Orbital Involvement in Cherubism

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Purpose: To demonstrate the clinical, radiologic, and histopathologic features of a patient with orbital involvement in cherubism that prompted surgical treatment.

Design: Single interventional case report.

Intervention: Findings of the ophthalmic evaluation, computed tomography (CT) scans, intraoperative examination, and light microscopy of the specimens were analyzed.

Main Outcome Measures: Globe displacement, orbital bony lesions detected on CT scans, histopathology, and postoperative results were assessed.

Results: A 27-year-old female was seen with a slowly progressive superonasal globe displacement and a temporal orbital mass bilaterally of 6 years’ duration. She had a history of cherubism, but her cheeks and jaws had a normal appearance instead of the bilateral fullness of the lower half of the face typical of the disease. CT scans demonstrated multicystic bony lesions arising from the orbital floors bilaterally. The masses were excised using an anterior transcutaneous transseptal orbitotomy. Histopathology demonstrated numerous giant cells in a fibrovascular stroma, confirming the clinical diagnosis of cherubism. Postoperative recovery was complete.

Conclusions: Orbital involvement in cherubism may develop beyond puberty, after stabilization or regression of the lesions in the jaws. Patients with cherubism should be routinely evaluated by an ophthalmologist.


In 1933, Jones 1 described three siblings affected by a condition of the jaws characterized clinically by a painless expansion of the region of the cheeks and jaws. He reported that “the full round cheeks and the upward cast of the eyes give the children a peculiarly grotesque, cherubic appearance.” This originated the term “cherubism.” The disease usually worsens progressively until puberty, at which time it stabilizes and then gradually resolves. 2–6 It displays a typical radiographic appearance of bilateral, multicellular, radiolucent areas within the jaw bones. 2–5,7 Histopathologically, the lesions show numerous giant cells in a stroma of spindle-shaped cells. 2–6,8 Lesions involving the orbit are rare. 9–11 To our knowledge, only two patients have been reported in the ophthalmic literature. 11 We describe a patient who had orbital manifestations of cherubism develop after stabilization of the lesions in the jaws, prompting surgical treatment.

Case Report

A 27-year-old female was seen with a slowly progressive superonasal displacement of both eyes—more accentuated in the right eye—and a mass visible through the conjunctiva in the temporal area bilaterally (Fig 1). At age 9, an irregular mandible was noticed. Radiology demonstrated bilateral multicystic lesions in the mandible and in the maxilla compatible with cherubism, which prompted referral to a maxillofacial service. An incisional biopsy was performed. Microscopically, the lesion showed giant cells in a vascularized fibrous stroma, confirming the diagnosis of cherubism. One year later the patient underwent extraction of four teeth that were malformed or partially resorbed. The mandibular irregularity became less perceptible over the years. At age 21, a “bone-hard prominence” in the right lateral canthus was noticed. Six years later, the ophthalmic evaluation revealed bilaterally a fixed bony tumor located in the anterior orbit temporally. The globes were displaced supernasally. Exophthalmometry readings were 21 mm in the right eye and 19 mm in the left eye. The rest of the examination was unremarkable except for an A-phenomenon and a slight reduction in oblique inferior muscle function. Computed tomography (CT) scans showed bilaterally a multicystic bony tumor of the orbital floor temporally, extending from the orbital rim deep into the orbit (Fig 2). Because the patient was anxious about the nature of the tumor and the tumor was cosmetically unacceptable, surgery was performed. The right orbit was operated on first. The mass was exposed using an anterior transcutaneous transseptal orbitotomy. It showed a grayish, thin bony surface and, when incised, a cavity partially filled with a jellylike tissue (Fig 3). The lesion was curettaged and reduced to the level of the orbital floor. The left orbit was operated on in the same manner 5 months later. Histopathologically, the lesions showed numerous multinucleated giant cells scattered in a fibrovascular stroma (Fig 4). Postoperatively, recovery was uneventful (Fig 5). The jaw lesions of childhood had regressed, and our patient showed a normal configuration of the jaws and cheeks in adulthood (Fig 6).

Discussion

Cherubism is a rare inherited disease of childhood characterized by expansion of the mandible and/or the maxilla.
resulting in different degrees of bilateral fullness of the lower half of the face. To our knowledge, this is the third case published in the ophthalmic literature. Two patients were previously reported by Hawes in 1989. One was an 18-year-old female who had orbital manifestations of cherubism develop at age 6 in one orbit and at age 11 in the contralateral orbit. CT scans showed involvement of the floor and lateral walls of the orbits. The lesion was subtotally resected. Three years postoperatively there was no clinical evidence of regrowth. The other patient was a 45-year-old female (the mother of the previous case) who had a mass develop in her mandible at age 5. Fifteen years later there was proptosis of the right eye. CT scans demonstrated bony lesions of the orbital floor bilaterally. At age 45, the right orbital lesion was subtotally resected. One year postoperatively there was no evidence of recurrence. The patient described here is unusual in that the orbital involvement arose in early adulthood, after the jaw lesions had subsided.

The disease is generally inherited as an autosomal dominant trait, with incomplete penetrance and variable expressivity. In a recent study of two families affected by the disease, the gene locus was localized to chromosome 4p16.3. Few patients without apparent familial involvement have been reported. Clinically, the size of the lesions varies from minimal to massive involvement of both jaws. Intraorally, a V-shaped palate; delay in the eruption of teeth; and missing, displaced, malformed, and resorbed teeth may be present. Enlargement of the submandibular

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**Figure 1.** A 27-year-old patient with bilateral superonasal displacement of both eyes and an orbital mass visible through the conjunctiva temporally (arrows).

