

## Ocular findings in elderly cases of homozygous sickle-cell disease in Jamaica

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Sickle-cell disease is characterized by recurrent vascular occlusive episodes and a progressive obliteration of capillary beds. This process can be directly observed in the eye and its occurrence in the peripheral retina has been well documented (Welch and Goldberg, 1966; Goldberg, 1971; Condon and Serjeant, 1972a, b, c). The effects of such thrombotic episodes might be expected to accumulate with age and to be most marked in elderly patients. The results of ocular examinations in 60 patients aged over 40 years with homozygous sickle-cell (SS) disease in Jamaica are presented below.

### Patients and methods

The patients attended the sickle-cell clinic of the University Hospital of the West Indies. Ocular examination of 56 out of 66 patients aged over 40 years (born before 1 January 1935) attending the clinic was possible. In addition, the cases of four patients (cases 2, 31, 47, 54) aged over 40 years at the time of previous examinations, but who had since died, were studied. The overall group therefore consisted of 60 patients (27 men, 33 women) whose ages ranged from 40–66 years.

Homozygous sickle-cell disease was diagnosed on criteria reported elsewhere (Serjeant, 1974). Methods of ocular examination have been previously described (Condon and Serjeant, 1972a). Retinitis proliferans and angioid streaks were confirmed in each case by fluorescein angiography.

### Results

The findings are summarized in Table I. Visual acuity was decreased in 40 eyes (25 patients) and was 6/60 or less in eight eyes (eight patients). The causes included astigmatic refractive errors in four patients, trauma in three, retinal detachment in two, macular degeneration of unknown origin in seven, a toxoplasma lesion, long-standing optic atrophy, cataracts, and vitreous haemorrhage in

one each, and was unknown in five patients. Traumatic causes were more common in younger patients and macular degeneration more common in the older group.

Tortuosity of the major retinal vessels was present in 18 (30 per cent) patients affecting the veins alone in 13 and the arteries and veins in five. Peripheral retinal vessel disease was classified as previously described (Condon and Serjeant, 1972a) into three grades. Grade I consisted of narrowing of peripheral arterioles with tortuosity and abnormal looping of peripheral venules. Grade II included tortuosity, dilatation, and microaneurysmal formation in the peripheral capillary network; coarsening of the network with loss of some fine vessels; and abnormal branching of peripheral venules. Grade III changes were arteriolar occlusions. The grade of vessel disease was usually identical in both eyes (37 patients), although differences between eyes of one grade (12 patients) or even two grades (six patients) did occur. Grade I changes were present in 40 eyes, grade II in 21, and grade III in 40. The peripheral retinal vessels appeared normal in 15 eyes. Arterio-venous fistulae occurred in four eyes (four patients) and was associated with grade III vessel disease in all cases. Retinitis proliferans occurred in 12 eyes (eight patients), the lesions being often multiple and affecting large areas of the peripheral retina. In four of the eight patients the lesions had fibrosed, presumably after spontaneous vessel occlusion.

In order to assess the effect of age on peripheral retinal vessel disease and retinitis proliferans the group was divided into those aged 45 years or under (29 patients) and those aged 46 years or over (31 patients). The results are summarized in Table II, which shows that mild grades of vessel disease (I and II) were more common in the younger groups and that the more severe grade III and retinitis proliferans predominated in the older group. Women also seemed to have more normal retinal vasculature and accounted for 5/7 (71 per cent) patients with normal vessels and 12/14 (86 per cent) of those with grade I vessel disease.

Chorioretinal scars known as 'sunburst' spots

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**Table I** Ocular findings in 60 patients aged 40 or over with homozygous sickle-cell disease. Arabic figures refer to number of lesions in eye. See text for criteria for grading retinal vessel disease

