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Ophthalmic manifestations of cherubism

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Abstract

Cherubism is a rare craniofacial disorder characterized by progressive replacement of mandibular and maxillary bone with multicystic fibro-osseous tissue, potentially resulting in significant deformity and morbidity. The severity of the disorder is variable; more advanced disease may affect the orbit and impact vision. We detail the ophthalmological findings in 2 patients, 7 and 8 years of age, with cherubism.

The database of the Craniofacial Clinic at UCLA was queried to identify patients presenting between 1992 and 2012 with a diagnosis of cherubism. Medical records were retrospectively reviewed with attention to orbital manifestations of the disease. The patients underwent complete ophthalmological evaluation at the Jules Stein Eye Institute. Both had bilateral but asymmetric cherubism involving the mandible and maxilla, with proptosis on the more affected side, and anisometropia. One patient had decreased visual acuity in the proptotic eye, strabismus, and acquired nasolacrimal duct obstruction. Dilated fundus examination showed normal optic nerves in both patients. Ophthalmic involvement in cherubism can vary significantly; these cases demonstrate that cherubism may involve the orbit and lead to abnormal vision, disturbances in ocular motility, proptosis, and nasolacrimal duct obstruction.

Case 1

An 8-year-old boy with cherubism involving the left maxilla and bilateral mandible was evaluated for left eye proptosis. Cherubism had been diagnosed at 6 years of age after a left mandibular biopsy. The patient had undergone excision and debridement of the left maxillary and bilateral mandibular lesions at 7 years of age. There was no known family of cherubism. His visual acuity was 20/20 in each eye. Pupils were normal. The anterior segment and fundus examinations were normal. No strabismus was noted. Exophthalmometry showed 2 mm relative proptosis in the left eye (Figure 1). Cycloplegic refraction revealed mild anisometropia of +1.00 sphere in the right eye and +1.75 + 0.75 × 180 in the left eye. Cystic lesions of both mandibular rami and the left maxilla were present on

computed tomography. Since the surgery at 7 years of age, the lesions and left eye proptosis had been stable.

Case 2

An 8-year-old girl with cherubism asymmetrically involving the maxilla and mandible was referred for left eye proptosis and tearing. Cherubism had been diagnosed at 5 years of age based on a panoramic radiograph ordered by her dentist. Her father also had cherubism involving the mandible for which he underwent surgery in his teens. Visual acuity was 20/20 in the right eye and 20/30 in the left eye. Cycloplegic refraction measured $-0.75 + 2.75 \times 090$ in the right eye and $-2.25 + 4.25 \times 095$ in the left eye. Color vision, pupils, confrontation visual fields and intraocular pressures were normal. She was orthophoric in all gaze positions with full ductions. There was 4 mm relative proptosis in the left eye with upward displacement of the globe. The tear meniscus was increased on the left. Dilated fundus examination revealed normal optic nerves without edema in both eyes. She underwent debulking of a left maxillary mass and returned at 9 months postoperatively with an exuberant recurrence of the left maxillary lesion with more significant orbital effect that had worsened over time (Figure 2). Her visual acuity was unchanged, but stereoacuity decreased from 100 arcsec to <4800 arcsec. She developed 16° of alternating exotropia and 16° of left hypertropia, with limited downgaze. She subsequently underwent excision of the recurrent left maxillary mass. Histopathology demonstrated multinucleated giant cells with fibroblasts consistent with cherubism. Three months postoperatively, her visual acuity improved to 20/20 in both eyes, with 40 arcsec of stereopsis and orthophoria (Figure 3). She has remained stable with no recurrence of the lesions at last follow-up, 13 months after her second surgery.

Discussion

Ophthalmic manifestations of cherubism can vary greatly, depending on the level of involvement of the maxilla. Orbital involvement due to superior extension of maxillary lesions is considered rare and may occur later in the disease course, after mandibular lesions, which occur twice as often as maxillary lesions, stabilize or regress.¹⁻³ We describe 2 patients with cherubism with varying presentations and orbital involvement.

Cherubism is due to an autosomal dominant or de novo mutation with variable expressivity and reduced penetrance.⁴ *SH3BP2*, found on chromosome 4p16.3, is the only gene in which a mutation is known to cause cherubism.⁴ The disease prevalence is unknown. Genetic testing was not available for either patient; however, the father of case 2 also had a history of cherubism, presumably from the same mutation, but had only involvement of the mandible.

Both cases had asymmetric lesions despite the reported bilaterality and symmetry usually attributed to cherubism.⁴ Prior reports of patients with maxillary involvement of cherubism leading to orbital mass effect have varied in their ophthalmic sequelae and age of occurrence.^{2,5} Reported sequelae include proptosis, strabismus with diplopia, compressive

optic neuropathy, retinal vein occlusion, and macular folds and scarring, with age of occurrence ranging from 7 to 27 years of age.⁶

Several case reports describe the development or progression of lesions involving the orbit after 20 years of age, despite some reports that lesions stabilize and may regress after puberty.²⁻⁷ Both cases presented here were prepubertal. Case 2 had an active phase, with rapid recurrence of the left maxillary lesion following initial debulking. Rapid recurrence of lesions in cherubism after excision has been reported and may be due to the surgery being performed during the active phase.^{5,8} The active phase does not appear to be related to age at presentation, age during active phase, or pubertal status (although pubertal status was not provided in most reports).^{2,5-7}

Case 2 also developed an acquired nasolacrimal duct obstruction (NLDO). NLDO has been described in patients with fibrous dysplasia and other craniofacial disorders.⁹ NLDO in cherubism is likely due to bony stenosis of the duct by maxillary bone lesions. This may be an underreported sequela of cherubism in those with severe maxillary involvement. Alternatively, the nasolacrimal duct may be resilient to external compression. Lello and Sparrow¹⁰ described this resilience in patients with severe craniofacial fibrous dysplasia involving the maxilla, but with patent nasolacrimal ducts on imaging.

As seen in this case series, ophthalmic involvement may progress, especially in the active phase.^{2,5} Routine ophthalmologic screening is indicated in patients with cherubism, especially those with maxillary lesions.

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FIG 1.
Clinical photograph of case 1 showing maxillary prominence and left eye proptosis.

FIG 2.

A, Clinical photograph of case 2 with recurrence of the left upper maxillary lesion B, Ocular motility testing demonstrating severe mass effect on the left orbit and left hypertropia with limited downgaze in the left eye. C, Computed tomography and three-dimensional reconstruction showing lucent lesions involving the left maxilla and bilateral mandible.

FIG 3.

A, Clinical photograph of case 2 following her second craniofacial surgery with more symmetric maxillary and mandibular prominence. B, Ocular motility testing showing orthophoria and full ductions. C, Computed tomography and three-dimensional reconstruction with decreased mass effect on the left orbit.