Biometry in X linked megalocornea: pathognomonic findings

Françoise M Meire, J Willem Delleman

Abstract

Biometric study in a series of 11 affected males provides characteristic findings. The patients present with a large cornea with short radius, very deep anterior chamber depth (AC depth) exceeding the normal mean value of plus 2 SD, and a short vitreous length. Calculation of the postlimbal depth; a method applied in this study to obtain information about positioning of the iris and the lens, reveals a posterior positioning of the iris and lens. The posterior positioning of the iris and lens was proved to occur at the expense of the vitreous. The importance of biometric data for diagnosis and for differential diagnosis in primary infantile glaucoma and other diseases with megalocornea is discussed.

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The affected males in X linked megalocornea present with symmetrically enlarged clear corneas without evidence of elevated intraocular pressure. Corneal diameter is between 13-18 mm. Kayser, in 1914, was the first to describe the occurrence of megalocornea as an X linked recessive disease in a kindred with 17 affected males.¹ Nevertheless, for a considerable time, the disease was considered to be an abortive type of congenital glaucoma or an incomplete glaucoma.² Until the 1960s this unitarian theory was defended by some authors. Since then the existence of X linked megalocornea as a separate entity is accepted. Arcus lipoides, mosaic corneal dystrophy, pigment dispersion, cataract, and lens dislocation are associated ocular anomalies in the disease; those symptoms are age-related.^{3,4} The gene for X linked megalocornea has been mapped on the long arm of the X chromosome.^{3,5}

In this study we performed a biometric examination in 11 affected males. The importance of biometric data for diagnosis and for differential diagnosis with primary infantile glaucoma and other diseases with megalocornea is discussed. Biometric data also appear to clarify the pathogenesis of X linked megalocornea.

Patients and methods

We examined three families with proved X linked megalocornea with a total number of 20 affected males. Our examination in 11 patients included the measurement of refraction, corneal diameter with a ruler, corneal radius with the keratometer, and corneal thickness with optical pachymeter (Haag-Streit). Anterior chamber depth, lens thickness, vitreous and axial length were studied by ultrasonography (applied by contact). We referred to the mean values of biometry for normal eyes as given by Delmar-

celle.⁶ In this study we also used formulas that allow us to calculate the cupula (H) and the postlimbal depth (i); those are the two parts of the anterior chamber that are obtained by drawing a plane through the limbus AA' (Fig 1). The cupula (H), the anterior part of the AC depth, is related to the corneal diameter (D) and radius (R):

$$H = R - \sqrt{R^2 - \frac{D^2}{4}}$$

The cupula becomes constant by the age of 3 years, its mean value being $\bar{x}=2.55$ (SD 0.21) mm.⁶ The postlimbal depth (i), the posterior part of the AC depth, is calculated by subtracting the cupula from the AC depth. At age 20 years the postlimbal depth is about +0.20 mm.⁶ Since the lens thickness increases in the elderly, the anterior surface of the lens reaches the limbal plane by about the age of 50 years; the postlimbal depth then becomes negative. The postlimbal

Figure 1 The anterior chamber can be divided into two parts by drawing a plane through the limbus AA'. H=cupula; i=postlimbal depth.

University Hospital
Ghent, Department of
Pediatric
Ophthalmology,
Belgium
F M Meire

The Netherlands
Ophthalmic Research
Institute, Department of
Ophthalmogenetics,
Amsterdam, Netherlands
J W Delleman

Correspondence to:
Dr F M Meire, Department of
Ophthalmology, University
Hospital, De Pintelaan 185,
B-9000 Ghent, Belgium.

