Sir,

Accelerated radiation retinopathy in diabetes and pregnancy

Radiation retinopathy is a well-documented phenomenon which may occur after radiation therapy for primarily extracranial head and neck tumours or for intraocular pathology. Total dosage and daily fraction size of radiation are known to influence the incidence of radiation retinopathy.[1–3] Patients who are diabetic and have had previous chemotherapy are more susceptible to radiation retinopathy.[2,4] Here we describe a patient who presented with florid proliferative radiation retinopathy following radiation for rhabdomyosarcoma of the right maxillary antrum. She was an insulin-dependent diabetic who had had previous chemotherapy. She was 8 weeks pregnant when first seen with proliferative retinopathy.

Case report

A 24-year-old woman was diagnosed as having a stage 2/4, IV embryonal rhabdomyosarcoma in March 1995. The tumour involved the floor of the right orbit, filled the right maxillary antrum and involved the nasal septum. It has also involved the hypopharynx to the level of the uvula, as well as the right ethmoid. She was a well-controlled insulin-dependent diabetic since the age of 9 years.

She was treated with chemotherapy and radiotherapy. The chemotherapy comprised isosamide, vincristine, epirubicin, actinomycin D, etoposide and carboplatin given as 6 cycles over 20 weeks. Radiotherapy encompassing the anterior and lateral fields and including both ethmoids, nasal cavity, right orbit and maxilla was completed by August 1995. The treatment involved a total of 54 Gy comprising 30 fractions, each of 1.8 Gy, over 6 weeks. The dose prescribed was 100%. Shielding to the right lens, right lacrimal gland and to the left border of the field at the left inner canthus was provided. This resulted in regression of the tumour.

The patient was regularly screened by her optician for diabetic retinopathy. She was referred to us in May 1998 by her optician after a routine visit, with proliferative retinopathy confined to the right eye. She was asymptomatic and 8 weeks pregnant. Her right and left visual acuities were 6/5 and N5. Fundal examination of the right eye revealed two large neovascular fronds at 3 o'clock and above the superotemporal arcade and a large preretinal haemorrhage, overlying the frond (Figs. 1, 2). Fluorescein angiography revealed gross ischaemia extending clockwise from 11 o'clock to 7 o'clock, the worst area being in the inferonasal quadrant. The left fundus was normal with no obvious retinopathy. However, fluorescein angiography revealed ischaemia of the extreme nasal quadrant in this eye. There was no sign of diabetic retinopathy in either eye. Scatter laser photocoagulation was carried out to the ischaemic zones of both eyes. A total of 2963 burns (over three sessions) were applied to the right eye and 347 burns to the left eye. At follow-up, 2 months later, the neovascular fronds were showing signs of regression. Despite initial improvement, the proliferative changes worsened in the third trimester, although she maintained a visual acuity of 6/5. She was delivered of a stillborn child at 8 months of gestation. On review 2 months later, the new vessels had converted into fibrotic bands (Fig. 3).

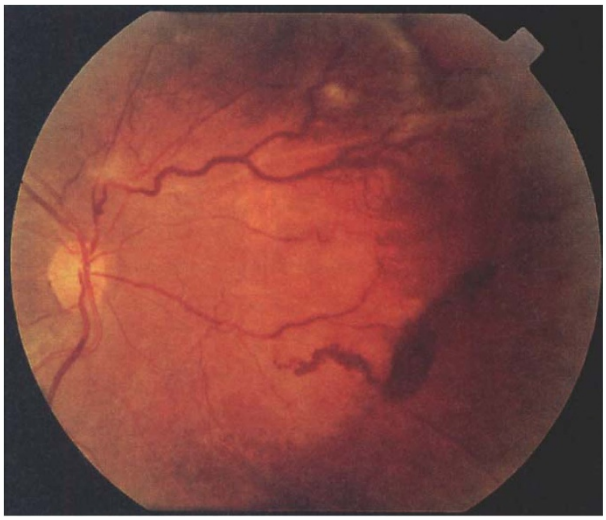

Fig. 1. *Neovascular fan along the nasal quadrant of the right eye, with a ridge demarcating the peripheral ischaemic zone.*

Comment

The clinical changes seen in radiation retinopathy include capillary dilatation, telangiectasias, microaneurysm formation and capillary closure.[1] Retinal oedema and exudative phenomena may result from the retinal vascular incompetence. Cotton wool spots occur transiently with later evolution of large areas of capillary non-perfusion. Retinal ischaemia may lead to retinal and disc neovascularisation, vitreous haemorrhage and retinal detachment.

The incidence of radiation retinopathy is dependent on both total dose and daily fraction size of radiation. In two reports, 50% of patients had retinal changes following 60 Gy of cephalic radiation, rising to 85–95% in patients exposed to 70–80 Gy.[5,6] The Intergroup Rhabdomyosarcoma Study 1 (IRS 1)[7] reported that only 3 of 37 children (8%) who received 50–60 Gy (2 Gy per fraction) to the orbit developed radiation retinopathy.

