

Familial bilateral macular colobomata

STEVEN ABBOTT MILLER AND G. BRESNICK

From the Department of Ophthalmology, Retina Service, University of Wisconsin, University Hospitals, Madison, Wisconsin, USA

SUMMARY A mother and daughter had a life-long history of poor vision and photophobia, bilateral macular colobomata, and retinal pigment epithelial abnormalities; psychoelectrophysiological testing indicated extensive loss of cone or cone-rod function. These cases suggest this is a genetically determined condition unrelated to infection.

Familial bilateral macular colobomata occur infrequently (Leonardi, 1909; Feilchenfeld, 1911; Clausen, 1921, 1928; Schott, 1921; Waardenburg, 1923, 1938; Car, 1925; Clarke, 1927; Davenport, 1927; Sorsby, 1935; Evans, 1937; Waardenburg *et al.*, 1961; Margolis *et al.*, 1977). The purpose of this paper is to present the clinical characteristics and psychoelectrophysiological findings in a 37-year-old mother and her 13-year-old daughter, who had a life-long history of poor vision and photophobia, bilateral macular colobomata, varying degrees of retinal pigment epithelial abnormalities, and whose colour vision, ERG, EOG, and dark adaptation findings indicated extensive loss of cone or cone-rod function.

Patients and methods

CASE 1

The 13-year-old daughter of Case 2 reported a life-long history of poor vision and photophobia but no nyctalopia. She had no known systemic abnormalities. With eccentric fixation the best-corrected visual acuity in either eye was 20/200. Paramacular retinoscopy and subjective refraction were variable but that of a low (less than 5) myopic astigmatic error. A jerk nystagmus was present on horizontal gaze. Biomicroscopy was normal. There were bilateral, $2\frac{1}{2}$ -3-disc diameter, macular-centred colobomata. These oval, discrete excavations were surrounded by a dark rim of retinal pigment epithelium. Only an occasional choroidal vessel of larger calibre was visible against the white scleral background of the defect. The internal limiting membrane surrounding the colobomata was contracted and wrinkled (Figs. 1, 2). A wedge of temporal pallor of the optic nerve was present. The arterioles were normal. There was a

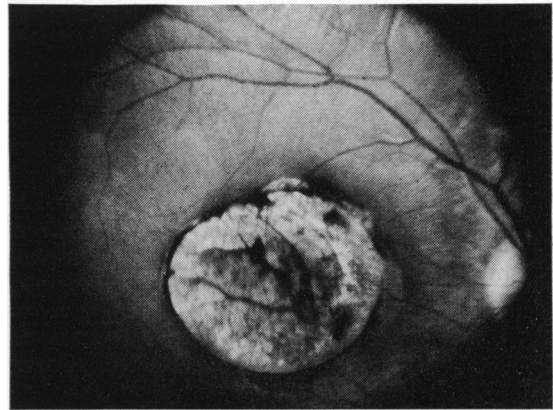


Fig. 1 *Black-and-white print from colour photograph of macular region of the right eye. The well demarcated macular-centred coloboma is surrounded by a discrete dark rim of retinal pigment epithelium. A few large-calibre choroidal vessels are seen against the white scleral background of the defect. There is wrinkling of the internal limiting membrane adjacent to the lesion*

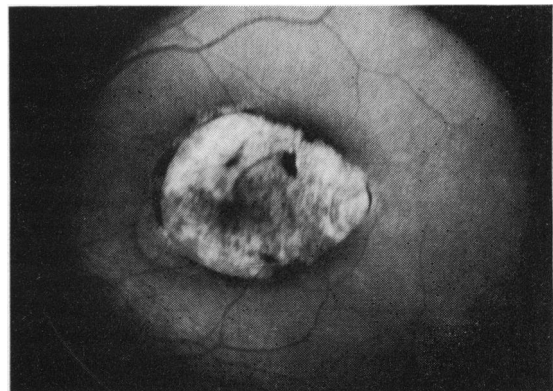
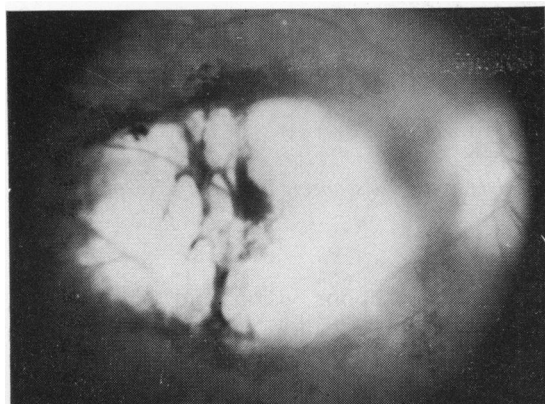