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Table 1 Biometric data for eyes of patients with X linked megalocornea

Case	AC depth (mm)		Refraction (dioptries)*		Vitreous length (mm)		Axial length (mm)		Vitreous index (%)	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
The A family										
II-3	4.20	3.66	-4	-2	14.83	15.53	23.95	24.19	61.92	64.20
II-5	3.80	3.66	-1.5	-1.75	15.50	15.57	23.80	23.80	65.13	65.42
III-14	3.90	3.90	+0.5	+2.0	16.00	16.00	23.80	23.80	67.23	67.23
III-15	5.10	5.60	-0.5	-1.75	16.00	16.40	25.00	25.40	64.00	64.57
IV-11	4.20	4.20	0	0	18.40	18.40	25.60	25.60	71.86	71.86
IV-23	6.00	6.25	0	-1	13.87	13.77	23.87	24.02	58.11	57.33
IV-35	5.60	5.80	-5.75	-5.75						
IV-38	6.00		-1.5	-1.5	15.40		24.90		61.85	
The B family										
II-1	5.70	5.70		0			24.97	24.73		
II-3		6.50				16.10	26.72	26.90		59.85
The C family										
III-6	5.23	5.25	+1	-6	13.64	14.23	23.59	24.02	57.82	59.24

*Spherical equivalent. Axial length, $\bar{x}=23.10$ (0.82) $^{\circ}$. Vitreous index $\bar{x}=69\%$.

Vitreous length, <25 years $\bar{x}=16.81$ (0.73) $^{\circ}$. 25-50 years $\bar{x}=16.57$ (0.79) $^{\circ}$. >50 years $\bar{x}=16.32$ (0.84) $^{\circ}$.

depth gives the clinician an estimation of the iris inclination and therefore of the width of the iridocorneal angle. The postlimbal depth depends not only on lens thickness but also on lens positioning. In the event of a large positive

postlimbal depth three possibilities should be considered: decreased lens thickness, posteriorly lens subluxation, or posterior insertion of iris and lens. In the case of a negative postlimbal depth in individuals younger than 50 years with normal lens thickness, the lens may be subluxated anteriorly or the iris and the lens may be inserted anteriorly. The postlimbal depth for the patients with X linked megalocornea was calculated in order to obtain information about the positioning of the iris and the lens.

In this study the vitreous index was also calculated. The vitreous index is defined as

$$\frac{\text{vitreous length}}{\text{axial length}} \times 100$$

and is normally about 69%.⁶

Results

Visual acuity in phakic and even in aphakic patients was normal. The distribution of spherical equivalents showed that patients were emmetropic or slightly myopic (Table 1). Astigmatism did not exceed 3 dioptres and was mostly with the rule.

The range of the corneal diameters was from 13 up to 14.5 mm. The corneal radii found for our patients and 26 reported cases¹⁷⁻²¹ are plotted in Figure 2. Most corneas with a diameter between 13 and 15 mm have short radii. A significant correlation between corneal diameter and corneal radius was found (right eye: $r=0.54$, $p<0.01$, $n=36$). For almost all patients the corneal thickness was below the mean value and a negative correlation between corneal diameter and corneal thickness was found (left eye: $r=-0.77$, $p<0.01$, $n=11$) (Fig 3). All AC depths, plotted in relation to age, were very deep, and exceeded the mean value plus 2 SD (Fig 4). The lens thickness in relation to age was found to be normal (Table 2). The cupula was found to be larger than the mean value plus 2 SD. The postlimbal depth in four patients younger than 40 years, who did not present with cataract or lens dislocation, was also very large ($i>+1.0$ mm) (Table 2) and therefore indicates a posterior positioning of the iris and lens. Both the large cupula and the deep postlimbal depth contribute to the very deep AC depth in the patients.

In all affected males the axial length exceeded

Figure 2 (A) Corneal radius in relation to corneal diameter for normal eyes. (Delmarcelle et al⁶). (B) Corneal radius in relation to corneal diameter for own patients with X linked megalocornea and reported cases,¹⁷⁻²¹ regression line.

