Central retinal artery occlusion (reversible) in sickle trait with glaucoma

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Retinal vascular occlusions of several types occur in the various sickle haemoglobin disorders (SS, SA, SC, S-Thal) (Edington and Sarkies, 1952; Henry and Chapman, 1954; Goldberg, 1971a; Kennedy and Cope, 1958; Isbey, Clifford, and Tanaka, 1958; Lieb, Geeraets, and Guerry, 1959). Occlusions are primarily of small vessels in the peripheral retina preceding the development of neovascularization (Welch and Goldberg, 1966; Goldberg, 1971a, b). Occlusions of small vessels in the macula have also been reported in SS and SC haemoglobinopathy (Knapp, 1972; Acacio and Goldberg, 1973; Ryan, 1974). They are probably due to intravascular emboli of sickled red blood cells (Welch and Goldberg, 1966; Goldberg, 1971a, b). Factors known to enhance sickling of red cells thereby influencing the risk of vascular thrombosis include hypoxia, dehydration, lowered pH, and hyperviscosity (Sherman, 1940; Griggs and Harris, 1956; Perillie and Epstein, 1962; Charache and Conley, 1964). Not surprisingly, therefore, under certain conditions occlusion of large vessels such as the central retinal artery occur (Kabakow, Van Wiemokly, and Lyons, 1955; Conrad and Penner, 1967; Stein and Gay, 1970; Michelson and Pfaffenbach, 1972). We report a case of central retinal artery occlusion in SA disease immediately after diuretic and hyperosmotic therapy for acute traumatic glaucoma. We believe that this treatment must be used cautiously in the sickle patient whose ocular circulation is already compromised by acute glaucoma.

Case report

An 18-year-old black woman presented to the Wilmer emergency room with a traumatic hyphaema 24 hours after a blunt ocular injury. Her medical and family history were unremarkable. Uncorrected visual acuity was light perception right eye, 20/20 left eye. The anterior chamber contained diffuse haemorrhage with a layered hyphaema of about 10 per cent. Ocular motility was normal. Intraocular pressure by applanation was 55 mmHg. The fundus could not be visualized through the anterior chamber blood. Examination of the left eye was normal in all respects.

Treatment consisted of atropine cycloplopia, topical dexamethasone, and 120 ml glycerol 75 per cent. Emesis followed shortly after osmotic therapy. Intraocular pressure remained raised at 55 mmHg. Subsequent treatment consisted of intravenous acetazolamide 500 mg and mannitol 100 g (1·5 g/kg) at an infusion rate of 5 g/minute. One hour later ocular tension was 55 mmHg. Vision in the right eye was no light perception when tested with the American optical indirect ophthalmoscope at maximum voltage.

The clinical impression was that the patient had suffered a central retinal artery occlusion. An anterior chamber paracentesis of 0·08 ml was performed. After this vision returned to brisk light perception. Intraocular pressure was subsequently controlled with oral acetazolamide. With clearing of the ocular haemorrhage fundus examination showed disc hyperaemia. Fluorescein angiography was essentially unremarkable. Electroretinography could not be performed. Subsequent serum electrophoresis showed sickle-cell trait (SA) haemoglobinopathy with 42 per cent sickle-cell haemoglobin. Visual acuity returned to the 20/30 level.

Discussion

Our patient presented with an intraocular pressure of 55 mmHg and brisk light perception vision. One hour after diuretic and osmotic therapy the pressure remained at 55 mmHg with no light perception. This time sequence suggests that increased intravascular tonicity and altered haemodynamics after these medications may have precipitated an occlusion in an already compromised vascular system. Intravenous infusion of mannitol is known to increase serum osmolality from 290–40 mosm/l depending on rate of infusion and dosage (Galin, Davidson, and Pasmanik, 1963; Weiss and Wise, 1962; Koller and Hetherington, 1970). Increased serum tonicity occurs rapidly throughout the infusion and returns to equilibrium...
over a period of from one to two hours (Galin and others, 1963; Weiss and Wise, 1962). The effect of intravenous acetazolamide is difficult to quantify.

The susceptibility of patients with sickle-trait haemoglobinopathy to central retinal artery occlusion at moderately raised or even normal ocular pressures has been well documented. Five cases of central retinal artery occlusion have been reported (Kabakow and others, 1955; Conrad and Penner, 1967; Stein and Gay, 1970; Michelson and Pfaffenbach, 1972). Bilateral vascular occlusions were described in a 36-year-old patient with active pulmonary tuberculosis, systemic lupus erythematosus, and sickle-cell trait (Kabakow and others, 1955). Conrad and Penner described central retinal artery occlusion in a 32-year-old pilot with sickle-trait haemoglobinopathy (unassociated with active flying duties) (Conrad and Penner, 1967). No other precipitating ocular or systemic conditions were found; the proportion of sickle haemoglobin was 42 per cent. Vision remained at no light perception in the affected eye. Stein and Gay reported bilateral arterial occlusions in a six-month-old infant suffering from high fever and marked dehydration (Stein and Gay, 1970). They suggest that metabolic abnormalities induced by pneumonia and renal failure in this SA infant might well have produced intravascular sickling leading to bilateral central artery occlusion. Finally, Michelson and Pfaffenbach described two sickle-trait youths with arterial occlusions after blunt trauma and ocular haemorrhage (Michelson and Pfaffenbach, 1972). Both these patients were treated with diuretic and osmotic agents to control raised intraocular pressures ranging from 20 to 50 mmHg.

