Aniridia associated with microcornea and subluxated lenses

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SUMMARY Four cases of aniridia associated with subluxated lenses and microcornea are presented. The triad occurred in both eyes of the 4 affected members in one Ndebele family (one of the South African Negro tribes). No other ocular or systemic defects were noted, and intelligence was normal. Chromosomal studies on both parents showed no abnormality, and gene marker studies failed to reveal any linkage between the disease locus and a wide range of polymorphic loci.

Aniridia is a congenital anomaly of ectodermal development with an incidence of 1:100 000 (Duke-Elder, 1964; Warkany, 1971; Podos, 1975) and is transmitted in an autosomal dominant fashion with high penetrance (Sorsby, 1972).

Several other ocular and systemic defects have been associated with aniridia. Among these are foveal aplasia (Warkany, 1971; Sorsby, 1972), subluxated lenses (Duke-Elder, 1964; Podos, 1975) and hypoplastic optic discs (Layman *et al.*, 1974). Associated systemic conditions include mental retardation (Warkany, 1971; Podos, 1975) and Wilms's tumour (Warkany, 1971; Haicken and Miller, 1971).

We report on a family in which four members in 2 generations exhibited the triad of aniridia, microcornea, and upwardly subluxated lenses (Fig. 1).

Case reports

CASE I/1

A 42-year-old man gave a history of bilateral lens extraction at 15 years of age. On examination the right eye had no light perception, while the left eye, with aphakic correction, had a vision of 6/24. The intraocular pressure by applanation tonometry was 20 mmHg in both eyes. Both corneae were 8 mm in the vertical and in the horizontal meridia. A rudimentary iris was visible as a temporal crescent on both sides (Fig. 2). The angle of the right eye was closed throughout 360°. On gonioscopy some iris

rudiment was seen all round and scar tissue in the upper half of the angle. The vitreous in this eye was organised, and no view of the fundus could be obtained. The angle on the left side was open all round

Fig. 1 Pedigree of family with aniridia-microcornea-subluxated lens syndrome

Fig. 2 Left eye of Case I/1 with microcornea and a rudimentary iris crescent

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with iris tissue in the periphery similar to the right eye. Both eyes were aphakic, presumably following the above-mentioned surgery, and the fundus showed no significant abnormalities. A mild horizontal nystagmus could be detected.

CASE I/2

This patient, a 38-year-old woman, was the wife of Case I/1. She became blind in early childhood after an unknown bilateral eye disease of which she could give us no details. She attended a blind school and it was there she met her husband. Examination revealed absence of light perception in both eyes. The right eye was phthisical with a pressure of 0 mmHg. The left eye had a pressure of 10 mmHg, a shallow anterior chamber, and a totally occluded pupil with a complicated cataract. Both corneae were normal in size.

CASE II/1

A 15-year-old girl, daughter of the previous two cases, had a visual acuity with aphakic correction of 6/24 in both eyes. She had a horizontal nystagmus, and the intraocular pressure was 20 mmHg in each eye. The corneal diameter measured 7.0 mm horizontally in both eyes, while the vertical measurements were 8.5 mm on the right and 7.5 mm on the left. Both lenses were subluxated upwards, with the lower margin of the lens just above the visual axis. The lens on the right was opaque (Fig. 3), while that on the left showed early cortical opacities. Gonioscopy revealed rudimentary iris tissue all round and an open angle with normal structures (Fig. 4). Both fundi were normal.

CASE II/2

A 13-year-old girl, sister of the previous case, had a visual acuity limited to light perception in the right eye and 6/18 in the left, with aphakic correction. The

Fig. 3 Right eye of patient II/1. Microcornea aniridia and subluxated cataractous lens

Fig. 4 Gonioscopic view of angle (black arrow) and iris rudiment (white arrow)

corneal diameters were 7.00 mm in the horizontal meridian of both eyes, while the vertical measurement was 8.0 mm on the right and 8.5 mm on the left side. Again, there was a horizontal nystagmus, and the intraocular pressure was 6 mmHg on the right and 18 mmHg on the left. The right eye had undergone lens surgery, and when seen had a long-standing detached retina with pronounced flare and cells in the anterior chamber. The left eye showed upward subluxation of the lens, identical to Case II/1. On gonioscopy, on the right side iris tissue was present only on the temporal periphery; on the left side iris tissue was present in a rudimentary form all round. The angles were open with similar normal structures as in the previous case. The fundus of the left eye was normal.

CASE II/3

A 9-year-old girl (Fig. 4), sister of the other 2, had a visual acuity of 6/9 on the right and 6/7.5 on the left, both with small myopic-astigmatic corrections. Intraocular pressures were 16 mmHg on the right and 14 mmHg on the left. The corneae were normal in size, the iris and pupil normal in appearance. Neither lens was subluxated, but early peripheral cortical opacities were present in both temporal aspects. The angles were open all round and normal. Both fundi were also normal.

