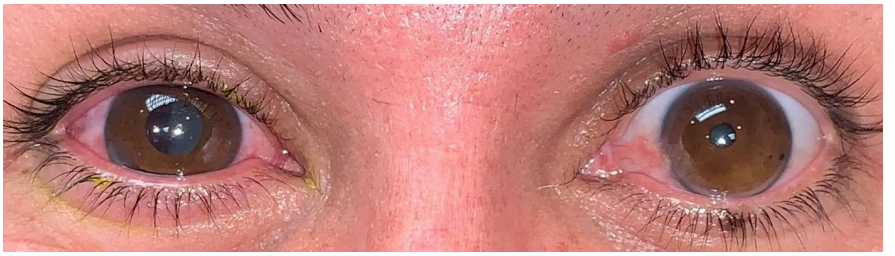
Fundamentals of Megalocornea

Megalocornea is a nonprogressive X-linked recessive congenital anomaly in which the corneas are symmetrically enlarged to a diameter of at least 13 mm. Awareness of megalocornea is important because it can be easily confused with buphthalmos, a more serious finding associated with congenital glaucoma. Furthermore, megalocornea is associated with early cataract formation, glaucoma, and crystalline lens subluxation in adults. Finally, the anatomic peculiarities of megalocornea have important implications for planning and performing cataract surgery.



MEGALOCORNEA. *Bilaterally enlarged corneal diameters in a megalocornea patient who underwent cataract extraction and IOL placement in the right eye. (The right pupil was pharmacologically dilated at a postoperative visit.)*

Epidemiology

Although megalocornea is rare, multiple cases have been reported in the literature. To our knowledge, there are no epidemiologic data on the prevalence, incidence, or geographic variation of the condition. Because of the X-linked recessive inheritance pattern of megalocornea, it occurs mostly in males.

Genetics and Pathophysiology

Most described cases of megalocornea demonstrate a mutation of the chordin-like 1 (*CHRDL1*) gene, located in the Xq13-q25 region. *CHRDL1* is expressed in the cornea, lens, and retina and encodes ventroptin, an antagonist of bone morphogenetic protein (BMP). Studies of families with known X-linked megalocornea have identified various abnormalities in the *CHRDL1* gene, including copy-number variation, frameshift, missense, splice-site, and nonsense mutations.

In the proposed pathogenetic mechanism of megalocornea, a mutation of *CHRDL1* leads to a relative absence of ventroptin and, consequently, to a relative excess of BMP, which in turn results in the relative overproliferation and overdifferentiation of limbal stem cells. The morphology and density of corneal endothelial cells are normal in megalocornea, suggesting it is secondary to failure of timely fusion of the anterior optic cup.

Clinical Features and Diagnosis

The primary clinical feature of megalocornea is an enlarged corneal diameter noted at birth in the setting of normal IOP. Most patients with megalocornea remain asymptomatic through adolescence, though astigmatism may be present. It is important to differentiate megalocornea from buphthalmos, the key differential diagnosis of the pediatric enlarged cornea. Whereas megalocornea is an anomalous finding of minimal acute concern, buphthalmos is caused by congenital glaucoma, which can potentially be devastating and therefore requires timely workup and management.

Buphthalmos usually presents with several findings not seen in megalocornea: elevated IOP, increased axial length, and horizontal breaks in the Descemet membrane (Haab striae) that can lead to corneal edema and haze. As these features are often associated with a diagnosis of congenital glaucoma, any patient with a putative diagnosis of megalocornea who is found to have one or more of these clinical signs requires further workup to exclude congenital glaucoma.

In contrast to patients with buphthalmos, those with megalocornea typically have clear corneas, normal IOP, and normal axial length. Furthermore, megalocornea patients commonly have pigment dispersion syndrome and iris transillumination defects, which are

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usually not seen in congenital glaucoma.

Ultrasound biometry may be useful in distinguishing megalocornea from buphthalmos; classically, the ratio of anterior chamber depth to axial length is relatively elevated in megalocornea compared with buphthalmos. Definitive diagnosis of megalocornea requires genetic testing of the complete coding region of the X chromosome.

