Reminder of important clinical lesson

Late onset of subfoveal choroidal neovascularisation following cerebral radiotherapy

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Summary

A report of choroidal neovascularisation (CNV) associated with radiation retinopathy. A 43-year-old Caucasian man presented with a 4-week history of sudden loss of central vision in the left eye, 8.5 years following radical radiotherapy for left temporo-parietal anaplastic astrocytoma. His visual acuity was 6/6 in the right eye and 6/60 in the left eye. Ophthalmoscopy of the left eye showed central macular pigmented area surrounded by subretinal fluid, haemorrhage and exudates. Fundus fluorescein angiography revealed left subfoveal CNV with surrounding macular oedema and peripheral retinal ischaemia. Radiation retinopathy associated CNV is a late ocular complication of cerebral radiotherapy. It should be investigated as a possible aetiology of severe visual loss in long-term survivors of cerebral tumours who have previously received radiotherapy.

BACKGROUND

Anaplastic astrocytoma has a median survival of 2 years.¹ Patients surviving longer are susceptible to relatively rare, later complications of their condition and treatment. Radiation retinopathy can occur several years after cerebral radiotherapy for cancers of the head and neck. Severe visual loss in radiation retinopathy occurs from macular oedema, foveal non-perfusion, retinal ischaemia, retinal detachment and neovascular glaucoma. Choroidal neovascularisation (CNV) is a rare cause of sudden and severe visual loss in radiation retinopathy.^{2–4} The authors report the case of a young patient who developed CNV associated with radiation retinopathy 8.5 years following cerebral radiotherapy.

CASE PRESENTATION

A 43-year-old Caucasian man presented with a 4-week history of sudden loss of central vision in the left eye. His medical history included a surgical excision followed by high dose radical radiotherapy for left temporo-parietal anaplastic astrocytoma 8.5 years ago previously. The total dosage was 55.07 Gy delivered in 30 fractions of which one was 2.0 Gy and 29 were at a slightly reduced dose of 1.83 Gy in view of the presence of a large amount of healthy brain tissue. All or part of the left retina received the complete 55.07 Gy of radiotherapy (figure 1). This was subsequently followed by chemotherapy for 9 months. He remained on long-term carbamazepine to control his epilepsy, dexamethasone for headaches and hydrocortisone for adrenal suppression. There was no history of diabetes, hypertension or serum lipid abnormalities. He is a non-smoker.

Visual acuity was 6/6–1 in the right eye and 6/60 in the left. Both the eyes had no significant refractive error. Anterior segment examination and intraocular pressures were normal in both eyes. Fundal examination of the left eye revealed considerable macular oedema, haemorrhage and exudation in the macular region (figure 2). Right fundal

examination was normal with no evidence of age-related macular degeneration. There were no signs of vitreous or choroidal inflammation in either eye.

INVESTIGATIONS

Fundus fluorescein angiography (FFA) revealed a left subfoveal CNV, which showed hyperfluorescence with filling of the CNV in early phase and progressive leakage in late phase. This was associated with surrounding macular oedema and peripheral retinal ischaemia (figure 3). FFA of the right eye showed mild telangiectasia in the macular region and peripheral retinal ischaemia.

DIFFERENTIAL DIAGNOSIS

In view of the significant medical history, other causes of CNV were eliminated and the patient was diagnosed as having radiation retinopathy associated with CNV.

OUTCOME AND FOLLOW-UP

Despite receiving thorough advice and counselling about his condition, the patient declined any active medical intervention. Over the next 6 months the left visual acuity deteriorated to 1/60 with a further increase in subretinal fluid and exudates.

DISCUSSION

Our patient had made an excellent systemic recovery following his primary treatment for anaplastic astrocytoma and was doing very well to survive beyond 8 years. Long-term survivors of such malignancies are susceptible to relatively rare effects of their condition and treatment. Specific ocular effects include atrophy and telangiectasia of the periorbital skin, dry eye syndrome, neurotrophic corneal ulceration, neovascular glaucoma, cataract, radiation retinopathy and optic neuropathy.⁵

Figure 1 External beam radiotherapy plan indicating the area that the radiotherapy was delivered to. This included all or part of the left retina.

The incidence of radiation retinopathy depends on both the total radiation dose and fraction size. In a retrospective study of 43 eyes of 25 patients exposed to fractionated external beam irradiation for treatment of advanced nasal and paranasal cancer, Takeda *et al*⁶ reported that the radiation dose and the area of retina irradiated are the most important factors in the development of severe complications in radiation retinopathy. The incidence increases in doses more than 50 Gy,⁶ although it has also been reported in doses that were considered safe.⁷ Amoaku and Archer⁸ found that the interval between external beam radiation treatment and the detection of radiation retinopathy was between 1.0 and 8.5 years (mean 4.7 years). Our patient received 55.07 Gy of radiation, which was higher than recommended dose and directed over a large area due to the

aggressive nature of the tumour. Although he presented with ocular symptoms 8.5 years following the treatment, examination suggested chronic maculopathy of no less than 6 months' duration.