Figure 3 Corneal thickness in relation to corneal diameter.

the mean value for normal individuals, and in eight of 19 cases (42%) it exceeded the mean value plus 2 SD (Table 1). Nevertheless, the vitreous length was less than the mean value minus 2 SD in four of 16 eyes (25%) and less than the mean in 10 of 16 eyes (62.5%). The vitreous index (the contribution of the vitreous length to the axial length) was below normal in 14 of 16 cases (87%) (Table 1). Moreover, a negative correlation between the AC depth and vitreous index was found: $r = -0.67$ $p < 0.003$, $n = 8$ (the AC depths of right and left eyes were correlated: $r = 0.96$ $p < 0.001$, $n = 7$; in case IV-38 of the A family, only unilateral biometry was performed).

Discussion

A biometric study in a series of 11 patients with X linked megalocornea provided characteristic findings. The patients present with a large cornea with short radius, very deep AC depth exceeding the mean value plus 2 SD, and a short vitreous length.

In patients presenting X linked megalocornea with corneal diameters up to 15 mm keratometry showed short radii. This finding is important since for normal eyes it was observed that corneas with a diameter between 12 and 13 mm always have large radii.⁶ As the large corneas have short radii, they are clinically observed as globular corneas. In our experience the cornea globosa is a pathognomonic finding of X linked megalocornea and one should always look for it. It appears that only if the cornea is too large with a corneal diameter equal to or larger than 15 mm, does it become stretched and, therefore, flatter. Biometry revealed a very deep AC depth in all patients exceeding the mean value plus 2 SD. The very deep anterior chamber could be observed by slit-lamp examination. The presence of a short vitreous in X linked megalocornea, as observed in this study, has never been reported. The pathognomonic biometry of X linked megalocornea is illustrated in Figure 5. We believe that the name introduced in 1931 by Vail¹⁰ 'anterior megalophthalmos' refers very properly to the enlargement of the anterior eye segment in the disease.

BIOMETRY FOR DIFFERENTIATION BETWEEN X LINKED MEGALOCORNEA AND PRIMARY INFANTILE GLAUCOMA

The differentiation between X linked megalocornea and primary infantile glaucoma is often difficult, but very important, for in the latter surgical treatment may prevent blindness. Elevated intraocular pressure in children results in distension of the eye globe with progressive enlargement of the cornea and the appearance of Descemet's ruptures. Nevertheless, Descemet's ruptures are only evident in 60% of the infants presenting with primary infantile glaucoma.²² The corneal curvature always becomes flat and could therefore be distinguished easily from the 'cornea globosa' typical of X linked megalocornea. An increase in the AC depth, a decrease of lens thickness, and an increase of vitreous length are reported in glaucomatous eyes.²³ The decrease of the lens thickness is caused by the enlargement of the ciliary ring and the increase of vitreous length is related to the elasticity of the connective tissue in children that allows distension of the globe. An increase of vitreous length indicates uncontrolled glaucoma and, therefore, the measurement of the vitreous length is a valuable method for the follow up of glaucoma in children. The biometry for five patients with primary infantile glaucoma and five patients with X linked megalocornea is given in Figure 5. This figure illustrates the quite different characteristics of biometric data for both diseases. It is important to mention that biometry should be performed in both eyes. In X linked megalocornea there is always symmetry between the eyes, while in primary infantile glaucoma asym-

Figure 4 Anterior chamber depth in right eyes in relation to mean values.

Table 2 Relation between AC depth, cupula, and postlimbal depth in right eyes for patients with X linked megalocornea

Case	Age (years)	Diameter (mm)	Radius (mm)	AC depth (mm)	Cupula (mm)	Post-limbal depth (mm)	Lens thickness (mm)
The A family							
II-3	67	13	7.21	4.20	4.09	0.11	4.92*
II-5	57	13	7.49	3.80	3.77	0.03	4.50*
III-14	43	13	7.68	3.90	3.59	0.31	3.90
III-15	35	14	7.68	5.10	4.52	0.58	3.90
IV-11	10	13	8.86	4.20	2.84	1.36	
IV-23	14	13.5	7.66	6.00	4.04	1.96	4.0
IV-35	12	13.5	7.93	5.60	3.77	1.83	
IV-38	6	14.5	7.83	6.00	4.87	1.13	3.5
The B family							
II-1†	56	14	7.74	5.70	4.56	1.14	
II-3	60	14	7.83	6.50	4.32	2.18	4.30†
The C family							
III-6	64	14	7.49	5.23	4.83	0.40	4.72*

* Mature cataract.

