mandible	+	+	—	+
4	12/M	+	—	4	+	Mandible, maxilla, orbit	+	+	—	+
5	20/M	+	—	4	+	Mandible, maxilla, orbit	+	+	—	+

cherubism regress spontaneously. However, the underlying cause of this regression is not known. Affected children are normal at birth. Progression of the bone lesions usually slows down after the age of 5 years, and stops at the age of 12 to 15 years. Mandibular lesions are usually painless and symmetrical. In general, cherubism does not affect other parts of the skeleton or osseous metabolism.^{2,6-10}

Cherubism is reported to be associated with some well-described syndromes, including neurofibromatosis type 1, Noonan-like/multiple giant cell lesion syndrome, Ramon syndrome, and Jaffe-Campanacci syndrome.^{11,12}

Ramon and Engelberg have proposed a grading system for cherubism based on the area of involvement, as follows:¹³

- grade 1 — involvement of both mandibular ascending rami
- grade 2 — grade 1 plus involvement of both maxillary tuberosities
- grade 3 — massive involvement of the maxillae and mandibles except for the condylar processes
- grade 4 — grade 3 plus involvement of the floor of the orbits, causing orbital compression.

According to Ramon and Engelberg's classification,¹³ 3 patients in this study were classified as having grade 1 disease and 2 had grade 4 disease.

Conventional radiography and CT scanning are sufficient for the radiological diagnosis of cherubism. Bilateral multiloculated cystic expansion in the mandible is the characteristic radiological appearance.^{6,7,9} The most prominent radiological characteristics of the patients in this study were the presence of expansile reformatting in the involved bones and distinctive cortical thinning. There was no accompanying periosteal reaction in the lesions. Mandibular involvement is typically bilateral — only 1 patient with unilateral involvement has been

described in the literature¹⁴ — and maxillary involvement always accompanies mandibular involvement. Lesions often begin near the angle of the mandible and expand into the body and ramus of the mandible. Expanding lesions often cause thinning of the cortex and, in the maxilla, may cause obliteration of the maxillary sinus. In this study, extension of the lesions to the mandible and the maxilla was clearly demonstrated. CT investigation is the best method for demonstrating expansile lesions and the soft tissue components in these lesions. Additionally, 3D formatting contributes to the diagnosis.^{3,4,15} For the patients in this study, CT scanning helped to provide a clear delineation of the extent of disease, which was difficult to see on radiographs due to the overlap of the facial bones. Using CT, the bilateral osseous involvement, cortical thinning, and expansile remodelling of involved bones were depicted. CT scan showed a multilocular appearance in the mandible created by the presence of bone septa and expansile remodelling and perforation in some places. Preservation of the mandibular condyles is accepted as the pathognomonic finding of cherubism. In all of the patients in this study, the mandibular condyles were preserved. The panoramic radiograph and CT findings were concordant with reports in the literature.

The MRI findings of cherubism were first described by Beaman et al, who described cherubic lesions as non-specific homogeneous isointensity to skeletal muscle on T1W images and heterogeneous isointensity on fat-suppressed T2W images.⁷ Recently, Jain and Sharma reported that MRI showed the presence of heterogeneous signal intensity lesions, with areas of isointensity to skeletal muscle on T1W images, which were correspondingly hyper- to isointense on T2W images.¹⁶ In contrast to the description of Beaman et al,⁷ cherubic lesions were isointense to the muscle tissues in T1W SE images and heterogeneously hyperintense to normal bone and muscle in T2W FSE images in this study. The

authors hypothesise that these findings are not specific to cherubism, and MRI is only useful for determining the extent and localisation of the lesions, and the relation of the lesions to the orbit and the optic nerves. Mnari et al reported that MRI is helpful for determining soft tissue involvement in patients with aggressive cherubism and for assessing the vascular structures preoperatively.¹⁷

The differential diagnosis of cherubism includes giant cell granuloma of the mandible, odontogenic cyst, ameloblastoma, odontogenic fibroma, myxoma, haemorrhagic bone cyst, aneurysmal bone cyst, craniofacial fibrous dysplasia (McCune-Albright syndrome), familial gigantiform cementoma, brown tumour of hyperparathyroidism, and Jaffe-Campanacci syndrome. Giant cell granuloma is usually unilateral and involves patients aged 20 to 40 years. Unlike cherubism, osteoclastoma rarely involves the mandible. Bilateral odontogenic cysts are not common in the first 5 years of life. Familial gigantiform cementoma is a rare osseous lesion, characterised by cementum production in the lesions, and usually involves the maxilla rather than the mandible. Vascular tumours of facial bones usually follow trauma and should not be confused with cherubism. Brown tumour and Jaffe-Campanacci syndrome are readily distinguished clinically and are easily eliminated from the differential diagnosis. Cherubism should be distinguished from giant-cell reparative granuloma and McCune-Albright syndrome on clinical and radiological grounds, and from hyperparathyroid lesions on biochemical studies. Hypertrophy of the bilateral masseter muscles and pathologies related to the parotid glands should be considered in the differential diagnosis of cherubism.^{1,4-21}

There are some limitations to this study. The number of patients was small; the data were collected retrospectively; and MRI and histopathological findings were not available for all patients.

