Familial iris melanosis—a misnomer?

BRIAN C JOONDEPH AND MORTON F GOLDBERG

From the Department of Ophthalmology, Eye and Ear Infirmary, University of Illinois College of Medicine at Chicago, USA

SUMMARY Iris melanosis is an unusual condition characterised by the presence of minute, discrete, pigmented elevations arising from the anterior surface of the iris. We encountered two unrelated Mexican families in which all children, but no parent, had varying degrees of the condition bilaterally. Some family members also gave findings suggestive of ocular hypertension. No family member had any other ocular or cutaneous pigmentary changes with the exception of a hairy naevus on the thigh of one member. To our knowledge these are the first families reported with more than one member having isolated iris melanosis. This is also the first report of a possible relationship with ocular hypertension. Finally we suggest that the term ‘melanosis’ may be a misnomer, since the condition is characterised not by abnormal iris hyperpigmentation but by discrete, round elevations on the anterior iris surface.

Iris melanosis is an unusual condition characterised by minute, discrete, pigmented elevations arising from the anterior surface of the iris.^{1–6} Although it usually is unilateral, a bilateral case was recently described.⁴ The entire iris surface or just a sector may be involved. Iris melanosis, as opposed to the more generalised ocular melanosis, is not associated with any other ocular, cutaneous, or systemic abnormalities. While most cases of generalised ocular melanosis are sporadic, an autosomal dominant mode of inheritance has been suggested.¹

We present here what is to our knowledge the first two family pedigrees for iris melanosis, as well as the first report of a possible association with ocular hypertension.

Material and methods

Our study is based on two families in which iris melanosis was present in all children but in none of the parents. Both families were Mexican but were from different parts of Mexico and were unrelated to each other (Figs. 1, 2). Each of the family members underwent a complete ophthalmic examination (Tables 1, 3), including best corrected visual acuity,

manifest refraction, slit-lamp examination of the anterior segment, Goldmann applanation tonometry, slit-lamp gonioscopy (family A only), and dilated fundus examination. Goldmann visual fields were performed on three of the children in family A (patients II-3, II-4, and II-6). In addition home tonometry was performed on these three patients using a self-tonometer as described elsewhere.⁷ Tonometry readings were obtained on three to nine separate days during a one-month period, with three random measurements performed on each day (Table 2). Finally, a detailed history regarding skin lesions or systemic diseases was obtained.

Fig. 1 Pedigree of family A. Squares indicate male members; circles indicate female members.

Correspondence to Morton F Goldberg, MD, Wilmer Ophthalmological Institute, Johns Hopkins Hospital, Baltimore, Maryland 21205, USA.

Fig. 2 Pedigree of family B. Squares indicate male members; circles indicate female members.

Results

FAMILY A

Family A comprised six siblings (two males, four females) ranging in age from 13 to 27 years (Table 1). Both parents were Mexican, and there was no known consanguinity. Best corrected visual acuity was 20/20 in all family members, with plano, myopic, or mixed astigmatic refractive errors. Applanation tonometry revealed intraocular pressures of 20 mmHg or greater in three children (patients II-3, II-4, and II-6). These patients then underwent home tonometry, which revealed abnormal pressure elevations in patients II-3 and II-4 (Table 2). Patient II-4 had a maximum intraocular pressure of 27 mmHg OD and 26 mmHg OS, while patient II-3 had maximum pressures of 24 mmHg OD and 25 mmHg OS. Slit-lamp gonioscopy gave normal results except for the father and patient

Table 2 Home tonometry measurements in family A

Patient	Number of days tested	Maximum IOP (mmHg)	
		OD	OS
II-3	9	24	25
II-4	7	27	26
II-6	3	20	22

II-6, who both had prominent iris processes. None of the patients had abnormal angle pigmentation or angle maldevelopment.

