An unusual pedigree with microcornea-cataract syndrome

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Abstract

A pedigree with 14 patients affected with microcornea-cataract (MC) syndrome is described. MC syndrome is very rare and this pedigree is probably the sixth to be reported. Transmission is most likely autosomal dominant, but the unusual feature of the present family is the fact that the proportion of affected members is so high that one is tempted to suspect preferential transmission of the chromosome carrying the MC gene.

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Microcornea means an abnormally small cornea which is present in an otherwise normal eye. According to Franceschetti and Klein¹ the normal diameter of the cornea varies between 10.5 and 13 mm and is most frequently between 11 and 12 mm, while "the corneae with diameter of 10 mm or less should be considered as microcorneae...". According to Duke Elder,² a diameter of less than or equal to 11 mm is diagnostic of the condition. Microcornea affects only the anterior part of the eye, hence the historical term "anterior microphthalmos". The size of the eyeball, contrary to what is found in microphthalmos, is normal (the average axial length of the eye in adults is 24 mm; at birth it is 16.7 mm in males and 16.5 mm in females³) and the demarcation line between the cornea and sclera is well defined; in cornea plana it is not distinct. Typical of the condition is cataract which is present in most cases. Friedman and Wright,⁴ who described a large pedigree of five generations,

found that "at least 20% of the cases develop glaucoma during their life time".

In McKusick's catalogues⁵ the condition is termed cataract-microcornea syndrome (116150), although the alternative term microcornea-cataract (MC) would seem to be more appropriate because the presence of cataract is not the rule. Among the cases of Friedman and Wright⁴ and of Mollica *et al*⁶ there were single patients without cataract.

The pathogenesis of microcornea is unknown; Salmon *et al*,⁷ based on observation of their large pedigree and the available embryological data, presented a hypothesis that the anterior segment of the eye, including the cornea, originates from neural crest cells.

Case reports

We present an unusual pedigree of four generations with 14 members affected with MC syndrome (fig 1). Of these, eight were operated on for cataract.

Details of the affected subjects are provided in the table. Both horizontal and vertical diameters of the corneae were measured. In 13 cases both diameters were less than 10 mm; in one case (IV.1) the diameter was between 10 and 11 mm. In fact it was the only case in which there was doubt about the diagnosis. This was a boy aged 9 who was operated on because of the cataract. He had glaucoma of the right eye and the axial length of each of his eyes was well above the average (table). His mother, III.2, was affected with MC syndrome. However, as one can see from the pedigree (fig 1) he could have inherited cataract of another type from his father (III.1) who had cataract and glaucoma (the paternal grandmother and great grandmother also had cataract). In order to exclude microphthalmos, ultrasonographic measurements of the axial lengths of the eyes were taken in most of the cases (table). In only one case (III.2) was the axial length of one of the eyes less than normal, but this was because of postoperative phthisis of the eyeball. Peters' anomaly was excluded in all patients by slit lamp biomicroscopy and by gonioscopy in adults.

Fig 2 shows one of the cases of MC syndrome (III.6). One of the characteristic features (present in eight of 14 cases) was a white strip of a sclera, which could be seen between the cornea and the margin of the lower lid, giving the impression of the cornea hiding itself under the upper lid (fig 2). In some cases the pupils were excentric (fig 3), in two cases there was a convergent squint, and in another case the palpebral fissures were shortened. Myopia of

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Figure 1 Pedigree of the family.

