

Angioid streaks and sickle haemoglobinopathies

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Doyne (1889) described the clinical picture of angioid streaks. Groenblad (1929) reported the association of skin disease with angioid streaks. Strandberg (1929) carried out histopathological examinations of skin biopsies from Groenblad's patients and proved the abnormality to be that of pseudoxanthoma elasticum. Subsequently, angioid streaks have been reported in association with several other diseases, such as Paget's disease (Paton, 1972), acromegaly (Holloway, 1927; Howard, 1963; Paton, 1963), and Ehlers-Danlos syndrome (Green, Friedman-Kien, and Banfield, 1966).

The association of angioid streaks with sickle cell disease was first reported by Geeraets and Guerry (1960a) who described an incidence of angioid streaks of 6 per cent in a selected population of sickle cell patients (five of 69 cases). Subsequent reports have not substantiated such a high incidence of angioid streaks concomitant with sickle cell disease (Welch and Goldberg, 1966; Paton, 1972). Geeraets and Guerry (1960b) also reported elastic tissue degeneration in sickle cell patients and speculated whether intraocular and general elastic tissue degeneration in sickle cell disease represented a coincidental or true causative relationship. Skin biopsy studies in two sickle cell patients (Paton, 1972) failed to show any abnormality of elastic tissue.

Since we had an opportunity to examine a large series of sickle cell patients, the purpose of this communication is to report the incidence of angioid streaks in various sickle haemoglobinopathies. It is also our intention to demonstrate that no other disease, such as pseudoxanthoma elasticum, Paget's disease, or acromegaly, was associated with angioid streaks in our sickle cell patients. Because others have found elastic tissue alterations in sickle cell patients, we examined the skin of all our patients, specifically looking for elastic tissue changes histopathologically.

We also investigated the relationship between the severity of sickle cell retinopathy and the presence of angioid streaks.

Clinical data and methods

A total of 356 patients had been screened in the Sickle Cell Eye Clinic of the University of Illinois by May 1975. The haemoglobin electrophoresis of these patients showed that 162 had sickle cell anaemia (Hb SS); 101 sickle cell-haemoglobin C disease (Hb SC); 49 sickle cell trait (Hb AS); 34 haemoglobin S-thalassaemia (Hb S-thal); eight haemoglobin AC; and two haemoglobin CC.

Of these 356 patients five had angioid streaks and were investigated in detail. Investigations included detailed physical examination and the following laboratory determinations: Hb levels, Hb electrophoresis, serum calcium (normal 5.0 ± 0.5 mEq/litre and phosphate (normal 1.5-2.9 mEq/litre) levels, alkaline phosphatase (normal 20-124 international units/ml), skull and pelvic x-ray films, and skin biopsy. Haematoxylin and eosin stain, Verhoeff-van Gieson stain for elastic tissue, and von Kossa stain for calcium deposition were done in all cases to rule out elastic tissue abnormalities.

Ocular examination included visual acuity determination in both eyes and anterior segment examination with the slit lamp. A detailed fundus drawing with the binocular indirect ophthalmoscope, fundus photography, and fluorescein angiography were carried out in all cases.

Case reports

Case 1, a 42-year-old black woman with Hb SS, was first seen in November 1972. Her history included several episodes of sickle cell crises with episodic fever, joint pain, abdominal pain, and jaundice. She also had a history of mild systemic hypertension. Her blood pressure on systemic examination was 195/95 mm Hg.

Visual acuity was 20/30 in both eyes. Slit-lamp examination revealed positive conjunctival sickling sign. The right fundus showed small angioid streaks localized in the peripapillary region and two black sunbursts (chorio-retinal scars) at 12 and 2 o'clock in the retinal periphery. The macula was not involved.

The left eye also showed peripapillary angioid streaks without involvement of the macula. An area of neovascularization at 1.30 o'clock in the equatorial region leaked dye on fluorescein angiography; argon laser photocoagulation successfully occluded the feeder vessels.

Follow-up in August 1974 showed no change in angioid streaks or sickle retinopathy. Laboratory evaluation showed Hb level 9.6 g/100 ml; Hb SS by electrophoresis; serum calcium 4.8 mEq/litre; phosphate

2.6 mEq/litre; alkaline phosphatase 67 units/ml. Skull and pelvic x-ray films were normal. Skin biopsy showed no evidence of subepithelial or dermal elastic tissue alterations.

Case 2, a 46-year-old black man with Hb SC, was first seen in October 1971 with the diagnosis of vitreous haemorrhage in both eyes. His past history was unremarkable. Systemic examination was normal.