Various factors affect the severity of the symptoms in patients with sickle-cell disease. Percentage of abnormal haemoglobin as well as oxygen tension, lowered pH, fever, vascular stasis, hyperkalaemia, raised carbon dioxide level, and serum hyperosmotic increase the amount of erythrocyte sickling and subsequent clinical symptoms (Sherman, 1940; Griggs and Harris, 1956; Perillie and Epstein, 1962; Charache and Conley, 1964). Increased serum tonicity after diuretic and osmotic medications in combination with vascular stasis, presumably coincident with raised intraocular pressures, may have precipitated vascular occlusion in this patient with sickle-cell trait.

The possibility that ocular hypotensive medications may have aggravated the situation calls for re-evaluation of the management of raised ocular tension in black patients. We recommend an emergency sickle cell preparation as part of the initial examination of every black patient with hyphaema. In those with sickle-cell haemoglobin an intraocular pressure over 40 mmHg requires careful monitoring of vision for the earliest sign of vascular occlusion. Osmotic agents should be given with caution and vision must be checked frequently thereafter. Only experience with similar cases will show whether such medications must always be avoided.

In our case good visual function returned after retinal blood flow had apparently ceased. Recent reports emphasize that retinal function may return even when vascular occlusion lasts up to one hour or more. Neuronal function may be much more resistant to absolute ischaemia than previously recognized. After reversible ligation of the central retinal artery in Squirrel monkeys Kroll (1968) showed that a period of retinal ischaemia limited to 15 minutes produced no significant gross or histological damage. Only after one hour of obstruction was the earliest neuronal damage seen. Reinecke, Kuwabara, Cogan, and Weis (1962) produced retinal ischaemia in cats by increasing intraocular pressure above systolic arterial pressure by external massage. In cases in which ischaemia was limited to less than 1½ hours only minimal histopathological changes were noted. Lessell and Miller (1975) produced total cerebral as well as retinal ischaemia by cross-clamping the ascending aorta in adult Rhesus monkeys. When the arterial obstruction was released after periods of 14 to 24 minutes of the 22 monkeys had survived this vascular insult, and when periods of post-arrest hypotension were avoided, histopathological retinal abnormalities were not seen.

These histopathological studies have been corroborated by a number of experiments to assess the functional resistance of retinal tissue to ischaemia. After reversible occlusion of the retinal vascular supply in rabbits electroretinograms have returned to pre-insult levels when anoxia was limited to 10 minutes (Arden and Greaves, 1956). Popp (1955) found that even after 60 to 90 minutes of ischaemia partial recovery was seen in the rabbit ERG. Working with Squirrel monkeys, Hamasaki and Kroll (1968) produced reversible retinal artery occlusion by placing a ligature round the surgically exposed vessel. Remarkably, they showed that more than two hours of occlusion were required to produce irreversible changes in electrical activity of the retina and optic nerve. Gouras and Hoff (1970) made similar observations using an isolated, perfused mammalian eye system. Extending these studies to man, Wegner (1928) produced retinal ischaemia in pre-enucleation specimens by raising ocular tension well above systolic pressures. When the period of retinal ischaemia was limited to 15 minutes visual recovery was full: even after 45 minutes of ischaemia some function returned. Under similar experimental conditions Böck, Bornschein, and Hommer (1963, 1964) showed that complete recovery of both electrical and physiological retinal activity can be
obtained even after so long as one hour of absolute retinal ischaemia. Such investigations suggest that moderate periods of ischaemia may be expected to show significant functional recovery if adequate blood supply is restored and maintained.

We emphasize that the sickle-cell patient with an intraocular pressure over 40 mmHg is approaching a precarious situation which may be exacerbated by osmotic therapy. In our case function returned from no light perception to 20/30 vision. A review of the literature on experimental occlusion suggests that efforts to restore vision even after one to two hours of known occlusion should not be considered only heroic.

**Summary**

We report a case of central retinal artery occlusion in an 18-year-old black woman with sickle-trait haemoglobinopathy and acute glaucoma after hyphaema. The central retinal artery occlusion occurred immediately after treatment of the glaucoma with osmotic agents, raising the possibility that they played a precipitating role. We suggest that osmotic agents be used with extreme caution in sickle patients with glaucoma. The occlusion was treated by anterior chamber paracentesis with eventual return of good vision. The reversibility of retinal and optic nerve function after total ischaemia is discussed.

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