† Cataract + lens subluxation.

‡ Values for left eye.

Lens thickness, mean value for age.¹⁵

Diameter, $\bar{x}=11.78$ (0.37)⁶. Radius, $\bar{x}=7.86$ (0.26)⁶. AC depth, $\bar{x}=3.0$ (0.3)¹⁴.

Cupula, $\bar{x}=2.55$ (0.21)⁶.

metry between the eyes is common and is also reflected in the biometry.

The present study shows the importance of biometry for differentiation between X linked megalocornea and primary infantile glaucoma.

BIOMETRY FOR DIFFERENTIATION BETWEEN X LINKED MEGALOCORNEA AND MEGALOCORNEA IN ASSOCIATION WITH OCULAR DISEASES OR SYSTEMIC DISEASES

Megalocornea is always present in X linked megalocornea, but it can also be observed sporadically in association with other ocular disorders such as ectopia lentis et pupillae,^{24,25} congenital miosis,²⁶ and Rieger's anomaly.²⁷ Megalocornea is reported in systemic diseases such as congenital Marfan syndrome,²⁸ albinism,²⁹ and Neuhäuser syndrome.³⁰

The findings for 49 patients presenting with megalocornea have been analysed.³¹ In this study megalocornea was observed in 16 different conditions (inclusive X linked megalocornea), irrespective of an association with systemic diseases. Biometric characteristics of X linked megalocornea were not found in those conditions

and therefore they appear to be pathognomonic for the disease.

PATHOGENESIS

Calculation of the postlimbal depth was the method applied in this study to obtain information about positioning of the iris and the lens (Fig 1). In the patients a very large postlimbal depth was calculated and could be related to a posterior positioning of the iris and lens. Gonioscopy too revealed a wide open angle. The posterior positioning of the iris and lens occurred at the expense of the vitreous and was proved by the negative correlation between the AC depth and the vitreous index.

This posterior positioning of the iris and lens not only clarifies the pathognomonic biometry of X linked megalocornea but also supports the pathogenesis of the disease suggested by Mann.³² Mann advanced the following hypothesis for the pathogenesis of X linked megalocornea. Under normal conditions the optic cup is first bell-shaped; it then gradually changes to a more spherical form. If the early embryonic relation between the diameter of the anterior opening of the cup and the equatorial diameter persists for a longer time, the result may well be a permanent increase in the relative diameter of the ciliary ring and hence an apparently larger size of the entire anterior part of the eye and a shorter size of the posterior segment. It is likely that if arrest of growth occurs at the time of the ingrowth of mesodermal cells (12 mm stage) a normal distribution of endothelial cells can be expected. Endothelial cell densities have been measured in X linked megalocornea and found to be normal.¹⁹ On the other hand, since stretching in congenital glaucoma occurs in the last trimester or neonatally it always results in an enlarged cornea with an increased radius and decreased endothelial cell densities.

Histopathological examination has only once been performed in X linked megalocornea.³³ Kayser³³ observed a large dome-shaped cornea with a deep AC in a normal sized globe; the overgrowth was limited to the anterior segment. Kayser also noted a posterior positioning of the iris and the ciliary body. Calculation of the vitreous index for this eye indicates a short vitreous (57.4%). Our biometric data are in accordance with this report.

Figure 5 Biometry for the normal eye (mean values for ages 20–30 years) for primary infantile glaucoma (mean values for five patients) and for X linked megalocornea (mean values of five patients without cataracts: III-14, III-15, IV-11, IV-23, and IV-38 of the A family).

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