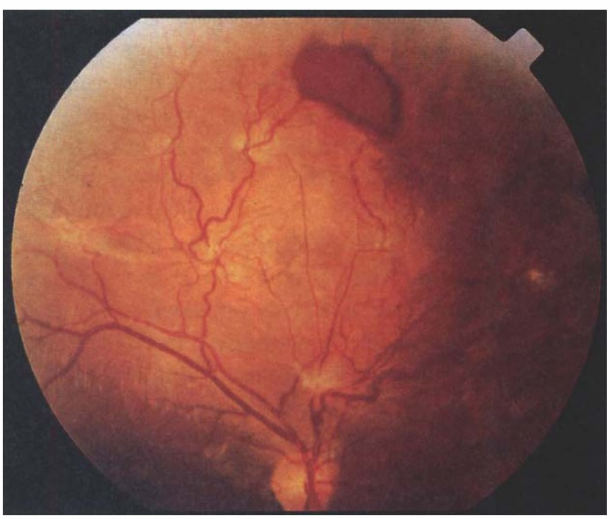

Fig. 2. *Neovascular frond in the superonasal quadrant of the right eye.*

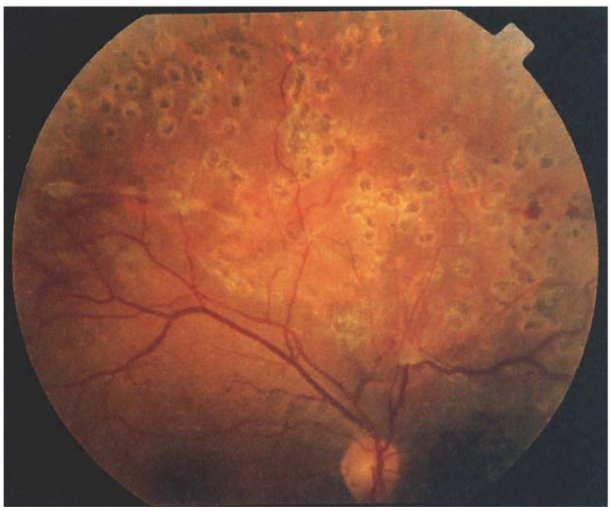

Fig. 3. *Regressed new vessels following laser photocoagulation and delivery.*

Fraction size of radiation has been shown to be an important factor in contributing to susceptibility to radiation retinopathy. In the 45–55 Gy dose range, the risk of radiation retinopathy increases with fraction size and individual dose fractions to the retina should not exceed 1.8–1.9 Gy.[3]

The two known factors exacerbating radiation retinopathy are chemotherapy and diabetes. A 4-fold increase in the risk of radiation retinopathy was noted by Chan and Shukovsky[8] in patients who received concurrent systemic 5-fluorouracil compared with patients treated with the same doses of radiation alone for nasal cavity or paranasal sinus cancer. The study by Parsons *et al.*[3] revealed that of their 12 patients who received 45–51 Gy, 4 of 10 patients treated with irradiation alone developed radiation retinopathy compared with 2 of 2 treated with radiation and chemotherapy.

Histopathological and ultrastructural studies by Archer *et al.*[4] confirm that the primary vascular event in radiation retinopathy is endothelial cell loss and capillary closure, similar to diabetic retinopathy. In a case report, Viebehn *et al.*[2] describe a diabetic patient who developed fulminant radiation retinopathy after receiving 30 Gy in 15 fractions over 3 weeks to one eye. Similarly, the lowest dose associated with radiation retinopathy in a series of 64 patients was 45 Gy delivered as 52 fractions (0.87 Gy twice per day) over 38 days to the nasal half of each retina for advanced skin cancer in a 61-year-old diabetic.[3]

Pregnancy has been shown to aggravate diabetic retinopathy, probably secondary to the increase in level of clotting factors.[9] It would be tempting to assume that pregnancy is an additional risk factor that could accelerate radiation retinopathy. Although the retinopathy in our patient initially appeared to respond to laser photocoagulation, its worsening in the third trimester followed by quiescence following delivery, without further laser, would tend to support this hypothesis.

Radiation-induced retinal changes develop over a long period. Amoaku and Archer[10] found the interval between radiation treatment and detection of radiation retinopathy varies between 1 and 8.5 years (mean 4.7 years). They suggest that radiation retinopathy has a long latency and that long-term follow-up and sequential fundoscopy will increase early detection and optimise treatment with laser photocoagulation. This point has been borne out by our patient, who presented 3 years after radiotherapy with advanced proliferative retinopathy.

While spontaneous improvement of radiation retinopathy may occur, this is an infrequent event.[1] Kinyoun *et al.*[11] found that new vessels had resolved in 91% (10/11 cases) of patients who were treated with panretinal photocoagulation for proliferative radiation retinopathy. They conclude that panretinal photocoagulation has long-term effectiveness in decreasing the proliferation of new vessels in radiation retinopathy.

This case highlights the importance of long-term follow-up for all cases of cephalic radiation. In particular, those patients with added predisposing factors such as chemotherapy and diabetes need to be reviewed more frequently, especially during pregnancy.

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