Associated Conditions

Once megalocornea is diagnosed, attention should turn to identifying any associated comorbidities or syndromes. While megalocornea is often an isolated anomaly, several syndromic conditions have been described, such as Neuhauser syndrome (megalocornea–mental retardation syndrome), Frank–Ter Haar syndrome (megalocornea, skull malformation including brachycephaly and wide fontanelle, other bone deformities, and hypertelorism), and others.[1,2]

When megalocornea is identified in a newborn, collaboration with the pediatrician is crucial to monitor for the development of potential skeletal, cardiac, and neurological developmental abnormalities and to coordinate prompt treatment and referral to subspecialty care. Although patients with megalocornea tend to be asymptomatic early in life, they should be followed closely by an ophthalmologist, as they can develop presenile cataracts and crystalline lens subluxation as adults.[3]

Management

The management of megalocornea consists of refractive correction and treatment of associated ocular conditions in both primary and syndromic cases. Primary megalocornea patients generally have favorable ophthalmic outcomes with early screening and consistent follow-up. However, complications and associated ophthalmic conditions in these patients are challenging to treat because of their abnormal ocular anatomy.

Associated myopia and astigmatism can be managed with spectacles or contact lenses. Although there are reports of successful keratorefractive surgery in megalocornea, data are limited due to the low prevalence of this condition.[4] Therefore, surgeons must consider each case individually and inform patients of potential complications and unknown risks prior to surgery.

Patients with megalocornea are also predisposed to developing glaucoma, given the possibility of iris and angle abnormalities. Treatments focus on standard antihypertensive eyedrops and filtering procedures if necessary.

Cataract Surgery

Megalocornea poses challenges to cataract surgery. Patients have a large anterior chamber and ciliary ring, which frequently leads to zonular insufficiency, an abnormally large lens capsule, phacodonesis, and ectopia lentis.[3,5-7]

IOL selection and placement. Several principles are important to keep in mind when planning for and performing surgery. First, megalocornea patients have a white-to-white measurement of at least 13 mm. Lens selection is challenging in these patients because most standard-sized posterior and anterior chamber IOLs will be too small for the capsular bag, the ciliary sulcus, or the anterior chamber; this size mismatch predisposes the patient to postoperative IOL decentration and potential development of uveitis-glaucoma-hyphema (UGH) syndrome from iris or ciliary chafing.[6]

The first option is to insert an IOL into the sulcus or capsular bag, coupled with posterior optic capture or anterior optic capture, respectively.[3,8,9] With this approach, it is best to select an IOL with a large optic and total diameter to minimize potential for decentration in case optic capture is unsuccessful. Given the possibility of postoperative lens decentration, multifocal and extended depth of focus IOLs should be avoided in megalocornea patients.

The second option is to use iris fixation techniques for IOL placement or specially designed iris-claw lenses.[10] Anterior chamber IOLs with a sufficient total length are often unavailable, and most conventional models are not an ideal choice because of the risk of decentration, substantial pseudophakodonesis, and UGH syndrome.[3]

Additionally, there are reports of postoperative hyperopic surprise in megalocornea patients.[5] It is postulated that, given megalocornea patients' wide corneas, large anterior chambers, and large capsules, standard IOL formulas do not accurately predict refractive outcomes. Therefore, some authors recommend aiming for a degree of myopia as a postoperative refractive target in these patients.

Other considerations. Certain considerations and adjustments to cataract surgery technique may be necessary. First, the patient's unusual anatomy should be kept in mind when performing the continuous curvilinear capsulorrhexis, as the surgeon cannot rely on the pupillary border alone to size the capsulotomy. Second, given the predisposition for zonular insufficiency, care must be taken when spinning the nucleus, performing chopping or grooving maneuvers, and maintaining a formed anterior chamber. Although there are no studies indicating higher incidence of postoperative wound leak in patients with megalocornea, suture closure of a corneal wound may decrease the risk of postoperative wound leak.[5]

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