Slit-lamp examination disclosed no abnormal eyelid, conjunctival, fundus, or scleral pigmentation in any of the family members. The irides of the children were brown and contained minute, discrete, pigmented elevations on the anterior surface (Figs. 3, 4). The extent of involvement varied from as many as 30 to 40 excrescences per clock hour of iris (Fig. 3) to as few as one to five per clock hour (Fig. 4). These excrescences tended to be more concentrated on the midperipheral and inferior portions of the iris (Table 1). The disease was bilateral and symmetrical. The mother's irides were brownish green and had no pigmented elevations (Fig. 5). The father's irides were brown, with a smooth anterior surface. Two flat iris freckles, with a smooth anterior surface, were noted (Fig. 6).

Fundus examination disclosed no abnormal choroidal pigmentation. Cup-to-disc ratios were within normal limits except for patient II-6, who had a moderate amount of asymmetry (Table 1). Goldmann visual fields were full in those family members tested (patients II-3, II-4, and II-6).

No family member had any known abnormal skin pigmentation.

Table 1 Ocular findings in family A

Patient/age (yr)/sex	Visual acuity (OU)	Refraction	IOP (mmHg)	Gonioscopy	Iris involvement	Other
II-1/27/F	20/20	Plano OU	17 OU	Normal	Moderate, midperipheral, more inferiorly OU	C/D 0.30 OU
II-2/23/F	20/20	Plano OU	18 OU	Normal	Mild, midperipheral OU	C/D 0.30 OD, 0.25 OS
II-3/21/M	20/20	-3.50+0.50×90° OD -2.25+0.25×105° OS	24 OD 22 OS	Normal	Mild, inferiorly only OU	C/D 0.30 OU, full GVF
II-4/19/M	20/20	Plano OU	20 OU	Normal	Moderate, midperipheral OU	C/D 0.30 OU, full GVF
II-5/18/F	20/20	-1.75 sphere OU	18 OU	Normal	Mild, midperipheral, more inferiorly OU	C/D 0.20 OU
II-6/13/F	20/20	-2.25+2.25×90° OD -3.50+2.50×90° OS	22 OD 20 OS	Prominent iris processes OU	Extensive, entire anterior surface OU	C/D 0.25 OD, 0.50 OS; full GVF
I-2/48/F	20/20	-0.75 sphere OU	18 OU	Normal	None	Breast carcinoma metastatic to choroid
I-1/54/M	20/20	-0.50 sphere OD -0.75+0.50×80° OS	18 OU	Prominent iris processes OU	2 Brown freckles, no discrete elevations	

OU=both eyes. IOP=intraocular pressure. OD=right eye. OS=left eye. C/D=cup-to-disc ratio. GVF=Goldmann visual fields.

Fig. 3 Iris of patient II-6 (family A) showing numerous minute, discrete, pigmented elevations on the anterior surface.

Fig. 4 Iris of patient II-4 (family A) showing fewer iris excrescences than his sister (Fig. 3). They tend to be more concentrated on the mid-peripheral and inferior iris.

FAMILY B

Family B comprised two children, a boy aged 13 years and a girl aged 8 years (Table 3). Both parents were Mexican, and there was no known consanguinity. The father was deceased. Best corrected visual acuity was 20/25 or better, with myopic or mixed astigmatic refractive errors, in all family members. Applanation tonometry revealed normal intraocular pressures.

Slit-lamp examination disclosed no abnormal eyelid, conjunctival, scleral, or fundus pigmentation in any family members. The irides of the children were brown and contained minute, discrete, pigmented elevations of the anterior surface. Patient II-1 had extensive involvement of the entire mid-peripheral iris with 20 to 30 excrescences per clock hour of iris (Fig. 7), while his sister (patient II-2) had only a few excrescences along the inferior mid-peripheral iris. Involvement was bilateral and symmetrical. The mother's irides were brown with a smooth anterior surface.

Fundus examination revealed no abnormal pigmentation and a normal cup-to-disc ratio. Patient II-1 had a hairy naevus on his left thigh.