Visual acuity was 20/50-2 in the right eye and 20/25 in the left. Fundus examination revealed angioid streaks near the disc and a large patch of neovascularization in the right eye at 10 o'clock with a small vitreous haemorrhage in the temporal equatorial zone. The left eye showed sea-fans at 9.30, 12, 1, and 3 o'clock and angioid streaks around the disc.

Follow-up in September 1974 showed small angioid streaks in both eyes, which were confined to the peripapillary area; the maculae were not involved.

Laboratory findings were as follows: Hb 10.2 g/100 ml; Hb SC by electrophoresis; serum calcium 4.9 mEq/litre; phosphate 2.1 mEq/litre; alkaline phosphatase 34 units/ml. Skull and pelvic x-ray films showed findings consistent with sickle cell anaemia. Skin biopsy was normal.

Case 3, a 36-year-old black man with Hb SS, was seen in July 1974 for sickle cell retinopathy. The patient had had a few sickle cell crises, urinary tract infection, renal vein thrombosis, and upper respiratory tract infection. General physical examination was normal.

Visual acuity was 20/20 in both eyes. Slit-lamp examination showed positive conjunctival sickling sign. Fundus examination revealed prominent angioid streaks in both eyes (Figs 1 and 2) radiating from the peripapillary region. The maculae were not involved. The retinal periphery showed arteriolar occlusions typical of sickle cell disease. No neovascularization was seen.

Laboratory findings were as follows: Hb 10.9 g/100 ml; Hb SS by electrophoresis; serum calcium 4.9 mEq/litre; phosphate 2.4 mEq/litre; alkaline phosphatase 40 units/ml. Skull and pelvic x-ray films were normal; abdominal x-ray films revealed gallstones. Skin biopsy showed no elastic tissue degeneration.

Case 4, a 47-year-old black man with known Hb S-thal, was first seen in May 1970 with the complaint of poor vision in the right eye. He had had several episodes of sickle cell crises for which he had received symptomatic treatment.

Ocular examination showed visual acuity of perception of light in the right eye and 20/20 in the left. Slit-lamp examination was unremarkable. Vitreous haemorrhage prevented fundus examination of the right eye. The left eye showed prominent wide angioid streaks radiating from the peripapillary region; the macula was not involved.

Patches of neovascularization at 1 and 3 to 4 o'clock in the equatorial region of the left eye were photo-coagulated in 1971.

A cataract was removed from the right eye in September 1974. The retina showed extensive degeneration

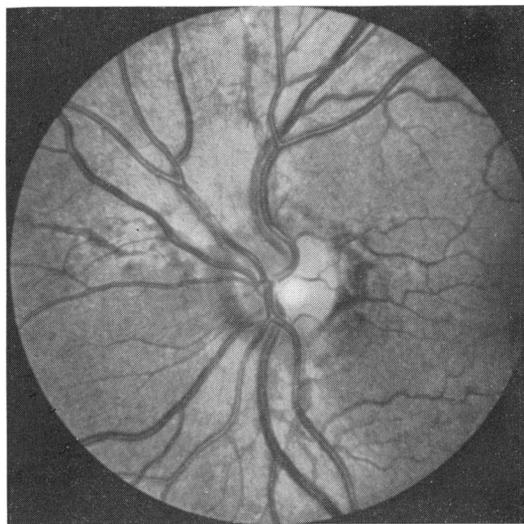


FIG. 1 *Case 3, left eye. Fundus photograph showing angioid streaks*

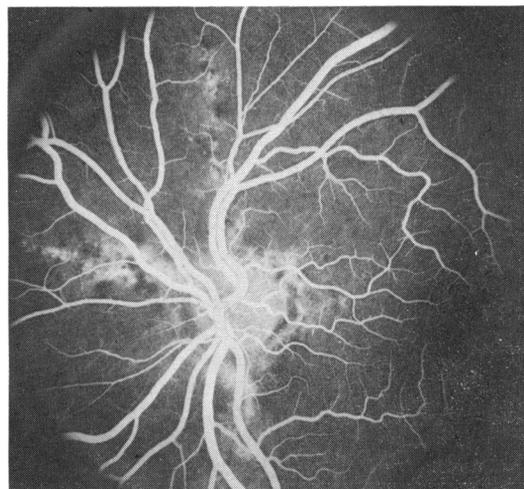


FIG. 2 *Case 3. Fluorescein angiogram of same eye as in Fig. 1, showing hyperfluorescence of angioid streaks*

with retinal pigmentary changes and vascular occlusions in both the central and the peripheral area. The inferior retina not involving the macula was detached with vitreous traction and breaks in this area. White fibrous tissue was seen at 8 o'clock. There was no improvement in vision after cataract extraction.