Case no.	Age and sex	Visual acuity		Tortuous major retinal vessels (A=arterial, V=venous)	Grade of retinal vessel disease		Arterio-venous fistulae		Retinitis proliferans		Chorio-retinal sunburst lesions		Micro-aneurysms of posterior pole		Angioid streaks		Comments
		R	L		R	L	R	L	R	L	R	L	R	L	R	L	
1	40 M	6/6	6/6	—	II	II	—	—	—	—	2	—	—	—	—	—	
2	40 M	6/6	6/60	—	II	II	—	—	—	—	—	—	—	—	—	—	(L) long-standing optic atrophy
3	40 F	6/6	6/6	V	I	I	—	—	—	—	—	—	—	—	—	—	
4	41 M	6/6	6/6	—	III	I	—	—	—	—	—	—	—	—	—	—	
5	41 M	6/6	6/6	AV	II	II	—	—	—	—	—	—	—	—	—	—	
6	41 M	6/6	1/60	V	III	—*	—	—*	—	—*	—	—*	—	—	—	—	Traumatic maculopathy
7	41 M	6/6	6/6	—	—	—	—	—	—	—	—	—	—	—	—	—	
8	41 F	6/6	6/6	—	III	III	—	—	—	—	—	—	—	—	—	—	
9	42 M	HM	6/6	V	—*	III	—*	—*	—*	—*	—	—	—	—	—	—	Traumatic lesion (R) eye
10	42 M	6/6	6/6	V	I	I	—	—	—	—	—	—	—	—	—	—	
11	42 M	6/6	6/6	V	III	II	I	—	—	—	—	—	—	—	—	+	
12	42 F	6/6	6/6	—	I	III	—	—	—	—	3	I	—	—	—	—	Myopic astigmatism
13	42 F	6/9	6/12	—	I	I	—	—	—	—	—	—	—	—	—	—	
14	42 F	6/6	6/6	—	I	III	—	—	—	—	—	—	—	—	—	—	
15	42 F	6/6	6/6	—	II	I	—	—	—	—	—	—	—	—	+	—	
16	43 M	6/6	6/6	—	—	II	—	—	—	—	I	I	—	—	—	—	
17	43 M	6/6	6/6	—	III	III	—	—	—	—	I	—	—	—	+	+	
18	43 M	6/18	6/24	—	II	III	—	—	—	—	—	I	—	+	+	+	
19	43 M	6/36	6/6	—	—	—	—	—	—	—	—	—	—	+	+	+	Healed toxoplasma lesion (R) macula
20	43 M	6/6	6/6	—	II	II	—	—	—	—	I	—	—	+	+	+	
21	43 F	6/6	6/6	V	I	I	—	—	—	—	—	—	—	+	+	+	
22	44 F	6/6	6/6	—	I	I	—	—	—	—	—	—	—	—	—	—	
23	44 F	6/6	6/6	V	I	I	—	—	—	—	—	—	—	—	—	—	
24	44 F	6/6	CF	—	I	I	—	—	—	—	—	—	—	—	—	—	Traumatic lesion (L) eye
25	44 F	6/6	6/6	V	III	III	—	I	2	I	—	I	—	—	—	—	
26	44 F	6/6	6/6	—	—	—	—	—	—	—	—	—	—	—	—	—	
27	45 F	6/6	6/6	—	III	II	—	—	—	—	—	—	—	—	—	—	
28	45 M	6/6	6/6	—	I	I	—	—	—	—	—	—	—	—	+	+	+
29	45 F	6/6	6/9	V	I	I	—	—	—	—	—	—	—	—	—	—	Macular degeneration
30	46 M	6/12	6/12	—	III	III	—	—	—	—	I	—	—	+	+	+	
31	46 M	6/6	6/6	—	II	I	—	—	—	—	—	—	—	—	—	—	
32	46 F	6/12	6/6	—	II	I	—	—	—	—	I	I	—	—	—	—	Macular degeneration
33	46 F	6/6	6/6	—	I	I	—	—	—	—	—	—	—	—	—	—	
34	47 M	6/12	6/12	V	II	I	—	—	—	—	I	—	—	+	—	—	Macular degeneration
35	47 F	6/6	6/6	—	II	III	—	—	—	—	—	—	—	—	+	+	
36	48 M	6/12	6/9	—	III	I	—	—	—	—	I	I	—	—	—	—	
37	48 F	6/9	6/9	—	I	I	—	—	—	—	—	—	—	—	—	—	
38	49 M	6/6	6/6	—	III	III	—	—	9	3	I	—	—	—	—	—	
39	49 M	6/6	6/6	—	III	III	2	—	2	I	I	—	—	—	+	+	
40	49 M	6/6	6/6	—	I	III	—	—	—	—	—	—	—	—	—	—	
41	49 F	6/6	6/6	—	I	I	—	—	—	—	—	—	—	—	—	—	
42	49 F	6/6	6/6	AV	—	—	—	—	—	—	—	—	—	—	—	—	
43	49 F	6/18	6/18	—	I	I	—	—	—	—	—	—	—	—	—	—	Macular degeneration
44	50 M	Nil	6/12	—	—*	III	—*	I	—*	3	—*	I	—*	+	—*	—	?Retinal detachment (R)
45	53 M	6/6	6/6	V	II	I	—	—	—	—	—	—	—	—	+	+	
46	53 F	6/9	6/9	—	II	III	—	—	—	—	2	—	—	—	—	—	
47	53 F	6/18	6/12	—	II	III	—	—	—	I	—	—	—	—	—	—	Macular degeneration
48	55 F	6/12	6/12	V	II	I	—	—	—	—	—	—	—	—	—	—	Myopic astigmatism
49	55 F	6/6	6/6	—	I	I	—	—	—	—	—	—	—	—	+	+	
50	56 F	6/6	6/24	AV	III	III	—	—	2	3	—	—	—	—	—	—	(L) perimacular fibrosis from vitreous haemorrhage
51	57 F	6/6	6/6	—	III	III	—	—	—	—	I	—	—	—	—	—	
52	58 F	6/24	6/6	—	III	III	—	—	—	—	—	—	—	—	+	+	Amblyopia
53	59 F	6/6	Nil	—	III	—*	—	—*	6	—*	—	—*	—	—	—	—	Retinal detachment (L)
54	59 F	6/36	2/60	—	I	III	—	—	—	—	—	—	—	—	—	—	Senile macular degeneration and cataracts
55	59 F	6/12	6/24	AV	III	III	—	—	—	4	—	—	—	—	+	+	(L) vitreous haemorrhage
56	60 M	6/6	6/6	—	III	III	—	—	—	—	—	—	—	—	+	+	
57	60 F	6/36	6/24	AV	—	—	—	—	—	—	—	—	—	—	+	+	Macular degeneration
58	60 F	6/6	6/6	—	—	—	—	—	—	—	—	—	—	—	—	—	
59	61 F	6/36	6/60	—	—	—	—	—	—	—	—	—	—	—	—	—	Senile cataracts
60	66 M	6/6	6/6	V	III	III	—	—	—	—	—	—	—	+	—	—	