Discussion

Melanosis of the eye (melanosis oculi) refers to increased pigmentation of the iris, ciliary body, and choroid, as well as the sclera, conjunctiva, and optic disc.¹ It may exist in two forms, either congenital or acquired. Iris melanosis was first described by Coats in 1912 as a unilateral iris condition in which the iris 'anterior surface is sown all over with minute, discrete, hemispherical, pigmented prominences, arranged quite regularly, the appearance being comparable with "goose-skin" or the surface of a golf ball'.² He found an otherwise normal function of the eye, including visual acuity and pupillary reactions. He believed the condition to be non-progressive, though the more generalised ocular melanosis may be associated with an increased risk of uveal

Fig. 5 Mother of family A (patient I-2). She has greenish brown irides with no abnormal iris excrescences.

Fig. 6 Father of family A (patient I-1). He has brown irides with a smooth anterior surface.

Table 3 Ocular findings in family B

Patient/age (yr)/sex	Visual acuity (OU)	Refraction	IOP (mmHg)	Iris involvement	Other
II-1/13/M	20/25	-3.00 sphere OU	10 OU	Extensive, midperipheral OU	C/D 0.20 OU, hairy naevus on left thigh
II-2/8/F	20/25	-1.75 sphere OU	12 OU	Mild, midperipheral, more inferiorly OU	C/D 0.10 OU
I-2/32/F	20/20	-1.50+1.25×180° -2.00+1.25×180°	10 OU	None	C/D 0.10 OU

OU=both eyes. IOP=intraocular pressure. C/D=cup-to-disc ratio.

malignant melanoma.^{2,3} No relationship between race and risk of malignancy was discovered for iris melanosis. While most cases of generalised ocular melanosis occur sporadically, autosomal dominant and recessive forms of transmission have been described.¹

Other authors have noted a sectorial involvement of the iris by these 'evenly distributed small mammillations with bases radiating in minute folds'.^{5,6} Recently, Traboulsi and Maumenee described a single case of bilateral iris melanosis without other ocular or systemic involvement or family history.⁴ They claim that this was the first reported case of bilateral iris melanosis.

We have described two Mexican families in which all children but none of the parents have varying degrees of discrete, pigmented elevations of the anterior surface of each iris. The extent of involvement varies from as many as 30 to 40 to as few as one to five protuberances per clock hour of iris. These protuberances tend to be more concentrated in the midperipheral and inferior iris. Involvement is bilateral and symmetrical. Except for prominent iris processes in one child (patient A-II-6), gonioscopic examination did not reveal hyperpigmentation or angle maldevelopment. Interestingly, that same child had the greatest number of iris lesions. Visual acuity and iris motor function were normal in

all children. No other ocular or skin hyperpigmentation was noted in any of the family members except for a hairy naevus on the thigh of patient B-II-6.

The possible relationship to ocular hypertension is interesting. Two of the six children in family A (patients II-3 and II-6) had a raised intraocular pressure (24 mmHg OD, 22 mmHg OS; and 22 mmHg OD, 20 mmHg OS, respectively), on their initial examination. The conclusion that some of these pressures are abnormal is based on the distribution of applanation pressures in normal subjects aged 20–29, where the mean pressure plus two standard deviations above the mean yields an upper limit of normal of 20 mmHg.⁸ One of the children (patient II-6) had a moderate degree of cup to disc asymmetry (0.25 versus 0.50). No visual field defects could be demonstrated by Goldmann perimetry. As a further investigation into these findings, home tonometry was performed on three of the children, showing abnormal pressure peaks in two of them (Table 2). The clinical significance of these findings is unknown, and periodic examinations are warranted because these children are considered to be at risk of developing glaucoma.

Detailed histological study of this disorder has not been undertaken. Some suggest that the iris excrescences may be due to irregular thickening of the anterior iris surface, with the remainder of the iris being normal.¹ They may also represent collections of large uveal melanocytes as seen in ocular melanosis.⁹

The relationship of iris melanosis to malignant melanoma is questionable. Incidences from 10 to 27% have been reported.^{2,3} However, inspection of the actual case reports reveals that all such cases occurred in eyes with hyperpigmentation of the sclera, conjunctiva, or choroid, so that they had more generalised ocular melanosis, not the localised iris 'melanosis' as shown in our patients. In addition, these series do not specify the patient's race, nor do they make any distinction between congenital and acquired ocular melanosis, the latter of which is known to be associated with an increased incidence of malignant melanoma of the choroid in white patients.

