Retinal vascular remodelling in radiation retinopathy

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SUMMARY A 34-year-old female developed bilateral radiation retinopathy three months after external beam radiotherapy for pituitary adenoma. The clinical symptoms, fundus abnormalities, and microvascular pathology noted on fluorescein angiography resolved spontaneously over a few months. The most dramatic aspect was the progressive improvement and partial reperfusion of the retinal capillary bed.

A retinopathy may follow radiation treatment for intraocular malignancies, for lesions adjacent to the eye, or for intracranial lesions. The latency period is variable but is usually a few months to a few years.

The abnormalities are probably a result of damage to the retinal vessels resulting in obliterative endarteritis. Clinical manifestations include microaneurysms, telangiectasias, haemorrhages and exudates (superficial and deep), vessel wall sheathing, capillary non-perfusion, and neovascularisation. Progression of these lesions is not uncommon.

We report herein a case of radiation retinopathy following external beam irradiation for pituitary adenoma. On follow-up examination there was dramatic resolution of many of the microvascular abnormalities.

Case report

A 34-year-old white female was diagnosed as having a pituitary adenoma 11 years previously, at which time she underwent an intracranial subtotal removal of the tumor. The preoperative amenorrhoea and bitemporal visual field defect resolved after surgery.

In November 1978 she received external beam radiotherapy (4500 rads) to the remaining tumour for symptoms of acromegaly (changes in facial contour and increasing hand size). Three months after therapy she complained of spots in front of both eyes and progressive visual blurring in the left eye. An increase in growth hormone and an abnormal glucose tolerance test prompted the diagnosis of diabetic retinopathy by the consulting ophthalmologist.

At the time of our initial evaluation in August 1979 the visual acuity was 6/6- (20/20-) OD and 6/18 (20/60) OS. The pupils were 4 mm round and reactive to light with a 2+ afferent pupillary defect OS. The versions were full. Colour vision testing with the Ishihara plates showed multiple errors in each eye, but they were more marked in the left eye. Tangent screen visual fields showed a temporal defect to a 3 mm red OD and a slight superotemporal depression to a 3 mm white OS.

The fundus examination revealed scattered posterior polar superficial haemorrhages and exudates,

Fig. 1 Initial examination. Both eyes showed superficial haemorrhages and exudates in the posterior pole with a macular star figure in the left eye.

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Fig. 2A Fluorescein angiography. Large areas of capillary non-filling were seen in the left eye which corresponded to the areas of superficial haemorrhage and exudate.

Fig. 2B The late phase shows intraretinal oedema and vessel wall staining.

which were more extensive in the left eye. There was a macular star exudate in the left eye (Fig. 1). The fluorescein angiogram showed extensive abnormalities in the retinal circulation, including large areas of capillary non-filling, focal microaneurysms, and dilated anastomotic channels. In the late-phase

angiogram there was evidence of posterior polar intraretinal oedema and staining of the vessel walls (Fig. 2).

After this examination she underwent a transphenoidal hypophysectomy with decompression of the chiasm. While the bitemporal field defects

Fig. 3A Seven-month follow-up examination. There is reperfusion of the retinal capillary bed with a few dilated capillaries evident in the macula.

Fig 3B The retinal oedema and vessel wall staining is less apparent.

Fig. 4A One-year follow-up examination. On fundus examination there is little evidence of the previous injury save for a few dilated tortuous retinal vessels.

Fig. 4B The angiogram shows capillary reperfusion without evidence of retinal oedema.

improved the visual acuity remained unchanged. The fundus picture and fluorescein angiogram were slightly worse in the left eye two months later. In view of the extensive areas of retinal capillary disease throughout the posterior pole of the left eye it was decided that treatment with photocoagulation would not prove beneficial for improving central vision.

In March 1980 the vision was 6/6– (20/20–) OD and 6/9 (20/30) OS. There were only a few superficial haemorrhages and exudates in each eye, and the macular exudate had partially resolved. The angiogram showed reperfusion of much of the retinal capillary system (Fig. 3A). The retinal oedema was still present but had considerably lessened, and there was only minimal vessel wall staining (Fig. 3B). One year later the vision was unchanged but the haemorrhages and exudates had disappeared. There were a few dilated tortuous vessels and focal microaneurysms of the left eye (Fig. 4).

Discussion

The retinopathy following radiation treatment to the eye and orbit has been well documented in a number of reports.^{1–7} The exact pathogenesis is uncertain. It is known that irradiation of other organs can result in a vasculopathy consisting of thickened vessel walls, an endarteritis, and capillary atrophy. This is a delayed effect of radiation and may progress with time.⁸ Histopathology of globes has revealed thickened hyalinised vessel walls.^{9–11}

Clinically the retinopathy resembles the vascular

changes seen in a variety of vaso-occlusive diseases such as diabetes, retinal vein obstruction, sickle cell retinopathy, or systemic hypertension, to name some of the more common aetiologies. Interestingly, retinal vascular disease—for example, diabetes mellitus—may potentiate the effect of radiation-induced retinitis. Chemotherapy also seems to have an additive effect.¹¹

The amount of capillary non-perfusion is considered to be a prognostic sign. When it occurs in the macula and affects the perifoveal capillary net, the prognosis for good central vision is grave. This is a result of either retinal atrophy or persistent macular oedema. Capillary non-perfusion is a finding prior to the appearance of intraretinal neovascularisation. Neovascularisation occurs at the interface of perfused and non-perfused retina, growing into the non-perfused retina. A final complicating factor with profuse areas of capillary non-perfusion is rubeosis iridis and haemorrhagic glaucoma.

The treatment for diseases with capillary non-perfusion has been to destroy ischaemic retina in an attempt to prevent new vessel formation or to hasten its regression. Panretinal argon laser photocoagulation has resulted in the complete regression of optic nerve and retinal neovascularisation in a case of radiation retinopathy.¹²

The patient in this case report presents a number of interesting findings. The onset of visual symptoms three months after radiation therapy is an extremely short latency period. At this time her initial eye examination elsewhere prompted the diagnosis of

diabetic retinopathy. Not only did the clinical appearance resemble this common retinopathy, but the abnormal glucose tolerance test (a result of an increase in growth hormone) reinforced this diagnosis. Elevated blood glucose levels secondary to increase in growth hormone may result in a minimal retinopathy of a few microaneurysms, but this never proceeds to the marked retinopathy seen in this patient. It is interesting to speculate whether this pituitary-induced diabetic state potentiated the effects of radiation, as has been stated to occur in diabetes mellitus.¹¹

The most dramatic aspect was the partial reperfusion of the retinal capillary bed. The reperfusion was noted seven months after the initial examination and continued to improve when assessed one year later. The most plausible explanation for this sequence of events is that the radiation-induced vessel wall oedema resulted in occlusion of the lumen. With resolution of this extra and intracellular swelling the lumen was reopened. Apparently the degree of retinal hypoxia was insufficient to induce secondary intraretinal neovascularisation.

Retinal vascular remodelling does occur in the healing stages of obstructive vasculopathies (vein occlusion, sickle cell retinopathy, Eales' disease, retrolental fibroplasia, periphlebitis of various aetiologies) and in the course of diabetic retinopathy. The reperfusion of the retinal capillary circulation to the degree presented in this case is to our knowledge unique.

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