\*Inapplicable: peripheral retina could not be seen

Severity of lesion: +, ++, +++

**Table II** Age distribution of peripheral retinal vessel disease and retinitis proliferans

Age (years)	No.	Eyes observed*	Eyes affected									
			Normal vessels		Grade of vessel disease						RP	
			No.	Percentage	I No.	I Percentage	II No.	II Percentage	III No.	III Percentage	No.	Percentage
40-45	29	56	7	12	22	38	13	22	14	24	1	2
46-60	31	60	8	13	18	29	8	13	26	42	7	11

\*Excludes four eyes in which assessment of the peripheral retina was impossible

occurred in 20 eyes (16 patients). Microaneurysms at the posterior pole were seen in 12 eyes (nine patients). Angioid streaks occurred in 25 eyes (13 patients). They were bilateral in 12 patients, in 11 of whom they were better developed on the right side. They occurred in 4/29 (14 per cent) patients aged 45 years and under compared to 9/33 (27 per cent) patients over this age. In one case (Case 20) angioid streaks developed over a four-year period of observation between ages 39-43. In another patient (Case 57) bilateral macular degeneration and reduced visual acuity occurred concurrently with early angioid streaks around the disc, but fluorescein angiography suggested that these lesions were probably unassociated. Clinical evidence of pseudoxanthoma elasticum was not present in any patient with angioid streaks.

## Discussion

Tortuosity of the major retinal veins has been reported in homozygous sickle-cell disease in between 10-96 per cent of cases (Klinefelter, 1942; Henry and Chapman, 1954; Smith and Conley, 1954; Hannon, 1956; Hook and Cooper, 1958; Lieb, Geeraets, and Guerry, 1959; Welch and Goldberg, 1966). Condon and Serjeant (1972a) noted this finding in 8/76 (11 per cent) patients with SS disease in an earlier report and in 18/60 (30 per cent) of the present series. The variable prevalence of this sign may reflect real differences in populations or may result from the subjective nature of tortuosity. Interpretation of this finding is further complicated by lack of valid control data. However, the available evidence suggests that tortuosity of the major retinal veins is associated with sickle-cell disease. Tortuosity of both arteries and veins may indicate an independently inherited genetically determined abnormality which can also coincide with sickle-cell disease (Condon and Serjeant, 1972a).