Laboratory findings were as follows: Hb 9.6 g/100 ml; Hb S-thal by electrophoresis; serum calcium 5.1 mEq/litre; phosphate 2.1 mEq/litre; alkaline phosphatase 26 units/ml. Skull and pelvic x-ray films suggested Paget's disease or metastatic carcinoma. Alkaline phosphatase levels were normal repeatedly. Systemic examination showed no evidence of malignancy. Skin

biopsy was normal; no elastic tissue degeneration was found.

Case 5, a 49-year-old black man with Hb SS, was first seen in January 1973. History showed that he had had several episodes of sickle cell crises and joint pain which had been treated symptomatically.

Visual acuity of 20/30 in both eyes improved to 20/20 with -0.5D sph. in both eyes. Slit-lamp examination showed positive conjunctival sickling sign. In both eyes fundus examination revealed asteroid hyalitis and small angioid streaks, particularly in the peripapillary region. The macular area was not involved with streaks, although there were multiple drusen of both maculae. The retinal periphery showed occluded retinal arterioles in both eyes, but no neovascularization.

Follow-up in September 1974 showed no change in ocular status. Laboratory determinations showed Hb 10.5 g/100 ml; Hb SS by electrophoresis; serum calcium 4.6 mEq/litre; phosphate 2.3 mEq/litre; alkaline phosphatase 33 units/ml. Findings on skull and pelvic x-ray films were consistent with sickle cell anaemia. Skin biopsy demonstrated no evidence of elastic tissue degeneration.

Discussion

Although the association of sickle cell haemoglobinopathies with angioid streaks is well documented, the reported incidence has varied from 0.95 to 6 per cent (Geeraets and Guerry, 1960a; Welch and Goldberg, 1966; Paton, 1972). These groups comprised a small number of patients. Since we examined a large number of patients, the occurrence of five cases in 356 patients (1.4 per cent) may represent the truer incidence of angioid streaks in sickle cell haemoglobinopathies. These data are close to the incidence reported by Paton (1972) who documented 1.33 per cent incidence of angioid streaks in various sickle haemoglobinopathies. The series described by Geeraets and Guerry (1960a) gave a very high incidence of angioid streaks in relation to sickle cell disease, perhaps because of their selection of patients. The incidence of angioid streaks in our series may not be entirely accurate either, because of a certain degree of patient selection.

Detailed investigations of our patients failed to show evidence of other diseases known to be associated with angioid streaks except in one case: the radiologist suspected Paget's disease or metastasis from a systemic malignancy in Case 4, but repeated serum alkaline phosphatase determinations and systemic examination were normal. Skin biopsy specimens, which were examined by an ophthalmic pathologist, a dermatologist, and a pathologist, revealed no evidence of elastic tissue degeneration. Moreover, we are not able to support the finding by Geeraets and Guerry (1960b) of widespread elastic tissue degeneration in sickle cell disease, which

might have been causally related to cracks in Bruch's membrane. Our findings lend support to the contention of Paton (1972) that it is highly unlikely that an elastic tissue defect exists in addition to Hb abnormality. We are unable to confirm Paton's hypothesis that chronic haemolysis results in deposition of iron in Bruch's membrane, thereby rendering it more brittle and prone to crack; however, this appears to be a more convincing argument than that involving elastic tissue degeneration.

The presence of angioid streaks could not be related to the severity of retinopathy. Two patients with sickle cell anaemia and angioid streaks had very mild retinopathy, whereas two patients with Hb S-thal and one with Hb SC had peripheral retinal neovascularization and severe retinopathy. These observations on the severity of the proliferative retinopathy agree with previous reports that retinal neovascularization is characteristic of certain varieties of sickle cell disease, particularly Hb SC and Hb S-thal (Welch and Goldberg, 1966; Goldberg, 1971a, b; Goldberg, Charache, and Acacio, 1971). Our observations also support the earlier hypothesis (Goldberg, 1975) that visual disability from the streaks is uncommon in patients with haemoglobinopathy. None of our patients had haemorrhagic macular involvement by the streaks.

An interesting observation that we are unable to explain is the age of patients reported by Geeraets and Guerry (1960a), by us, and by Paton (1972). All those described by Geeraets and Guerry (1960a) were younger than 30 years, whereas those reported by Paton (1972) and all those with angioid streaks in our series were over 30 years old. In our series of patients there was a large number of paediatric patients, yet we did not see a single case of angioid streaks in that group.

Summary

Five patients had angioid streaks associated with sickle cell haemoglobinopathy. Other diseases associated with angioid streaks were ruled out, as was elastic tissue degeneration in sickle cell patients. After studying over 350 patients, we believe the incidence of angioid streaks in sickle cell disease to be between 1 and 2 per cent.

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