Fig. 2 *The left macular region is similar to that in the right eye. The arterioles have a normal calibre*

Address for reprints: Steven A. Miller, MD, University of Wisconsin Hospital, 1300 University Avenue, Madison, Wisconsin 53706, USA



3



4

Figs. 3 and 4 The right (Fig. 3) and left (Fig. 4) fundus of patient also show bilateral macular colobomata. In addition, disc pallor, arteriolar narrowing, and prominent diffuse coarse pigment clumping are noted

subtle mottled pattern to the retinal pigment epithelium but no obvious pigment clumping.

Colour vision testing with the Farnsworth-Munsell D-15 panel was irregular and non-reproducible. The light-adapted ERG showed no response. The dark-adapted ERG to the dim white stimulus showed half normal amplitude (approximately 75 mV). To a bright stimulus there was a single 'A' wave of half normal amplitude (approximately 75 mV) and a larger than normal 'B' wave (approximately 650 mV). The EOG light-peak/dark-trough ratio was 1.52 in the right eye and 1.59 in the left (normal greater than 1.85). The dark adaptation of each eye was symmetrical, did not have a rod-cone break, and had a normal final rod threshold.

no nyctalopia. The best corrected visual acuity was 20/200 in each eye with eccentric fixation. A jerk nystagmus was present on horizontal gaze. Slit-lamp biomicroscopy showed a faint posterior subcapsular cataract in each eye. There were bilateral macular centred colobomata similar to but larger than those of the daughter (Figs. 3, 4). There was waxy pallor of the optic nerves. The retinal arterioles were markedly narrowed. Diffuse coarse pigmentary clumping was present throughout the fundus.

The patient was unable to distinguish any colour on the Farnsworth-Munsell D-15 panel. There was no response to the light- or dark-adapted ERG. The EOG noted was 1.05 in the right eye and 1.0 in the left. The dark adaptation curve showed that the eccentric cone threshold was normal. The eccentric rod threshold was elevated 1 log unit.

Eleven other members of the pedigree were examined (Fig. 5) and were found to have normal

CASE 2

The 37-year-old mother of Case 1 related a life-long history of poor vision and marked photophobia but

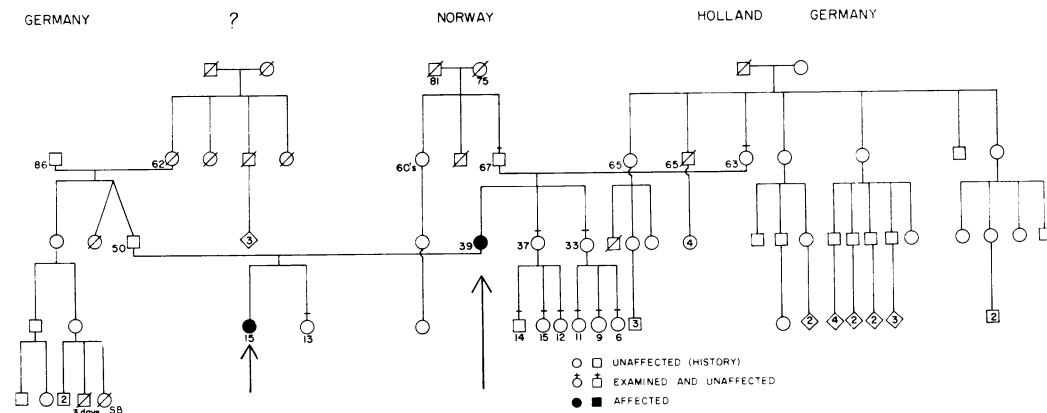


Fig. 5 Family tree of patients with bilateral macular colobomata

visual acuity and maculae. The family was of German, Dutch, and Norwegian descent.