Ocular findings in the family members

Affected subject	Age (y)	Sex	Corneal diameter (mm)*		Axial length of eyes (mm)		Cataract	Refraction defect	Nystagmus	Other ocular abnormalities
			R	L	R	L				
II-2	50	F	9.0 × 8.5	9.0 × 8.5	NM	NM	Aphakia	No	No	No
III-2	30	F	7.5 × 7.5	8.0 × 7.5	16.98	26.60	Aphakia	No	Yes	Phthisis of R eyeball
III-4	29	F	9.0 × 9.0	9.0 × 9.0	NM	NM	Posterior polar	Hypermetropia +3.0 D	No	L divergent squint
III-6	28	F	8.0 × 7.5	8.0 × 7.5	26.35	26.30	Posterior polar	Myopia -6.0 D	No	No
III-7	26	M	9.0 × 8.5	9.0 × 8.5	26.20	25.20	Posterior polar	Myopia -2.0 D	No	L convergent squint
III-8	25	M	8.0 × 8.0	9.5 × 9.0	22.46	24.21	R total, L posterior polar	No	No	Short palpebral fissures
III-10	22	F	8.5 × 8.0	8.5 × 8.0	25.24	25.88	Posterior polar	Myopia -2.0 D	No	Excentric pupils
III-11	21	M	9.0 × 9.0	9.0 × 9.0	24.34	24.80	Total	No	Yes	Excentric pupils
IV-1†	9	M	11.0 × 10.0	10.5 × 10.0	28.90	28.44	Aphakia (total)	No	Yes	R glaucoma
IV-2	8	F	8.0 × 7.0	8.0 × 7.0	20.76	20.39	Aphakia (posterior polar)	No	Yes	No
IV-3	10	M	9.0 × 8.5	9.0 × 8.0	24.86	23.79	Aphakia (total)	No	Yes	No
IV-4	8	M	8.0 × 7.5	8.0 × 7.5	NM	NM	R aphakia (L posterior polar)	No	No	No
IV-5	7	M	8.0 × 7.5	8.0 × 7.5	NM	NM	Aphakia (total)	No	Yes	No
IV-6	4	F	6.0 × 6.0	7.5 × 7.0	20.61	21.63	Aphakia (posterior polar)	No	Yes	No

* Horizontal × vertical, † doubtful case, NM not measured, () type of cataract recorded before operation.

Figure 2 Patient III-6 showing microcornea-cataract; note normal size of the eyeball and white strip of sclera between the cornea and margin of the lower lid.

up to -6.0 D was present in three cases (III-6, III-7, III-10) and hypermetropia + 3.0 D in one case (III-4) (table). The cataract was either posterior-polar or total. The size of the eyeballs was normal in all cases except III-2 in which there was postoperative phthisis of the right eyeball. Eight cases present postoperative aphakia. The expression of microcornea was

Figure 3 Patients III-10 and III-11 showing the same features as patient III-6, plus excentric position of the pupils.

more marked in females than in males: the mean diameter of the cornea in males was 8.4 mm and in females 7.9 mm (difference not significant).

The stature of most of the affected subjects was short: adult males (3) 161–164 cm, females (5) 142–154 cm. This, however, is probably an independent feature in the family.

In order to exclude chromosome abnormalities cytogenetic examination was performed in one of the affected subjects (III-10) and the karyotype was found to be normal.

Discussion

The inheritance in the family described here is most probably autosomal dominant, although we are not able to rule out X linked dominant transmission (male to male transmission was not observed). However, if the inheritance was X linked dominant, then one would expect microcornea to be expressed more often in males than in females, but this was not the case.

The most striking feature of this family, however, is the very high proportion of affected persons. Even if we considered subjects III-9 (who died at the age of 2 years and was reported by the family to have normal eyes) and a doubtful case IV-1 as being unaffected, there would still be a proportion differing significantly from the expected 50%, that is 12:2 ($p < 0.05$, $\chi^2 = 4.094$).

Microcornea-cataract is a very rare dominant syndrome and only a few pedigrees have been described.⁴⁻⁸ In the pedigree of Mollica *et al*⁶ myopia was also a characteristic feature; the axial length of the eyeball was normal. Salmon *et al*⁷ described a pedigree in which in some cases there was cornea plana, sclerocornea, and Peters' anomaly; they considered these as variant expressions of the same condition.

This was an interesting pedigree in view of the fact that both conditions, microcornea and cornea plana, are considered to be separate genetic entities.¹ In McKusick's catalogue⁵ cornea plana is a separate entity which can be either dominant (121400) or autosomal recessive (217300).

Recently it has been found that Peters' anomaly and a variety of anterior segment an-

omalies may be associated with a PAX6 gene mutation.⁹ Thus microcornea can be considered as one of the candidates for a PAX6 mutation.

Follow up of our family may bring a solution to whether the high proportion of affected subjects happened by chance or whether there is perhaps some, difficult to explain, preferential transmission of the chromosome carrying the MC gene.

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