Although the severity of peripheral retinal vessel disease generally increased with age, some elderly patients still manifested normal vessels or very mild changes. Arterio-venous fistulae, which

are presumed to precede the development of retinitis proliferans, occurred mainly in the younger patients, whereas retinitis proliferans (RP) was almost confined to older patients of the series. The relatively high prevalence of RP in patients over the age of 50 (29 per cent) is of especial interest since this complication has been considered uncommon in other series of patients with SS disease (Henry and Chapman, 1954; Lieb and others, 1959; Welch and Goldberg, 1966). In an earlier series that included Jamaican patients of all ages Condon and Serjeant (1972a) found this complication in only 2/76 (3 per cent) patients, one aged 34 and the other aged 55 (case 53 in present report). Since RP seems to be age-related, some variation in prevalence may reflect different age structures of other series. It was of interest that in 4/8 patients areas of retinitis proliferans had become spontaneously occluded and the vessels no longer leaked fluorescein on angiography. Although spontaneous obliteration of new vessels constitutes a progression of vascular disease in pathological terms, such a process would tend to halt the progressive nature of peripheral retinal ischaemia and render less likely complications such as vitreous haemorrhage and retinal detachment.

The aetiology of pigmented chorioretinal lesions, or 'sunburst' spots, is unknown although they may result from retinal or choroidal infarcts. This concept was supported by the presence of these lesions in 11/40 (28 per cent) eyes with grade III vessel disease compared with 9/76 (12 per cent) with milder grades of vessel disease.

Tortuosity and dilatation of the capillary network with microaneurysmal formation at the posterior pole was noted by Lieb and others (1959) and reported in 30/76 (40 per cent) patients with SS disease in Jamaica (Condon and Serjeant, 1972a). This finding appears more characteristic of homozygous sickle cell disease than of other variants such as sickle-cell-haemoglobin C disease and sickle-cell- $\beta$  thalassaemia (Condon and Serjeant, 1972b, c), and it is tempting to postulate that they are a retinal equivalent to the abnormal dilatations often seen in the conjunctival capillary bed (Serjeant, Condon, and Serjeant, 1972).

Angioid streaks are a recognized feature of sickle-cell retinopathy, although case reports are limited to a few patients. Paton (1959) and Lieb and others (1959) each described two cases with SS disease. Geeraets and Guerry (1960) reported five cases, three with probable SS disease and two with SC disease. Suerig and Siefert (1964) described a single case with SS disease, and Condon and Serjeant (1972b) reported a single case with SC disease. In two of these reports pseudoxanthoma elasticum was also present, but in the other nine cases the angioid streaks were attributed to sickle-cell disease. In view of these sparse case reports the finding of angioid streaks in 13/60 (22 per cent) patients in the present series is of especial interest and compares with an incidence of 3/150 (2 per cent) in younger Jamaican patients (affected cases aged 25, 27, and 32 respectively). Angioid streaks increased in frequency with age in sickle-cell disease and they have developed in two patients aged 25 and 43 in the Jamaican group.

Angioid streaks are characterized histologically by defects in Bruch's membrane, and most cases have been associated with either pseudoxanthoma elasticum or osteitis deformans (Paget's disease). The aetiology of angioid streaks in SS disease is unknown. Paton (1959) suggested that vascular obstructions affected the chorio-capillary circulation, whereas Geeraets and Guerry (1960) thought the cause could be an avascular degeneration of elastic tissue consequent on involvement of the posterior ciliary vessels. In this context it is of interest that three patients with evidence of posterior ciliary vessel obstruction developed segmented chorioretinal atrophies, but failed to show any

evidence of angioid streaks (Condon, Serjeant, and Ikeda, 1973). The clinical course of angioid streaks in sickle-cell disease seems more benign than when associated with other conditions. No associated haemorrhages or exudates were seen in the present group, and in the one case with macular degeneration fluorescein angiography suggested that the two lesions may have been coincidental.

In summary, a distinctive pattern of ocular pathology emerges from the present elderly group. Severe grades of peripheral retinal vessel disease are common, and the incidence of retinitis proliferans and of angioid streaks is high, especially in those patients over 50 years of age. Some patients are exceptions to this general pattern and have only mild retinal vascular changes despite relatively advanced age. These exceptions could be of great interest and may represent variations of homozygous sickle-cell disease in which the tendency to vessel obstruction is much diminished.

### Summary

The ocular findings in 60 patients with homozygous sickle-cell disease over the age of 40 years have been described. Peripheral retinal vessel disease was common and appeared to increase with age. Retinitis proliferans was common among older patients in the group. Angioid streaks occurred in 13 (22 per cent) patients.

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