Retinal revascularisation in diabetic retinopathy

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SUMMARY The case history of a 33-year-old diabetic patient who has had diabetes for 24 years is presented. When first seen in 1975 he had bilateral proliferative retinopathy with new vessels in the retinal periphery. He had large areas of capillary non-perfusion lateral to the macula in the right eye associated with the new vessels. Nine years later, after extensive repeated photocoagulation, revascularisation of large areas previously not perfused were seen. The vessels are in the plane of the retina and do not have the appearance of new vessels.

Capillary non-perfusion is a sign of ischaemia in diabetic retinopathy. It is a precursor and is thought to be a stimulus for the formation of new vessels in the retina.¹ While revascularisation of small areas of capillary non-perfusion have been recorded,² when large areas are involved the condition is thought to be irreversible. We report on a patient with proliferative retinopathy in whom revascularisation of a large area followed extensive photocoagulation.

Case report

A 33-year-old male patient was first seen in the Retinopathy Clinic at the Hammersmith Hospital in 1975. He had been a diabetic since the age of 9 years. Initially he was treated with a single daily dose of PZI and soluble insulin, but since 1969 he had had twice daily Rapitard in a total dose of 152 units daily. He was on a 160 gram carbohydrate diet. During the previous year his hitherto poor diabetic control improved, so that most of his urine tests were between 0 and 1/4%.

He had symptoms of peripheral neuropathy and stiffness in his fingers, but was otherwise well. He noted spots in front of his eyes and intermittent blurring of vision for about one year; this precipitated his referral to the clinic.

On examination he was of ideal body weight. He had a normal blood pressure of 120/75 mmHg, normal peripheral pulses, absent ankle jerks, and reduced vibration senses. Investigations showed a trace of proteinuria, normal blood urea of 6 mmol/l, creatinine 91 μ mol/l, and normal serum proteins. The only significant abnormality was in his eyes.

Visual acuity (VA) was 6/6 in both eyes uncorrected and the intraocular pressure was 15 mmHg. He had no cataract or rubeosis. He had extensive peripheral new vessels in all four quadrants of his retina (NVE) with areas of fibrous tissue proliferation but no new vessels on the disc (NVD) (Fig. 1a). A fluorescein angiogram confirmed extensive new vessels and demonstrated extensive areas of capillary non-perfusion lateral to the macula (Figs. 1b and 1c).

Because of the symmetry of the two eyes and because at that time the benefits of photocoagulation were not proved, he was advised to join the British Multicentre Study in which one eye was treated by

Fig. 1a Right macular area showing multiple microaneurysms, haemorrhages, and new vessels (arrows).

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Fig. 1b Fluorescein angiogram of area shown in Fig. 1a, in capillary phase. There is widespread leakage from new vessels. There is no capillary perfusion lateral to the macula.

Fig. 1c Same as Fig. 1b, but late phase shows that perfusion lateral to the macula is absent, not delayed.

xenon arc while the other eye was followed up as an untreated control. The right eye was chosen for treatment by a randomisation procedure and had several treatment sessions under retrobulbar anaesthesia with the xenon arc. In all he had 520 xenon arc

burns in the right eye between 1975 and 1977. In 1977, because of a haemorrhage from the new vessels in the left eye, this was also treated. In December 1978 his VA was 6/12 on the right and 6/6 on the left. The new vessels had improved and others had been replaced by fibrous tissues. The visual loss was thought to be due to preretinal fibrosis.

Between 1978 and 1983 he developed further new vessels in both eyes, especially in the left, including NVD and several preretinal haemorrhages. He needed further extensive treatment of panretinal photocoagulation, now with the argon laser. He had 1450, 500 μm spot size burns on the right and almost 4000 in the left. In 1983 the VA was 6/12 on the right and 6/9 on the left. Both retinæ were now more quiescent and fluorescein angiography showed striking revascularisation lateral to the macula. No further treatment was necessary.

The patient was last seen in February 1985. His diabetic control was then excellent on twice daily Actrapid and Monotard insulin, total daily dose of 50 units. His glycosylated haemoglobin (HbA1) has been between 7.7% and 9.7% in the last three years (upper limit of normal 8%). His blood pressure had risen to 150/88 mmHg. He had no proteinuria; urea was 3.6 mmol/l and the creatinine 88 $\mu\text{mol/l}$. His visual acuity was 6/18 and L 6/9. The retinopathy had not changed significantly in the last two years, though some activity was still present (Figs. 2a-c). The vessels seen on angiogram were in the plane of the

Fig. 2a Right macular area 10 years later after extensive photocoagulation, showing quiescent retinopathy with little fibrous tissue.

Fig. 2b Fluorescein angiogram shows revascularisation lateral to the macula in the plane of the retina.

Fig. 2c Late pictures show leakage from fibrous tissue and minimal leakage from capillaries.

retina and did not have the appearance of new vessels.

Discussion

This case demonstrates the occurrence of capillary revascularisation in a previously avascular area of the retina in a patient with advanced diabetic eye disease after extensive photocoagulation. Revascularisation of non-perfused areas has been demonstrated previously in experimental animals after exposure to high intensity light³ and branch vein occlusion.⁴ It has also been noted in humans in retinal branch vein occlusion.^{5,6} Recently a patient with radiation retinopathy in both eyes has been described in whom partial reperfusion of the capillary bed occurred.⁷

In the natural history of diabetic retinopathy capillary non-perfusion is one of the most important features, since the sight-threatening lesions of macular oedema and neovascularisation are secondary to capillary occlusion. Most areas of capillary closure are irreversible and enlarge progressively. It has been reported that in some areas of capillary closure, associated with cotton wool spots, capillaries may reopen.⁸ In a recent report Muraoka and Shimizu⁹ describe both 'recanalisation' and 'intra-retinal neovascularisation' to describe the vessels that appeared in their patients. However, in that study all patients initially had non-proliferative retinopathy and new vessels developed subsequently. In the patient presented here there was

extensive non-perfusion and proliferative retinopathy at presentation. The revascularisation occurred after extensive photocoagulation. The stimulus for the large area of revascularisation is not known. However, in a recent study, Marshall *et al.*⁹ have demonstrated in experimental photocoagulation proliferation of capillary and venous endothelium. This must be the result of the photocoagulation, though it is not clear whether it is a reaction to pigment epithelial damage or transfer of a vasoproliferative substance from the choroid. The findings reported here raise the interesting possibility that, at least in some patients, there may be a partially reversible component in diabetic retinopathy even at advanced stages of the condition.

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