CASE II/4

An 8-year-old boy, was the youngest child of Cases I/1 and I/2. The visual acuity with or without aphakic correction was 6/60 in both eyes, with the lower margin of the lens bisecting the visual axis,

Table 1 Summary of ocular findings in the 4 affected patients

Case	I/I		II/I		II/2		II/4	
Findings	RE	LE	RE	LE	RE	LE	RE	LE
Visual acuity	No PL	6/24	6/24	6/24	LP	6/18	6/60	6/60
Corneal diameter:								
Horizontal	8	8	7	7	7	7	8	7
Vertical	8	8	8.5	7.5	8	8.5	8	8
Intraocular pressure	20	20	22	20	6	18	14	14
Sublux. lens	Aphakic	Aphakic	Upwards	Upwards	Aphakic	Upwards	Upwards	Upwards
Iris on direct view	Temporal crescent	Temporal crescent	None	None	None	Temporal crescent	Temporal crescent	None
Angle	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Cataract	Aphakic	Aphakic	+	Early	Aphakic	—	—	—
Fundus	Not seen	Normal	Normal	Normal	Total retinal detachment	Normal	Normal	Normal
Nystagmus		±		+		+		++

The intraocular pressure was 14 mmHg in both eyes. The right cornea measured 8.0 mm in both meridians, while the left measured 7.0 mm horizontally and 8 mm vertically. Both lenses were clear and subluxated upwards in a similar manner to the previous cases. Examination of the angles revealed very rudimentary iris present throughout the angles with the rest of the angle appearing normal. Both discs and maculae looked normal. The child had a marked nystagmus. The ocular findings of the affected cases are summarised in Table 1.

Discussion

Aniridia is a well documented congenital anomaly, transmitted as an autosomal dominant trait with 85–90% penetrance (Sorsby, 1972). When aniridia is transmitted as a dominant trait, the associated ocular manifestations usually show great variability (Drenckhahn and Behnke, 1961). Among these either microcornea (Duke-Elder, 1964) or subluxated lenses (Duke-Elder, 1964; Drenckhahn and Behnke, 1961; Warkany, 1971) have been described. To the best of our knowledge, however, there has been no report in which both have co-existed in the same patient. Likewise no defect in the angle of the anterior chamber was apparent, and for this reason none of our patients showed features of glaucoma.

As microphthalmos has been frequently associated with aniridia or with subluxated lenses (Duke-Elder, 1964; Sorsby, 1972), we undertook ultrasound investigations, which demonstrated normal axial lengths on the A-mode (Fig. 5) and showed normal structures, with the subluxated lens detectable on the B-mode (Fig. 6). It is of interest to note that the posterior segment of the eye in all patients revealed neither a hypoplastic disc (Layman *et al.*,

Fig. 5 A-mode ultrasound of left eye of patient II/2; normal axial length

1974), nor macular or foveal aplasia (Warkany, 1971; Podos, 1975; Sorsby, 1972).

None of the patients was mentally retarded. The father is the breadwinner and supports his family, while the children, in spite of their visual handicap, contrive to attend regular school.

No specific search was made for Wilms's tumour, but the patients' apparent good health at ages ranging from 9 to 42 renders this association highly unlikely. This would support the view that Wilms's tumour is associated mainly with sporadic cases of aniridia (Haicken and Miller, 1971).

Chromosomal studies were performed on the 2 parents, and the results were normal.

Dominantly inherited conditions afford an opportunity for establishing the relationship of the disease locus to loci determining the inheritance of normal genetic traits like the blood groups. In this

Table 2 Serogenetic data on all family members*

	I/1 (A)†	I/2 (U)	II/1 (A)	II/2 (A)	II/3 (U)	II/4 (A)
<i>Red cell antigens</i>						
ABO	O	A ₁	O	A ₁	O	O
MNSs	Ms/Ns	Ms/Ms	Ms/Ns	Ms/Ms	Ms/Ns	Ms/Ns
Rhesus (probable)	R ₁ /R ₂	Ro/Ro	R ₁ /Ro	R ₁ /Ro	R ₁ /Ro	R ₁ /Ro
Duffy	Fy ^a /Fy	Fy ^a /Fy	Fy ^a /Fy	Fy ^a /Fy	Fy/Fy	Fy/Fy
ABH Secretor	Se/se	Se/	Se/se	Se/se	Se/se	Se/se
<i>Red cell enzymes</i>						
6GPD	AC	A	A	A	A	A
PepA	1-1	2-1	2-1	1-1	2-1	1-1
CAII	2-1	1-1	2-1	2-1	2-1	2-1
GPT	2-1	2-1	2-2	2-1	2-1	1-1
GSH	1-1	1-F	1-1	1-1	1-1	1-1
<i>Serum proteins</i>						
Hp	2-1	2-1	0-0	2-1	0-0	2-1

*Red cell antigen typing carried out according to standard methods (Race and Sanger, 1975), and enzyme and protein typing according to methods outlined by Giblett (1969)

†The letter A indicates individuals affected with the syndrome; U indicates an unaffected individual

Fig. 6 B-mode ultrasound of left eye of patient II/2 with subluxated lens seen below

family such a study has been attempted. All family members were tested for a wide range of genetic polymorphisms. No variation was found in the P and Kell blood group systems or in the following red cell enzyme systems: glucose 6-phosphate dehydrogenase (G6PD), adenosine deaminase (ADA), acid phosphatase (AP), phosphoglucomutases (PGM₁ and PGM₂), peptidase D (pep D) esterase (est D), adenylatekinase (AK), carbonic anhydrase (CA₁),

and isocitrate dehydrogenase (ICD). The serum transference pattern was C in all family.

The findings in the other systems are presented in Table 2, from which it will be seen that very close linkage is excluded between the locus for the aniridia-microcornea-subluxated lens syndrome and the MNS, rhesus, Duffy, 6-phosphogluconate dehydrogenase, and carbonic anhydrase II loci. The data are presented in full to enable those workers with access to families suffering from the same condition to combine their findings with these in an attempt to establish genetic linkage.

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