Discussion

Sorsby (1935) has reviewed the literature up to 1935 on congenital coloboma of the macula (20 cases of bilateral macular coloboma, 36 unilateral, and 3 to 5 familial cases). The paucity of reports since then may reflect the awareness of congenital toxoplasmosis, cytomegalic inclusion disease, and other colobomata-simulating entities.

Central areolar choroidal sclerosis (Krill and Archer, 1971), cone degenerations (Krill *et al.*, 1971), and dominant foveal dystrophy (Frank *et al.*, 1974) may have round or oval (macula-centred) sharply punched-out lesions with various degrees of visible choroid and sclera resembling a coloboma. However, central areolar choroidal sclerosis (Krill and Archer, 1971) is an autosomal dominant or recessive disorder with onset between 20 to 40 years. This 'regional' choroidal atrophy demonstrates atrophy of the choriocapillaris and pigment epithelium, with preservation of the larger choroidal vessels. There is no selective rod or cone abnormality, but the preserved electrophysiological response is decreased more than expected from the ophthalmoscopic examination. An occasional member in a pedigree with central areolar choroidal dystrophy will have diffuse choroidal atrophy.

In the cone degenerations (Krill *et al.*, 1971) loss of visual acuity and photophobia are the chief complaints. The age at which severe visual loss is noted is frequently within the first 2 decades. Three types of macular lesion noted in descending frequency are: (1) 'bull's-eye', (2) diffuse pigment clumping, and (3) choroidal vascular atrophy. Krill *et al.* (1971) noted the latter appearance—i.e., loss of the choriocapillaris and some of the larger choroidal vessels—in only 2 patients. There was no apparent excavation. In their review of cone dysfunction syndromes Goodman *et al.* (1963) reported 1 patient with macular coloboma. Severe early loss of colour vision and abnormalities of the portion of the electroretinogram related to cone function are characteristically present.

Lastly, dominant progressive foveal dystrophy (Frank *et al.*, 1974), occurring in a North Carolina family of Irish descent, is characterised by drusen and pigmentary changes in the macula. The ERG, EOG, dark adaptation, and colour vision are normal. The lesions reach their final stage by puberty and in the advanced stage are characterised by total atrophy in the macular area, with visualisation of the underlying sclera.

The association between macular colobomata,

familial and non-familial, and tapeto-retinal degeneration, has been noted. Phillips and Griffiths (1969) described a brother and sister with bilateral macular colobomata, 'ring' lesions resembling primary pigmentary degeneration of the retina, and skeletal abnormalities. Freedman and Gombos (1971) reported a case of bilateral macular coloboma, keratoconus, and 'retinitis pigmentosa'. Leighton and Harris (1973) describe retinal aplasia (Leber's congenital amaurosis) in association with macular coloboma, keratoconus, and cataract. Electrophysiological testing was not recorded in the above 3 reports. Margolis *et al.* (1977) found no recordable response of the electroretinogram of two siblings with macular colobomata and Leber's congenital amaurosis.

The present 2 patients, of Dutch, German, and Norwegian descent, according to their medical histories had been affected 'all their life'. The chief complaints were poor visual acuity and marked photophobia. Each had bilateral, macular-centred, discrete, oval colobomata and retinal pigment epithelial abnormalities. Both had severe loss of colour vision. The daughter had marked abnormalities of the photopic component of the dark adaptation curve and of the electroretinogram. The mother's electrophysiological responses to light were unrecordable.

This and previous reports (Leonardi, 1909; Feilchenfeld, 1911; Clausen, 1921, 1928; Schott, 1921; Waardenburg, 1923, 1938; Car, 1925; Clarke, 1927; Davenport, 1927; Sorsby, 1935; Evans, 1937; Waardenburg *et al.*, 1961; Phillips and Griffiths, 1969; Margolis *et al.*, 1977) support the concept that the familial occurrence of bilateral macular colobomata is a genetically determined condition unrelated to infection.

