Ocular findings in children with sickle cell haemoglobin C disease in Jamaica

PATRICK I. CONDON, ROBERT GRAY, AND GRAHAM R. SERJEANT

From the Medical Research Council, Epidemiology Unit, University of the West Indies, Kingston, Jamaica

The development of severe retinal vascular disease and retinitis proliferans in sickle cell haemoglobin C disease (SC disease) is well recognized (Welch and Goldberg, 1966; Goldberg, 1971; Condon and Serjeant, 1972a). In a recent survey in Jamaica, Condon and Serjeant (1972a) noted retinitis proliferans in 23 (33 per cent.) of seventy adults with SC disease. The changes were found in some patients as early as 15 years of age. The present study was designed to observe the pattern of retinal vessel pathology in children with SC disease before this age.

Patients and methods

All children with SC disease between the ages of 2 and 15 years on the registers of the paediatric and adult sickle cell clinics at the University Hospital of the West Indies were asked to attend for ophthalmoscopic study in April and May, 1973. Children below the age of 2 years were excluded because of difficulties in cooperation. Of a total of 71 children older than 2 years, sixty (85 per cent.) attended for examination. Five patients aged 2, 2½, 3, 3½, and 6 years failed to cooperate, and it was impossible to examine one boy aged 11 years because of a jerky nystagmus. The age and sex distribution of the remaining 54 children is shown in Table I.

Table I *Age and sex distribution and severity of peripheral retinal vessel disease*

Age group (yrs)	Sex		Total cases	Severity of peripheral retinal vessel disease*				
	Male	Female		Normal	Mild	Moderate	Severe	RP
2-8	9	7	16	1	6	6	3	1
9-12	6	13	19	2	4	8	5	2
13-15	12	7	19	0	4	6	9	3
Total	27	27	54	3	14	20	17	6

* Condition of worse affected eye
N.B. All cases of RP are grouped under "Severe" vessel disease

Received for publication September 27, 1973
Address for reprints: Patrick I. Condon, M.Ch., F.R.C.S. South-East Area Health Board Regional Eye Department, Ardkeen Hospital, Waterford, Ireland

This study was supported by the Wellcome Trust, The South-East Metropolitan Regional Hospital Board, and the Medical Research Council

The diagnosis of SC disease was based on positive metabisulphite sickling tests, on the presence of two bands in the positions of Hb S and Hb C on starch gel electrophoresis at pH 8.6, and on typical red cell morphology.

The fundus was examined by direct and indirect ophthalmoscopy, and with the use of a slit lamp and 3-mirror contact lens where indicated. If there were visible abnormalities in the peripheral retina, the extent of peripheral retinal vessel disease was assessed by retinal and fluorescein (5 per cent.) photography. Where fluorescein photography could not be carried out because of lack of cooperation the peripheral retinal vessels were observed through an indirect ophthalmoscope fitted with appropriate filters (Keith, 1968). Peripheral retinal vessel disease was classified as previously described (Condon and Serjeant, 1972a).

Eleven children examined 2 years previously and included in an earlier report (Condon and Serjeant, 1972a) were re-examined in the present study.

Results

There were no ocular symptoms, but the fundus was abnormal in all cases except two boys aged 7 and 10 years. The pathological findings are summarized in Table II.

Table II Prevalence of ocular lesions in 54 children with SC disease

Ocular lesions		No. of patients	No. of eyes	Per cent. patients involved
Retinal	Whitening of the peripheral retina	47	91	87
	Peripheral retinal vessel disease	51	102	94
	Retinitis proliferans	6	8	11
	Retinoschisis	1	1	2
	Pigmented chorio-retinal lesions	4	6	7
	Brown pigmented areas	12	14	22
	Iridescent glistening spots	9	11	17
Central retinal capillary	Microaneurysmal formation on optic disc	4	5	7
Arterio-venous anomalies	Tortuosity of major vessels	17	34	32
	Peripheral AV anomalies	10	16	19
	True AV fistulae	9	15	16

WHITENING OF THE PERIPHERAL RETINA

This was seen in 47 (87 per cent.). This sign, which has been described in detail elsewhere (Condon and Serjeant, 1972b), is thought to reflect peripheral retinal hypoxia rather than complete ischaemia. It is more commonly associated with mild peripheral retinal vessel disease than with severe forms. In 192 quadrants (85 eyes) with mild and moderate retinal vessel changes, peripheral retinal whitening occurred in 180 (94 per cent.) compared with a frequency of 42 per cent. in 43 quadrants involved with severe retinal vessel disease.