Usually there is no need for active treatment of cherubism. Since the lesions undergo spontaneous regression, it is better if surgical intervention is delayed until after puberty. However, for patients with functional and/or cosmetic problems, limited surgical excision can be considered.¹⁶

Cherubism should be considered in the differential diagnosis of children and young patients presenting

with bilateral mandibular swelling. Radiological and histopathological features of cherubism are not pathognomonic. Comprehensive evaluation of the clinical, radiological, and histopathological features can confirm the diagnosis.

REFERENCES

1. Khalifa MC, Ibrahim RA. Cherubism. *J Laryngol Otol.* 1988;102:568-70.
2. Gomes MF, de Souza Setubal Destro MF, de Freitas Banzi EC, dos Santos SH, Claro FA, de Oliveira Nogueira T. Aggressive behaviour of cherubism in a teenager: 4-years of clinical follow-up associated with radiographic and histological features. *Dentomaxillofac Radiol.* 2005;34:313-8.
3. Ozkan Y, Varol A, Turker N, Aksakalli N, Basa S. Clinical and radiological evaluation of cherubism: a sporadic case report and review of the literature. *Int J Pediatr Otorhinolaryngol.* 2003;67:1005-12.
4. Yamaguchi T, Dorfman HD, Eisig S. Cherubism: clinicopathologic features. *Skelet Radiol.* 1999;28:350-3.
5. Regezi JA, Sciubba J. *Oral pathology: clinical-pathologic correlations.* 2nd ed. Philadelphia: Saunders; 1993. p 345-54.
6. Kalantar Motamedi MH. Treatment of cherubism with locally aggressive behavior presenting in adulthood: report of four cases and a proposed new grading system. *J Oral Maxillofac Surg.* 1998;56:1336-42.
7. Beaman FD, Bancroft LW, Peterson JJ, Kransdorf MJ, Murphey MD, Menke DM. Imaging characteristics of cherubism. *AJR Am J Roentgenol.* 2004;182:1051-4.
8. Timosca GC, Galesanu RM, Cotutiu C, Grigoras M. Aggressive form of cherubism: report of a case. *J Oral Maxillofac Surg.* 2000;58:336-44.
9. Ongole R, Pillai RS, Pai KM. Cherubism in siblings: a case report. *J Can Dent Assoc.* 2003;69:150-4.
10. Ayoub AF, el-Mofty SS. Cherubism: report of an aggressive case and review of the literature. *J Oral Maxillofac Surg.* 1993;51:702-5.
11. Lakhkar BN, Lakhkar BB, Ghosh MK, Shenoy DP, Patil UD. Cherubism. *Indian Pediatr.* 1990;27:1305-7.
12. Cohen MM Jr, Gorlin RJ. Noonan-like/multiple giant cell lesion syndrome. *Am J Med Genet.* 1991;40:159-66.
13. Ramon Y, Engelberg IS. An unusually extensive case of cherubism. *J Oral Maxillofac Surg.* 1986;4:325-8.
14. Reade PC, McKellar GM, Radden BG. Unilateral mandibular cherubism: brief review and case report. *Br J Oral Maxillofac Surg.* 1984;22:189-94.
15. Lannon DA, Earley MJ. Cherubism and its charlatans. *Br J Plast Surg.* 2001;54:708-11.
16. Jain V, Sharma R. Radiographic, CT and MRI features of cherubism. *Pediatr Radiol.* 2006;36:1099-104.
17. Mnari W, Ennouri S, Jlassi H, Mighri K, Driss N, Hamza HA. Cherubism: a new case with review of literature. *Ann Otolaryngol Chir Cervicofac.* 2005;122:260-4.
18. Zachariades N, Papanicolaou S, Xypolyta A, Constantinidis I. Cherubism. *Int J Oral Surg.* 1985;14:138-45.
19. Reed MH. *Pediatric skeletal radiology.* 1st ed. Baltimore: Williams & Wilkins; 1992. p 267-76.
20. Colombo F, Cursiefen C, Neukam FW, Holbach LM. Orbital involvement in cherubism. *Ophthalmology.* 2001;108:1884-8.
21. 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.