Radiation retinopathy is characterised by delayed onset of slowly progressive occlusive vasculopathy. Histological findings show a thickening of arteriolar and capillary walls and loss of endothelial cells. Associated retinal lesions include microaneurysms, intraretinal oedema, exudation, cotton wool spots and haemorrhage. Cotton wool spots occur transiently with later evolution of large areas of capillary non-perfusion. Widespread capillary closure and retinal ischaemia may lead to retinal and disc neovascularisation, vitreous haemorrhage and retinal detachment. The posterior pole is more sensitive to radiation than the

Figure 2 Fundus photograph of the left eye showing oedema, haemorrhage and exudation in the macular region.

Figure 3 Fundus fluorescein angiography of the left eye demonstrates subfoveal choroidal neovascularisation (CNV). Note hyperfluorescence in early phase, with filling of the CNV in the mid phase and progressive leakage in late phase.

peripheral retina. CNV is a rare manifestation of radiation retinopathy.^{2–4} Our patient had most of the above mentioned retinal lesions involving the posterior pole. The authors did not observe any cotton wool spots due to chronicity of the maculopathy.

Current options for the management of radiation retinopathy include pan retinal photocoagulation for proliferative disease and focal laser or photodynamic treatment for radiation maculopathy. Radiation maculopathy has also been treated with corticosteroids, anticoagulation and hyperbaric oxygen treatment.⁵

Vascular endothelial growth factor (VEGF) is an angiopoietic growth factor, which is known to play an integral role in the formation of CNV.⁹ Recently, several anti-VEGF

agents (bevacizumab, pegaptanib and ranibizumab) have become available, which have shown unprecedented efficacy in treating CNV due to age-related macular degeneration and other inflammatory conditions. In a recent series of 21 patients, Finger PT¹⁰ reported an improvement in radiation maculopathy following intravitreal bevacizumab with 86% of his patients showing stable or improved visual acuities. Our patient developed radiation maculopathy with CNV and the treatment options would have been photodynamic treatment with intravitreal triamcinolone or intravitreal anti-VEGF treatment. Unfortunately the authors were unable to assess the potential benefits of anti-VEGF treatment in our patient as he refused any active medical intervention.

Learning points

- ▶ Median survival of anaplastic astrocytoma is 2 years. Patients surviving longer should be actively monitored for the relatively rare late effects of the medical condition and treatment.
- ▶ Patients who have been exposed to high doses of radiation over a large treatment area have the potential to develop radiation retinopathy, which can present as a reduction or distortion in vision. These patients should urgently be referred for further ophthalmic investigation.
- ▶ Intravitreal anti-VEGF agents, which are highly effective in treating many types of CNV, have the potential to effectively treat radiation retinopathy related CNV and preserve vision in such patients.

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Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Laws ER**, Parney IF, Huang W, *et al.* Survival following surgery and prognostic factors for recently diagnosed malignant glioma: data from the Glioma Outcomes Project. *J Neurosurg* 2003;**99**:467–73.
2. **Boozalis GT**, Schachat AP, Green WR. Subretinal neovascularization from the retina in radiation retinopathy. *Retina* 1987;**7**:156–61.
3. **Spaide RF**, Borodoker N, Shah V. Atypical choroidal neovascularization in radiation retinopathy. *Am J Ophthalmol* 2002;**133**:709–11.
4. **Berker N**, Aslan O, Batman C, *et al.* Choroidal neovascular membrane in radiation retinopathy. *Clin Experiment Ophthalmol* 2006;**34**:625–6.
5. **Durkin SR**, Roos D, Higgs B, *et al.* Ophthalmic and adnexal complications of radiotherapy. *Acta Ophthalmol Scand* 2007;**85**:240–50.
6. **Takeda A**, Shigematsu N, Suzuki S, *et al.* Late retinal complications of radiation therapy for nasal and paranasal malignancies: relationship between irradiated-dose area and severity. *Int J Radiat Oncol Biol Phys* 1999;**44**:599–605.
7. **Gupta A**, Dhawahir-Scala F, Smith A, *et al.* Radiation retinopathy: case report and review. *BMC Ophthalmol* 2007;**7**:6.
8. **Amoaku WM**, Archer DB. Cephalic radiation and retinal vasculopathy. *Eye (Lond)* 1990;**4**:195–203.
9. **Ferrara N**. Vascular endothelial growth factor: basic science and clinical progress. *Endocr Rev* 2004;**25**:581–611.
10. **Finger PT**. Radiation retinopathy is treatable with anti-vascular endothelial growth factor bevacizumab (Avastin). *Int J Radiat Oncol Biol Phys* 2008;**70**:974–7.

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