Retinal changes in sickle cell/hereditary persistence of fetal haemoglobin syndrome

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SUMMARY We describe for the first time retinal changes in sickle cell/hereditary persistence of fetal haemoglobin syndrome, which is a rare and benign disorder. The changes are qualitatively similar to retinal disease seen with sickle haemoglobin and sickle C haemoglobin, but are mild.

The syndrome resulting from the inheritance of both the sickle cell gene and the gene for hereditary persistence of fetal haemoglobin results in a syndrome called sickle cell/hereditary persistence of fetal haemoglobin (S/HPFH). It is a benign syndrome in which 25-35% of fetal haemoglobin (Hb F) is distributed evenly throughout the red cell population with a marked inhibitory effect on sickling. As a result, accelerated haemolysis is unusual and symptoms attributable to vaso-occlusion rare. The clinical pattern of the syndrome is not well documented since it is uncommon, and no extensive reviews are available.¹ There are no published reports on retinal findings in this condition, which is surprising, since the retinal vasculature would provide a sensitive indicator of whether vaso-occlusion occurs. Recently an opportunity has arisen to perform retinal examinations in 6 patients with S/HPFH and the results are presented.

Material and methods

The patients attended the sickle cell clinic at the University Hospital of the West Indies. Four patients aged 16-46 years were detected during family studies of relatives with sickle cell disease, and 2 patients (aged 8 years) were part of a cohort study of sickle cell disease followed up prospectively following diagnosis at birth. The diagnosis was based on major haemoglobin bands in the positions of HbS and HbF on haemoglobin electrophoresis under alkaline and acid conditions, low HbA₂ levels, HbF levels greater than 20% and manifesting a relatively even intracellular distribution, and family studies where possible. Techniques of retinal examination were as previously described.²

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Results

Some clinical and haematological details in the 6 patients are summarised in Table 1. Retinal closure was present on angiography in 3 patients, and in one (case 2) there were other signs of sickle retinopathy.

In this patient visual acuity was normal in both eyes. Ophthalmoscopy revealed no abnormalities in the right eye, but in the left eye there was an irregular area of retinal pigment epithelial disturbance (sunburst spot) in the superotemporal periphery with an overlying vitreous opacity. An arteriole crossing

Fig. 1 Fluorescein angiogram of a sunburst spot in an 8-year-old girl with sickle cell/hereditary persistence of fetal haemoglobin syndrome, showing a chorioretinal anastomosis.

Table 1 Some details of haematological findings and retinal closure

Case	Age/sex	HbF (%)	Hb A ₂ (%)	Hb (g/dl)	MCV (fl)	Reticulo-cytes (%)	ISCs (%)	Retinal closure	
								Right	Left
								(degrees included)	
1	8M	31.2	1.7	12.6	76	3	0	0	0
2	8F	30.0	1.6	13.6	71	2	0	60°	60°
3	16F	34.8	1.9	14.0	80	1	0	0	0
4	22F	25.7	2.1	11.6	79	3	0	0	0
5	24F	27.6	2.0	12.8	74	2	0	90°	60°
6	46M	30.4	2.1	16.2	82	1	0	Trauma	60°

this area appeared to terminate over it. Fluorescein angiography indicated this arteriole to be entering into a choroidoretinal anastomosis (Fig. 1). There were transmission defects at the site of the pigment epithelial disturbance, and capillary closure peripheral to the chorioretinal lesion. There was also capillary closure in the superotemporal quadrant of the right eye.

Discussion

Three of the 6 patients examined had evidence of peripheral retinal vessel closure, typical of sickle cell disease, and one had a sunburst spot, presumed to result from deep retinal haemorrhage,³ through which an apparently spontaneous choroidoretinal anastomosis had developed. Although such anastomoses are common following photocoagulation therapy, especially with the xenon arc,⁴ spontaneous anastomoses are unusual and have only been described in one case of sickle cell disease.⁵

These findings suggest that, although the S/HPFH syndrome appears to run a very mild course, significant retinal vaso-occlusion may occur in this condition. This is compatible with other case reports which have detailed a variety of sickle cell related symptoms, including a mild haemolytic anaemia,^{6,7} splenomegaly,⁶ joint pains,⁸ avascular necrosis of the hip,^{8,9} and hemiparesis.⁹ However, the significance of these case reports is difficult to assess unless they are viewed against observations in a large representative sample of patients. Since most cases are asymptomatic and hence unlikely to present to medical attention, only by large-scale population screening would it be possible to define the medical abnormalities of such a group. Even this objective would be limited by the relative infrequency of the syndrome.

In a programme which screened 100 000 consecutive cord bloods in Jamaica 6 cases have been currently diagnosed, usually by the finding of the trait for hereditary persistence of HbF (AF genotype) in one parent. A conservative estimate would suggest a prevalence of approximately 10 cases in 100 000, or 1 in every 10 000 births. With such a low prevalence it would be desirable for retinal assessments to be made in all known cases, since these offer an elegant and sensitive method of detecting vaso-occlusion in a syndrome that could be an important model for learning more about sickle cell disease in general.

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