**Figure 2.** A, Coronal computed tomography (CT) scan showing bilaterally a multicystic bony tumor on the orbital floor (arrowheads). B, Axial CT scan showing that the lesions extend deep into the orbit (arrowheads).

**Figure 3.** Right orbital lesion exposed during surgery (arrows). It displayed a bony surface and a cavity (arrowhead) filled with a jellylike tissue (asterisks, eyelids N, nose).

**Figure 4.** Histologic section showing numerous multinucleated giant cells (arrows) scattered in a fibrovascular stroma. Note bony wall (arrowheads) (stain, hematoxylin–eosin; original magnification, ×100).
and, less frequently, the superior cervical lymph nodes has also been reported.² The disorder becomes noticeable within the first years of life, usually when the patient is 2 to 4 years old, and worsens progressively until puberty, at which time it stabilizes and then gradually resolves.²,³,⁵,⁶ Our patient showed in adulthood a normal configuration of the jaws and cheeks (Fig 6). In contrast to the typical natural history of the disease, she was 21 years old when the orbital abnormalities were noticed. Progression of the orbital involvement beyond puberty has been previously observed.¹⁰,¹¹ However, it is difficult to determine the frequency and characteristics of orbital involvement in this disease, because most reports have been published in the maxillofacial literature and do not include ophthalmic evaluations.²–⁵,⁷–⁹

Radiologically, patients with cherubism display bilateral, multilocular, radiolucent areas within the jawbones.²–⁵,⁷ These radiologic features in conjunction with the clinical picture are distinctive, and a biopsy is done only to confirm the diagnosis.²,³,⁵

Histopathologically, cherubic lesions exhibit numerous multinucleated giant cells scattered in a stroma of vascularized fibrous connective tissue.²–⁶ Cyst formation and newly formed bone may be present. Multinucleated cells in cherubic lesions show a strong positivity for monoclonal antibody 23c6 and tartrate-resistant acid phosphatase, which is characteristic of osteoclasts.⁶

The differential diagnosis of cherubism includes giant cell tumor of the jaw, central giant cell granuloma of bone, brown tumor of hyperparathyroidism, fibrous dysplasia, and aneurysmal bone cyst.²,³,⁶,¹¹,¹³ Giant cell tumor resembles cherubism histopathologically, but it is unusual in the jaw, affects patients between the ages of 20 and 40 years, and is seen unilaterally.²,³,¹³ Central giant cell granuloma of bone usually affects patients between the ages of 10 and 30 years and involves predominantly the anterior mandible.² In addition, similar to brown tumor of hyperparathyroidism, histopathologically it shows giant cells that are not scattered throughout the lesion—as in cherubism—but rather are grouped in areas where there may be hemorrhage (“zonal pattern”).¹³ Brown tumor of hyperparathyroidism, in contrast to cherubism, rarely affects the jaw in an isolated manner, and patients have abnormal serum concentrations of parathyroid hormone and calcium.³,⁶ Fibrous dysplasia exhibits prominent fibrous stroma containing Chinese-fig-urelike or C-shaped spicules of bone histologically.⁶,¹² Aneurysmal bone cyst may also show giant cells, but its main feature is a nonendothelium-lined cavity.¹³

Because the disease is generally self-limiting and subsides with age, treatment is indicated only in cases with esthetic or functional problems. Curettage alone or in combination with surgical contouring has been considered the treatment of choice.⁸ Some authors have reported a massive growth of the lesion after surgery, especially when this is performed during the active growth phase.⁸,¹⁰ Radiotherapy has been used, but it is not recommended because of the high incidence of complications.³,¹⁰

The word “cherub” originally designated a creature that belonged to the celestial chorus and that showed specific features (Fig 7A): severe, staring eyes; eyes on the wings and body; wheel below the feet. Angels with childish chubby faces became especially widespread in baroque art (Fig 7B): typical “angel” face with upward gaze and full cheeks. Nowadays, a cherub fits this latter description. The previously mentioned simile introduced by Jones¹ between the clinical appearance of affected patients and the baroque cherubs popularized the term “cherubism” to designate the disorder. The term “cherubism” for the disease actually is not fully correct, because the typical clinical picture does not resemble a classical cherub but a baroque angel.

In conclusion, we described a patient with cherubism who had orbital involvement develop unusually late. Lesions involving the orbits may appear and progress even after stabilization of the lesions in the jaws. Patients with cherubism should be routinely evaluated by an ophthalmologist.

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References

Availability of Donor Tissue and Histopathology Reports from Patients with Retinal Degeneration

The Foundation Fighting blindness sponsors histopathologic studies of donor eyes from patients with retinitis pigmentosa (RP), macular degeneration, Usher syndrome and related retinal diseases and from obligate and suspected carriers of these disorders. Detailed histopathologic reports on more than 300 eyes, including gross photography and light and electron microscopy, are available to interested researchers. These reports document the findings on patients from ages 2 to 100 (average age, 72) with different genetic forms of retinal degeneration at various stages of disease. Tissue samples and sections from many of these preserved donor retinas are available for distribution to qualified investigators. Most of the tissue samples are fixed in a buffered 1% paraformaldehyde-2.5% glutaraldehyde or a buffered 4% paraformaldehyde-0.5% glutaraldehyde solution, and later transferred to 2% paraformaldehyde. Frozen companion eyes and blood samples are also available from some cases.

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