Unusual chorioretinal degeneration in sickle cell disease

Possible sequelae of posterior ciliary vessel occlusion

P. I. CONDON, G. R. SERJEANT, AND H. IKEDA

From the Royal Eye Medical Ophthalmology Unit, Lambeth Hospital, London, and the Department of Medicine, University Hospital of the West Indies, Kingston, Jamaica

In the course of recent ophthalmological surveys of sickle cell disease, three cases of an unusual chorioretinopathy were seen. The patients all had reduced visual acuity and visual field loss which was associated with an unusual chorioretinal atrophic condition in two cases and a posterior polar retinal oedema in the third.

Clinical material and methods

Cases 1 and 2 were discovered during surveys of ocular pathology in sickle cell disease among patients attending the sickle cell clinic of the University Hospital of the West Indies. The group examined included 76 patients with homozygous sickle cell disease (SS), seventy with sickle cell haemoglobin C disease (SC), and fifty with sickle cell β -thalassaemia (S/Thal). The unusual chorioretinopathy here described affected one SC and one S/Thal patient.

Case 3 was observed in the retinal clinic of the Royal Eye Hospital, London, and had SC.

The methods of diagnosis have been described by Serjeant and Serjeant (1972). The case of S/Thal was of the Hb A containing type with 26.8 per cent. Hb A. Routine haematological methods were used. Clinical and haematological details are summarized in the Table.

Table *Clinical and haematological findings in three cases*

Case no.	Age (yrs)	Sex	Diagnosis	Hb (g. per cent.)	Serology	Comment
1	48	F	SC	12.5	WR + ve FTA + ve RPCFT + ve	Chronic chorioretinopathy
2	59	F	S-THAL	10.6	WR — ve	Chronic chorioretinopathy
3	22	F	SC	12.9	WR — ve FTA — ve RPCFT — ve	Acute chorioretinopathy

WR = Wassermann reaction

FTA = Fluorescent treponemal antibody test

RPCFT = Reiter protein complement-fixation test

+ ve = Positive

— ve = Negative

The methods of ophthalmological examination have been described by Condon and Serjeant (1972).

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Address for reprints: Patrick I. Condon, M.Ch., F.R.C.S., Research Dept. Ophthalmology, Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2

Case reports

Case 1, a 48-year-old Jamaican female, with SC disease had noticed sudden clouding of vision in the right eye, 9 years previously, within hours of completing a pressurized plane flight. The blurred sight cleared but recurred some weeks later when vision was reduced to bare perception of light. Since then, there have been no further attacks and there has been some visual improvement.

Examination

The visual acuity in the right eye was 2/60. Recording of the peripheral visual field with 20, 10 and 3 mm. white targets indicated a general constriction of all isopters, and a small absolute central scotoma with extensive surrounding annular loss was demonstrated with the Friedmann Analyser (Fig. 1).

FIG. 1 Static perimetry of central visual field in right eye of Case 1. I.S. signifies initial stimulus (log units intensity) for age of 48 years. Black dots indicate areas of absolute scotoma. Other figures refer to threshold strength of stimulus required in areas with relative scotoma. Shaded area represents blind spot.

The anterior segment was normal with no evidence of inflammatory disease. Chorioretinal degeneration affecting the inferior half of the fundus from below the disc and macula to the periphery had extended superiorly in the equatorial regions to involve the supero-temporal and supero-nasal periphery. Normal retina extended superiorly from the macula to the periphery and corresponded to the preservation of most of the inferior visual field. The abnormal retina had a mottled appearance with pale yellow tracks (approximately the size of retinal vessels) interspersed with areas of brownish red apparently normal retina (Fig. 2). This appearance was less marked at the equator, and between the equator and periphery there was a disturbance of pigmentation, not unlike that seen in retinitis pigmentosa (Fig. 3). Pigmentary disturbance was also obvious in the supero-temporal and supero-nasal areas where normal and abnormal retina merged. A localized pigmentary disturbance without evidence of elevation, oedema, or haemorrhage was also present at the macula (Fig. 4). The optic disc was normal in colour and the retinal vessels appeared normal in all areas.

