Case report

Central retinal vein occlusion and scleroderma: implications for sclerodermatous vascular disease

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SUMMARY A patient with scleroderma (progressive systemic sclerosis) who developed central retinal vein occlusion is described. The aetiology of this condition is discussed and the role of possible sclerodermatous vascular disease is highlighted. It is suggested that studies of fundal vasculature could be useful in the clinical assessment of sclerodermatous vascular disease.

Scleroderma, a disease of unknown aetiology, is associated with characteristic vascular lesions in many systems. These vessel changes may result in varying degrees of end-organ damage with resultant diversity of expression of clinical disease. Lesions of the fundal vasculature have not previously been highlighted despite the ease of accessibility of this area to examination. We report a case of central retinal vein occlusion in a patient with scleroderma and discuss the implications of sclerodermatous vascular disease in the aetiology of this complication.

Case report

A 52-year-old Caucasian male was well until 1974 when angina developed, characterised by typical chest pain and ST changes on exercise electrocardiogram. Raynaud's phenomenon developed in mid-1978, associated with arthralgia in the wrist, elbow, and knee joints, and the hands became stiff and swollen. There was no history of alopecia, photosensitivity, muscle weakness, mouth ulceration or skin rash. Because of mild hypertension, the patient was taking hydrochlorothiazide 50 mg/day and metoprolol 50 mg/day.

On examination in January 1979 the blood pressure was 135/85 mmHg and pulse 80/minute. The fingers were diffusely swollen and hands moist;

subcutaneous tissue was thickened and bound down to above the wrists. The skin in both malar areas was also thickened. Telangiectatic vessels were present at the base of most nails. Allen's test demonstrated poor filling of radial and ulnar arteries bilaterally, but otherwise cardiovascular examination was normal. Fine end-inspiratory pulmonary crepitations were present, and there were 20 tender joints with no effusions or deformity. Ophthalmological assessment showed 20/20 vision in both eyes with normal applanation pressures and slight rose Bengal staining of the cornea. Schirmer's test produced only 3 mm of wetting on both sides.

Investigations revealed mild anaemia with depression of serum iron and iron binding capacity, and the erythrocyte sedimentation rate was 53 mm/hour (Westergren). The following tests were normal: white blood count including differential count, platelet count, blood film, routine electrolytes, creatinine, urine analysis, creatinine clearance, blood sugar, fasting lipids, faecal fat, and d-xylose absorption. Protein electrophoresis indicated mild hypoalbuminaemia; VDRL, the Coombs test (direct and indirect), and RA latex tests were negative. ANF was positive at 1:100 with a diffuse pattern. Cryoglobulins were not detected. Radiography included a normal chest film and barium enema, with a barium swallow showing some irregular secondary contractile activity in the lower oesophagus. Electrocardiograms showed mild T-wave flattening in the inferior leads. Pulmonary function tests showed a reduction in all volumes with a FEV₁/VC of 83%.

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DCo was 6.5 ml/min/mm Hg (normal=15). A cold pressor test performed some 4 weeks off all hypotensive medications showed no change in the plasma renin activity level.

A diagnosis of systemic sclerosis was made and the patient was started on enteric-coated salicylate 2.6 g/day for joint symptoms and isosorbide dinitrate 120 mg/day for the ischaemic heart disease. Hypotensive medications were discontinued.

One month later the patient suffered 2 attacks of transient visual loss in the left eye, each lasting up to 30 minutes. The following day a third attack led to continued severe diminution of vision in the left eye.

Examination at that time showed the visual acuity to be 20/20 in the right eye and counting fingers at 1 metre in the left. There was a left afferent pupil defect. The anterior segments, ocular adnexae, and applanation pressures were normal. The right fundus was completely normal but the left showed disc swelling retinal oedema, and superficial haemorrhage (Fig. 1). The veins were dilated and segmented and a large number of cotton-wool patches were present. Fluorescein angiography showed attenuation of arteries and large areas of capillary closure in addition to the signs of venous stasis (Fig. 2). Central retinal vein occlusion was diagnosed. Investigations included normal haematology, clotting profile, and negative screen for intravascular coagulopathy.

Fig. 1 Left fundal photograph showing venous stasis, haemorrhage, cotton-wool patches, and retinal oedema.

Fig. 2 Fluorescein angiogram of left fundus in late venous phase showing venous dilatation and stasis. Extensive areas of retinal ischaemia and oedema block out the background fluorescence.

Prednisone 15 mg/day and sulphapyrazone 400 mg/day were added to the salicylate and isosorbide dinitrate. The left fundal findings gradually resolved over the next 3 months with improvement in the visual acuity to a level of 20/200. The left afferent pupil defect was unchanged.