We thank the Genetics Department at the University of Wisconsin, Madison, for assistance in constructing the family tree and Robert Jones for the psycho-electrophysiological testing.

This study was supported in part by Public Health Service Research Grant EY 00039 from the National Eye Institute.

References

- Car, A. (1925). Mikrozephalie und beiderseitiges Kolobom im Bereiche der Makula. *Zeitschrift für Augenheilkunde*, **57**, 618–627.
- Clarke, E. (1927). Coloboma at the macula (both eyes). *British Journal of Ophthalmology*, **11**, 97–99.
- Clausen, W. (1921). Typisches, beiderseitiges hereditäres Makula-Kolobom. *Klinische Monatsblätter für Augenheilkunde*, **67**, 116.
- Clausen, W. (1928). Zur Frage der Vererbung der Makula-

- kolobome. *Klinische Monatsblätter für Augenheilkunde*, **81**, 385.
- Davenport, R. C. (1927). Bilateral 'macular coloboma' in mother and son. *Proceedings of the Royal Society of Medicine*, **21**, 109-110.
- Evans, P. J. (1937). Familial macular colobomata. *British Journal of Ophthalmology*, **21**, 503-506.
- Feilchenfeld, H. (1911). *Zentralblatt für praktische Augenheilkunde*, **35**, 68.
- Frank, R., Landers, M. B. (III), Williams, R. J., and Sidbury, J. B. (1974). A new dominant progressive foveal dystrophy. *American Journal of Ophthalmology*, **78**, 903-916.
- Freedman, J., and Gombos, G. M. (1971). Bilateral macular coloboma, keratoconus, and retinitis pigmentosa. *Annals of Ophthalmology*, **3**, 664-668.
- Goodman, G., Ripps, H., and Siegel, I. M. (1963). Cone dysfunction syndromes. *Archives of Ophthalmology*, **70**, 214-231.
- Krill, A. E., and Archer, D. (1971). Classification of the choroidal atrophies. *American Journal of Ophthalmology*, **72**, 562-585.
- Krill, A. E., Deutman, A. F., and Fishman, M. (1971). The cone degenerations. *Documenta Ophthalmologica*, **72**, 562-585.
- Leighton, D. A., and Harris, R. (1973). Retinal aplasia in association with macular coloboma, keratoconus and cataract. *Clinical Genetics*, **4**, 270-274.
- Leonardi, E. (1909). Coloboma maculare in quatro fratelli. *Zentralblatt für die gesamte Ophthalmologie und ihre Grenzgebiete*, **22**, 649.
- Margolis, S., Schere, B. M., and Carr, R. E. (1977). Macular colobomas in Leber's congenital amaurosis. *American Journal of Ophthalmology*, **83**, 27-31.
- Phillips, C. I., and Griffiths, D. L. (1969). Macular coloboma and skeletal abnormality. *British Journal of Ophthalmology*, **53**, 346-349.
- Schott, K. (1921). Über das sogenannte Kolobom der Makula. *Klinische Monatsblätter für Augenheilkunde*, **67**, 415-424.
- Sorsby, A. (1935). Congenital coloboma of the macula: together with an account of the familial occurrence of bilateral macular coloboma in association with apical dystrophy of hands and feet. *British Journal of Ophthalmology*, **19**, 65-90.
- Waardenburg, P. J. (1938). Einige Beobachtungen bei erblichen Augenabweichungen. *Klinische Monatsblätter für Augenheilkunde*, **101**, 924-925.
- Waardenburg, P. J. (1923). Beiderseitige Makulaveränderungen bei drei Geschwistern. *Zeitschrift für Augenheilkunde*, **64**, 388.
- Waardenburg, P. J., Franceschetti, A., and Klein, D. (1961). *Genetics and Ophthalmology*, **1**, p. 788. Blackwell: Oxford.