FIG. 2 Mottled appearance of affected fundus inferior to optic disc in right eye of Case 1, showing irregular pale yellow tracks and interspersed areas of brownish red normal retina.

FIG. 3 Peripheral linear pigmentary disturbance in temporal fundus of right eye of Case 1. An occluded retinal arteriole to an area of retinitis proliferans crosses the photograph.

FIG. 4 Localised macular pigmentary disturbance, normal optic disc, and ring posterior vitreous detachment in right eye of Case 1.

FIG. 5(a) Pale tracks deep to inferior temporal retinal vessels in right eye of Case 1.

FIG. 8(a) Sectoral pigmentary chorioretinal degeneration inferior to optic disc and macula in right eye of Case 1.

FIG. 10(a) Indistinct pale areas at posterior pole of right eye in Case 3.

except for a small patch of white fibrous retinitis proliferans in the supero-temporal periphery, the feeder vessels to which had become white and occluded. The left eye was normal except for a small area of retinitis proliferans.

In the right eye fluorescein angiography revealed no abnormality of the optic disc, macula, or retinal circulation except in the occluded area of retinitis proliferans in which there was no retinal or choroidal fluorescence. The pale tracks seen in the degenerate retina (Fig. 5a) began to fluoresce in the preretinal phase, became more marked in the early venous phase (Fig. 5b), and persisted into the late venous phase when they became lost against the general choroidal fluorescence. These features suggested that the tracks in the abnormal retina may have represented exposed choroidal vessels. Areas of brownish-red retina showed no abnormality with fluorescein.

FIG. 5(b) Fluorescein angiogram showing fluorescence of pale tracks deep to inferior temporal retinal vessels in right eye of Case 1

Dark adaptation could not be recorded in the right eye but was normal in the left eye. Electro-oculography showed abolition of the light-induced response of the right eye, with a recorded light fall instead of a light rise in this eye. The light-induced response was 244 per cent. in the normal left eye (Fig. 6).

The scotopic and photopic electroretinogram in the right eye was grossly subnormal (Fig. 7A;B). Normal scotopic function, as shown by an increase in the β -wave with dark adaptation, was con-

FIG. 6 Changes in corneo-fundal standing potential determined by electrooculogram with dark and light adaptation of the eye in Case 1

FIG. 7 Electroretinogram Case 1

A β -wave amplitude as a function of dark adaptation (Intensity of flash used was 2 log units below the maximum intensity)

B β -wave amplitude as a function of log intensity of stimulating flash

siderably reduced in the affected eye (Fig. 7A) and the β -wave intensity curve was also flat (Fig. 7B). A flicker electroretinogram with a high-intensity flickering light of 30 cycles per second revealed cone function to be grossly subnormal in the affected eye with wavelets of 0.08 mV compared with 0.75 mV in the left eye.

Case 2, a 59-year-old female Jamaican with S/Thal, complained of gradual deterioration of vision in both eyes for 2 years and had had a senile cataract extraction in the left eye 3 months previously. The vision in this aphakic eye was limited to appreciation of hand movements only. Permanent anterior segment changes secondary to extracapsular lens extraction and vitreous loss prevented retinal examination in that eye. The visual acuity was 6/9 in the right eye and there was a dense superior altitudinal field defect extending almost to central fixation. A retinal degeneration (Fig. 8a) involved the inferior half of the retina from below the macula and disc out to the periphery and extended to the supero-nasal region. The margin between the normal and abnormal retina was sharply defined and the abnormal retina had a greenish-grey appearance with irregular scattered pigmentation and a linear branching pattern suggestive of choroidal vessels. The optic disc was normal in colour. The retinal vessels were normal at the disc but the inferior retinal arterioles became attenuated and disappeared as they entered the abnormal retina.