PERIPHERAL RETINAL VESSEL DISEASE

Changes in the peripheral retinal vessels were common (94 per cent. of patients) even in these young children, and only three patients aged 7, 10, and 12 years showed no evidence of vessel disease. Mild changes, consisting of arteriolar narrowing and tortuosity and abnormal

looping of peripheral venules, were present in 28 eyes (14 patients). Moderate changes, with dilatation, tortuosity, and coarsening of the peripheral capillary network with microaneurysmal formation, occurred in 32 eyes (20 patients). Severe changes with arteriolar occlusions were noted in 25 eyes (17 patients) and occurred as early as 6 years of age. The prevalence of peripheral retinal vessel disease in different age groups is shown in Table I. Vascular involvement became progressively more severe with advancing age.

RETINITIS PROLIFERANS

Retinitis proliferans (RP) occurred in six (11 per cent.) patients. It was possible to distinguish three types of lesions which may represent stages in development. The most minor change appeared as small localized clusters of abnormal new vessels (Figs 1*a* and *b*). More

FIG. 1 (*a*) *New vessels at site of arterio-venous fistula in temporal periphery of right eye in a 15-year-old male patient with SC disease. Ischaemic retina on left, normally perfused retina on right*
(*b*) & (*c*) *Fluorescein angiograms of same area indicating leakage of dye*

marked lesions were associated with condensation and whitening of the vitreous overlying the area of RP (Figs 2*a* and *b*). Both types of lesion remained flat on the retinal surface and were not associated with retinal traction. In the fully-developed lesion, contraction of the overlying vitreous and the mass of proliferative new vessels resulted in localized

FIG. 2 (*a*) *Retinitis proliferans in temporal periphery of right eye in a 15-year-old female patient with SC disease*
(*b*) *Fluorescein angiogram of same area with leakage of dye*

schisis or retinal detachment with subsequent retinal degeneration and tear formation (Figs 3a and b). The classical features of retinitis proliferans were common to all these lesions. They appeared to arise from abnormal arterio-venous connections at the junction of healthy and ischaemic retina, were perfused by at least one and often several feeding arterioles and were drained by at least one vein, and leaked intravenously-administered fluorescein into the vitreous.

FIG. 3 (a) *Retinitis proliferans and a localised traction retinoschisis with degenerative changes in the left eye of a 15-year-old male patient with SC disease*
(b) *Fluorescein angiogram of same area indicating slight leakage of dye*

OTHER CHORIO-RETINAL FINDINGS

Peripheral pigmented chorio-retinal lesions designated the 'black sunburst sign' by Welch and Goldberg (1966) were present in four patients (7 per cent.), three of whom were 15 years old and had severe retinal vessel disease. Peripheral mottled brown areas were seen in twelve patients (22 per cent.), eleven of whom were over 10 years. These areas develop at the site of previous retinal haemorrhage, and in one case in the present group, a vitreous opacity lay anterior to a mottled area, suggesting a previous retinal haemorrhage. Glistening spots occurred in nine patients (17 per cent.), and in five were associated with brown mottled areas. No recent retinal or vitreous haemorrhages were seen in the present group and there were no round red areas. Minute vessel abnormalities, resembling microaneurysms, were seen on the optic disc in four patients (7 per cent.).

ARTERIO-VENOUS ANOMALIES

Abnormal tortuosity of the major vessels at the disc and posterior pole was present in seventeen patients (32 per cent.); this affected the arteries alone in eleven, the veins alone in three, and both in three.

Peripheral arterio-venous anomalies in which the arteriole and vein lay in close proximity but without direct connection were seen in ten patients. True arterio-venous fistulae occurred in nine patients (17 per cent.) and were seen either as multiple direct arterio-venous (AV) communications developing at the interface of ischaemic and healthy retina, or as fistulae emanating new vessels at the site of retinitis proliferans.