Discussion

This patient had scleroderma with mild pulmonary fibrosis and early oesophageal motility dysfunction. No evidence of renal damage was present by routine tests, nor did cold pressor testing indicate any evidence of vascular involvement of the kidneys.¹ There was a 2-year history of mild hypertension without evidence of left ventricular hypertrophy on electrocardiogram or abnormality on fundal examination at the initial presentation.

The ophthalmological problem was that of central retinal vein occlusion (CRVO), though the usual picture was not present. The history of episodes of transient visual loss prior to the definitive event, the finding of an afferent pupil defect, and the fundoscopic and fluorescein observations all suggest that central retinal artery occlusion had also occurred at some stage. The fundoscopic picture observed corresponded with that described by Hayreh² as haemorrhagic retinopathy, or CRVO associated with retinal ischaemia. In this condition angiographic changes of retinal capillary obliteration, arteriovenous shunts, neovascularisation, and microaneurysms occur in addition to distended and engorged retinal

veins and venous stasis. This was the picture seen in our patient.

This type of CRVO thus implies involvement of the retinal artery as the primary pathological event. Occlusion of this vessel, whether partial or complete, transitory or prolonged, will result in stasis of retinal circulation. Subsequent ischaemia of capillary beds produces the characteristic haemorrhagic change. The effect of stasis on the venous system may include CRVO, and this is more likely if this vessel is itself diseased or affected by disease in the adjacent artery. At the level of the lamina cribrosa the central retinal artery and vein share a common adventitial sheath.³ Thus, disease of the artery may induce changes in the vein by extension of the primary process. Alternatively, because expansion and displacement of the vascular elements are restricted by the lamina cribrosa, the lumen of the vein may be diminished if the artery is enlarged by a pathological process. In situations where stasis is present this decrease in vein lumen size may lead to venous occlusion.

The central retinal artery is a true artery, with a diameter of about 130 μm . It seems not to be affected by hypertension but may be involved by atheromatous disease.⁴ Our patient may have atheromatous disease of the coronary arteries, and this disease could also be involved in the pathogenesis of the CRVO. An equally acceptable alternative possibility is that the vascular changes of scleroderma contributed to the visual loss. Lesions of the small arteries (150–500 μm diameter) are characteristic of scleroderma.⁵ Proliferation and swelling of endothelial cells lead to enlargement of the intima. A mucoid ground substance frequently appears. The adventitia will usually possess a fibrous cuff around the artery (and vein in the area of the lamina cribrosa), which frequently obliterates the periarterial capillaries and lymphatics. Goetz⁶ stated that lesions of this vessel size are to be found in every organ system. Smaller arteries (50–150 μm diameter) and arterioles may undergo intimal sclerosis, fibrinoid change, and necrosis. Capillaries have been noted to be dilated and decreased in number,⁷ and on electron micrographs thickening and reduplication of the capillary basement membrane is seen.⁸ While many large series fail to comment on involvement of retinal vasculature with these changes,^{5,9,10} other reports do indicate that the typical sclerodermatous vessel disease may also affect this area.

Retinal and choroidal arteries have been noted to show the typical changes of scleroderma.^{11–13} Farkas *et al.*¹³ also found choroidal capillary changes similar to those observed by Norton in muscle. Maclean and Duthie¹² reviewed data from 9 cases

of scleroderma with clinical fundal change. Most, but not all, were hypertensive. They concluded that ischaemic retinopathy in hypertensive patients with scleroderma occurred much earlier than otherwise expected and indeed was also seen in some normotensive patients. A study of the retinal vasculature of sclerodermatous patients, using fluorescein angiography¹⁴ demonstrated abnormalities of perfusion which affected the choriocapillaries and small choroidal arterioles. Most of these patients were normotensive. These observations suggest that end-organ disease due to retinal vessel involvement with sclerodermatous vascular change does occur, albeit uncommonly.

Any disease of the retinal vessels may be exaggerated by a superimposed Raynaud's phenomenon. Reflex vasospasm has been shown to affect the vasculature of the kidneys^{15,16} and lung,¹⁷ and similar changes may affect the retinal circulation.¹⁸ If the central retinal artery is affected by either atheromatous or sclerodermatous vessel changes, vasospasm may precipitate retinal ischaemia with risk of central retinal vein occlusion.

Although branch vein occlusion¹⁹ and branch artery occlusion²⁰ have been described in sclerodermatous patients, we could find no previous report of central retinal vein occlusion in this condition. This observation emphasises the importance of the vascular lesions of scleroderma, though by no means is a cause-and-effect relationship conclusively demonstrated by the findings in this case. Further studies of the retinal circulation with more sophisticated tools could make this easily observed area an important aspect of assessment in the patient with scleroderma.

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