The familial pattern in our two families suggests

Fig. 7 Iris of patient II-1 (family B) shows numerous elevations along the entire iris surface.

Fig. 8 Piece of 'dotted-swiss' fabric with a surface pattern very similar to the iris in the described patients.

the possibility of non-mendelian mechanisms (polygenic or multifactorial inheritance). The pedigree does not support an autosomal dominant pattern, and it would be unlikely for all children to be affected in a recessive pattern. There was no known parental consanguinity in either family.

The differential diagnosis of iris nodules is extensive, but two particular disorders deserve mention. The iris-naevus (Cogan-Reese) syndrome shares with iris melanosis its occurrence in young people and its association with raised intraocular pressure. However, the diffuse iris naevus in the iris-naevus syndrome can easily be distinguished from the discrete excrescences in iris melanosis. In addition the iris-naevus syndrome is unilateral and is associated with peripheral anterior synechiae and heterochromia, unlike iris melanosis. Neurofibromatosis (von Recklinghausen's disease) is another cause of bilateral iris nodules and congenital glaucoma, but the nodules tend to be larger than those in iris melanosis. Furthermore, the cutaneous, the central nervous system, and the systemic manifestations of neurofibromatosis serve to distinguish this condition from iris melanosis.

Finally, the term 'melanosis' refers to abnormally dark pigmentation of a specific tissue. The condition we are describing does not produce hyperpigmentation per se. Instead, the irides are characterised by discrete, round elevations on their anterior surfaces, which have previously been called mamillations. We therefore suggest another, possibly more descriptive name for this condition, such as 'dotted-swiss iris' (Fig. 8).

To our knowledge these are the first two families reported with more than one member having iris melanosis. This is also the first demonstration of a possible relationship to ocular hypertension. Further follow-up of intraocular pressures, visual fields, and optic discs will be necessary for a better understanding of the natural history of this condition.

We thank Kathleen Loudon for editorial assistance and Linda Warren for her illustrations.

This study was supported by core grant EY 1792 and training grant EY 7038 from the National Eye Institute, Bethesda, MD, and by an unrestricted research grant from Research to Prevent Blindness, Inc, New York, NY.

References

- 1 Duke-Elder S. *System of ophthalmology*. London: Kimpton, 1964; 3: 794–8.
- 2 Coats G. Unilateral diffuse melanosis of the uvea, with small elevations on the surface of the iris. *Trans Ophthalmol Soc UK* 1912; 32: 165–71.
- 3 Bronner A. Melanose congénitale avec dégénérescence maligne. *Bull Soc Ophthalmol Fr* 1948: 189–91.
- 4 Traboulsi E, Maumenee IH. Bilateral melanosis of the iris. *Am J Ophthalmol* 1987; 103: 115–6.
- 5 Mann I. *Developmental anomalies of the eye*. Philadelphia: Lippincott, 1957: 290–1.
- 6 Waardenburg PJ. Uveal membrane. In: Waardenburg PJ, Franceschetti A, Klein D, eds. *Genetics and ophthalmology*. Springfield: Thomas, 1961: 702.
- 7 Zeimer RC, Wilensky JT, Gieser DK, Welch DB, Mori MT, Kahanic D. Application of a self-tonometer to home tonometry. *Arch Ophthalmol* 1986; 104: 49–53.
- 8 Armary MF. On the distribution of applanation pressure. *Arch Ophthalmol* 1965; 73: 11–8.
- 9 Zimmerman LE. Melanosis, melanocytic nevi, and melanocytomas. *Invest Ophthalmol Vis Sci* 1965; 4: 11–41.

Accepted for publication 12 May 1988.