ANGIOID STREAKS

These were not observed in the present group.

Development of changes

In the eleven patients examined 2 years previously it was possible to make some observations on the progression and speed of development of retinal vessel disease. Three patients showed no change over this period, but in the remaining eight there was an increase both in the extent and severity of involvement. Arteriolar occlusions had developed in three patients, and one case with previous occlusions had developed true AV fistulae and RP. In a 13-year-old girl the number of RP lesions had increased from two to five, and in a 15-year-old boy a previous RP lesion had developed vitreo-retinal traction with retinoschisis and localized tears (Figs 3a and b).

Discussion

In this study severe retinal vessel pathology was strikingly frequent in children with SC disease. Peripheral arteriolar occlusions were noted as early as 6 years of age and retinitis proliferans at 7 years. Clearly the process of small vessel obstruction is well established at this age despite a relative lack of other significant clinical features. The cross-sectional evidence presented in Table I suggests that the degree of peripheral retinal vessel disease increases with age even within these young age groups. This suggestion is supported by our limited longitudinal studies in which eight out of eleven cases previously examined 2 years ago had shown unequivocal progression of retinal vessel disease.

The severity of retinal vessel disease in young children and its apparent rapid rate of progression suggested from this study is at variance with our findings in adults with SC disease. Significant retinal pathology is undoubtedly common among adults with SC disease but has not reached the degree or frequency that might be expected by extrapolations from the observations in childhood. A possible explanation is that the progression of retinal vessel disease is intermittent or may alternate with periods of spontaneous regression. In adults, areas of retinitis proliferans may become spontaneously occluded and infarcted, thus restoring the retinal vasculature to a more normal pattern. However, it is most unlikely that the avascular nature of the peripheral retina is reversible. An alternative possibility is that the progression of retinal vessel disease is truly more rapid in childhood but progresses at a slower rate once the periphery has been rendered generally ischaemic.

In adults with SC disease, the more severe grades of retinal vessel disease were associated with high haemoglobin levels and it was suggested that the higher viscosity in such cases may have been aetiologically related to the development of arteriolar occlusions and retinitis proliferans (Condon and Serjeant, 1972a). This relationship also appears to apply in childhood. Retinitis proliferans was not present in eleven patients with haemoglobin levels below 10.5 g. but occurred in one out of 29 (3 per cent.) of patients with levels between 10.6 and 11.9 g., and in five out of twelve (42 per cent.) of those with levels above 12 g. If further studies confirm the role of high haemoglobin levels and the resultant increased viscosity in the genesis of thrombotic lesions in SC disease, it may be considered desirable to maintain lower haemoglobin levels by venesection or the induction of a controlled iron-deficient state. The above findings indicate that any attempts to control the onset and progression of retinal vessel damage in SC disease must be applied in early childhood.

Summary

The ophthalmological findings in 54 Jamaican children with SC disease are reported. Evidence of peripheral retinal vessel disease was present in 94 per cent. and retinitis proliferans in 11 per cent. Retinitis proliferans was noted as early as 7 years of age and was more common in patients with high haemoglobin levels. There was an unequivocal progression in severity of retinopathy in eight out of eleven children examined 2 years previously. The pathological processes leading to sickle cell proliferative retinopathy are well established in childhood and attempts at prophylactic therapy should be instituted at an early age.

We wish to thank Miss Philpotts, Chief Photographer, Photographic Department, St. James' Hospital, Balham, SW.12., for assistance with the illustrations.

References

- CONDON, P. I., and SERJEANT, G. R. (1972a) *Amer. J. Ophthalm.*, **74**, 921
——— (1972b) *Ibid.*, **73**, 533
GOLDBERG, M. F. (1971) *Arch. Ophthalm. (Chicago)*, **85**, 428
KEITH, C. G. (1968) *Brit. J. Ophthalm.*, **52**, 862
WELCH, R. B., and GOLDBERG, M. F. (1966) *Arch. Ophthalm. (Chicago)*, **75**, 353