Fluorescein angiography confirmed the narrowing of the retinal arterioles, and the venous drainage from the abnormal area into the inferior temporal and nasal veins was markedly reduced. The choroidal circulation appeared to be almost absent in parts of this degenerate area, and only the larger vessels filled in the early preretinal phase (Fig. 8b). The greyish-green areas between these choroidal vessels failed to show any filling with dye, but thickening of the retina in these areas may well have masked the choroidal circulation from view. The macula was completely normal.

FIG. 8(b) Fluorescein angiogram of sectoral degeneration inferior to optic disc and macula in right eye of Case 2 ($\uparrow$) indicates areas of defective filling of choriocapillaris

Case 3, a 22-year-old Antiguan female with SC disease, noticed sudden impairment of central vision in the right eye. She had had a prophylactic diathermy to a small area of peripheral proliferative retinopathy in this eye 6 months earlier. Visual acuity in the right eye, previously 6/6, became reduced to 2/60 within 2 weeks of this episode of visual deterioration.

Examination

The visual fields showed peripheral constriction more marked superiorly and a dense central scotoma (Fig. 9, opposite).

FIG. 9 Static perimetry of central visual field in right eye of Case 3. I.S. signifies initial stimulus (log units intensity) for age of 22 years. Black dots signify areas of absolute scotoma. Other figures refer to threshold strength of stimulus required in areas with relative scotoma. Shaded area represents blind spot

In the fundus there were two indistinct pale areas along the inferior temporal vessels, apparently lying deep to the retina and surrounded by a choroidal halo. Overlying retinal pigment epithelial detachments were present, and there was evidence of subretinal oedema which was extending towards the macula. In the subsequent 2 weeks the number of these areas increased, especially around the posterior pole (Fig. 10a). The increase in subretinal oedema produced horizontal retinal folds across the posterior pole obscuring the deeper focal lesions, and the fluid later gravitated to produce a shallow non-rhegmatogenous retinal detachment inferiorly. The area previously subjected to diathermy was not affected by this process. The optic disc was initially normal but later became hyperaemic but not swollen. There were no signs of inflammatory activity in the vitreous or anterior chamber.

Initial fluorescein angiography revealed many localized areas of fluorescence (Fig. 10b, overleaf) which appeared in the early choroidal phase and corresponded to the focal abnormal areas seen on ophthalmoscopy of the posterior pole. Dye did not leak from the retinal vessels, but there was some leakage at the optic disc and gross leakage from the abnormal areas at the posterior pole. The electro-oculogram showed a subnormal light rise of between 275 and 375 mV (137.5 per cent.), and there was a markedly reduced β -wave amplitude with scotopic and photopic electroretinograms.

Fluorescein angiography repeated after 3 weeks showed that the posterior polar lesions had disappeared but subretinal oedema persisted. A course of systemic dexamethasone (8 mg. daily) was begun at the 5th week and by the 8th week most of the subretinal oedema had resolved leaving visual acuity of 6/9. At this stage a residual oedematous band was visible at the posterior pole and the retina appeared mottled along the temporal vessels. Fluorescein angiography showed that in extensive areas of the fundus there was heightened choroidal fluorescence in a segmental distribution superior and inferior to the disc and macula (Fig. 11, overleaf), which suggested a choroidal circulatory disturbance rather than a residual pigment epithelial thinning in these areas.

The visual acuity in the left eye had been reduced to 6/60 after a surgical procedure for advanced proliferative retinopathy and rhegmatogenous detachment several months earlier.

Discussion

The loss of visual function in areas affected by chorioretinal degeneration and the evidence of gross retinal epithelial disturbances in Cases 1 and 2 suggested a retinitis pigmentosa-like syndrome. The distribution of pigmentation, the visible choroidal vessels, and the grey-green background appearance were features resembling retinitis pigmentosa. The mottled hyperfluorescence of the fundus in the arterial phase and the increased visibility of the large choroidal vessels in the early retinal phase which are due to defects in the choriocapillaris and pigment epithelium are features of retinitis pigmentosa seen on

fluorescein angiography (Krill, Archer, and Newell, 1970) and were also present in Cases 1 and 2 of this report.

Although unilateral retinitis pigmentosa may exist (Henkes, 1966), the normal electrodiagnostic tests in the left eye and the absence of narrowing of the major retinal arterioles in the affected eye of Case 1 were features against the diagnosis of retinitis pigmentosa generally. Sectoral retinitis pigmentosa usually involves both eyes equally, but gross asymmetrical involvement may be present initially before the second eye becomes ophthalmoscopically involved (Pirodda and Cenacchi, 1959). The abnormal light fall instead of the usual light rise in the electro-oculogram with a recordable electroretinogram was unusual for retinitis pigmentosa. The equal reduction of both rod and cone-mediated

FIG. 10(b) Fluorescein angiogram of posterior pole of right eye in Case 3, showing multiple focal areas of fluorescence with leakage

responses in the electroretinogram and the diminished cone-mediated responses with flicker electroretinography, which suggested general involvement of all receptor elements and pigment epithelium, were also atypical. There was no relevant family history or history of consanguinity in any of the cases.

The lesion in Case 1 could have been an inflammatory choroidal lesion associated with the positive serological tests, but the restriction of the changes to one eye and the absence of other signs of inflammatory disease in the eyes make this unlikely.

The attenuation of the major branch retinal arterioles in the affected retina of Case 2 raises the possibility that these changes resulted from abnormalities of retinal vessel supply. An occlusion of both inferior nasal and temporal arteries at the optic disc was seen in one SS patient, but the ischaemic retinal area did not resemble the chorioretinal atrophy

FIG. 11 Fluorescein angiogram of posterior pole of right eye in Case 3 taken 3 weeks after onset, showing areas of heightened choroidal fluorescence superior and inferior to macula

described above. The appearances of the abnormal retina in Case 2 were not characteristic of a retinal branch arterial occlusion, and it is presumed that the vessel attenuation was secondary to degenerative changes in the underlying retina.

The association of normal optic discs, relatively normal retinal vessels, and specifically abnormal electrical tests in the two cases with sequential chorioretinal atrophy, suggested that the retinal dysfunction could have been secondary to a vascular disturbance of the choroid. The rapid development of the deep focal lesions with overlying retinal pigment epithelial detachments in Case 3 may have represented the acute stage of a primary choroidal vascular disturbance. The subretinal oedema, the pattern of fluorescence, and the greatly reduced β -wave amplitude of the scotopic and photopic electroretinograms were compatible with these lesions having been small choroidal infarcts following occlusion of the short posterior ciliary vessels which supply the choroid and retina at the posterior pole. The rapid resolution of these infarcts may have been affected by the highly vascular choroid but would leave a permanently affected choroid (Fig. 11).

Choroidal infarcts have been produced in Rhesus monkeys by occluding the medial, lateral, or both main posterior ciliary arteries (Hayreh and Baines, 1972). The resolution of white areas of choroidal ischaemia was subsequently followed by a widespread pigmentary disturbance, with atrophy of the retinal pigment epithelium and choroid most marked in the choriocapillaris. There was some progression of these atrophic changes during 6 months' subsequent observation. The segmental distribution of the short posterior ciliary arterioles to the choroid has been noted by Hayreh (1970) and confirmed by fluorescein angiography (Archer, Krill, and Newell, 1970).

The evidence from functional, ophthalmoscopic, and fluorescein studies, the subnormal β -wave pattern of the electroretinogram, and the segmental pattern of retinal involvement are all compatible with occlusive disease of either the main posterior ciliary artery or the short posterior ciliary artery. An acute occlusion of these vessels may have caused the lesions in Case 3 and it remains to be seen whether there will be a progression to the chorioretinal atrophy seen in the other two cases.

Summary

The vascular occlusive process characteristic of sickle cell disease may affect the retinal circulation, and the resulting pathological changes, from peripheral vessel obstructions to a proliferative retinopathy, are well recognized. In the present report, three cases of sickle cell disease are described with an unusual chorioretinopathy. It is suggested that these changes may have resulted from the vascular occlusive process affecting the posterior ciliary vessels.

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