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| Citation | Peeler, Crandall E., and Dean M. Cestari. 2016. “Radiation optic neuropathy and retinopathy with low dose (20 Gy) radiation treatment.” American Journal of Ophthalmology Case Reports 3(1): 50-53. doi:10.1016/j.ajoc.2016.06.008. http://dx.doi.org/10.1016/j.ajoc.2016.06.008. |
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| Published Version | doi:10.1016/j.ajoc.2016.06.008                                                                                                                                                                                                                                 |
| Citable link | http://nrs.harvard.edu/urn-3:HUL.InstRepos:35981972                                                                                                                                                                                                                  |
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Case report

Radiation optic neuropathy and retinopathy with low dose (20 Gy) radiation treatment

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ABSTRACT

Purpose: To report a case of optic neuropathy and retinopathy from a dose of radiation traditionally thought to be safe to the visual system and discuss strategies for preventing vision loss when using radiation to treat intraocular tumors.

Observations: A 44-year-old woman presented with new, painless vision loss in the left eye eighteen months after receiving proton beam radiotherapy (20 Gy dose delivered in two 10 Gy fractions) for a uveal metastasis of lung cancer. The dilated funduscopic examination revealed optic disc swelling and retinal hemorrhages and an MRI of the brain and orbits demonstrated enhancement of the left optic nerve head, findings consistent with radiation optic neuropathy (RON) and retinopathy. Risk factors for developing RON included coincident use of oral chemotherapy and relatively large fractionated doses of radiation.

Conclusions and importance: Though cumulative radiation doses to the anterior visual pathway of less than 50 Gy are traditionally felt to be safe, it is important to consider not just the total exposure but also the size of individual fractions. The single-dose threshold for RON in proton beam treatment has yet to be defined. Our case suggests that fractions of less than 10 Gy should be delivered to minimize the risk of optic nerve injury.

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1. Introduction

Ionizing radiation is frequently used in the treatment of brain, sinus, orbital, and intraocular tumors, and a small percentage of patients develop vision loss as a consequence of bystander injury to the anterior visual pathway. Radiation optic neuropathy (RON) is thought to result from dysfunction of the vascular endothelium, with endothelial cell loss leading to breakdown of the blood-brain barrier and subsequent exudation, vascular occlusion, and hypoxia.1-6 Vision loss from radiation is typically delayed, occurring an average of 18 months following treatment.5,6

Fortunately, the risk of RON is thought to be low at cumulative radiation doses of less than 50 Gy, though this threshold may be lower in patients receiving concurrent chemotherapy or with tumors compressing the optic nerves or chiasm.7-7 We report a case of a patient who developed RON and retinopathy from a relatively low dose (20 Gy) of proton beam radiation, delivered in two 10 Gy fractions.

2. Case report

A 44-year-old woman with a history of non-small cell lung cancer (NSCLC) with uveal metastases — treated 18 months prior with a 20 Gy dose of proton beam radiotherapy to the left macula (Fig. 1), delivered in two 10 Gy fractions — presented with a three-day history of new, painless vision loss in the left eye. Visual acuity was 20/20, right eye and 20/40, left eye. There was dyschromatopsia and an afferent pupillary defect on the left. Intraocular pressures were normal bilaterally and the anterior segment examination was unremarkable.

Ophthalmoscopy revealed swelling of the left optic nerve with adjacent nerve fiber layer hemorrhage and scattered dot-blot hemorrhages throughout the macula (Fig. 2). Also clearly apparent on the funduscopic examination were several small, white subretinal lesions along the vascular arcades in the peripheral retina of the right eye and a larger chorioretinal scar in the
superior macula on the left, corresponding to the patient’s previously diagnosed uveal metastases. Comparison to prior fundus photographs demonstrated stability of these lesions since the time of proton beam treatment and initiation of maintenance oral chemotherapy (crizotinib) 18 months earlier. Hummery visual field testing revealed an area of inferonasal depression near fixation in the left eye corresponding to the macular scar. MRI of the brain and orbits with gadolinium demonstrated enhancement at the left optic nerve head consistent with RON (Fig. 3). Her new visual symptoms, optic nerve swelling, and
Retinal findings were attributed to radiation injury to the optic nerve and retina.

Five weeks following presentation with RON, the patient returned with sudden worsening of her vision on the left. Visual acuity was 20/20, right eye and 20/600, left eye. Repeat ophthalmoscopy demonstrated neovascularization of the disc and a vitreous hemorrhage.

Over the next three months, her vitreous hemorrhage increased in density with further decline in her vision to light perception. She was therefore taken to the operating room for a pars plana vitrectomy. Intraoperatively, she was noted to have sclerotic retinal vasculature inferiorly with evidence of decreased retinal perfusion and this area was treated with endolaser photocoagulation. She also received an intravitreal injection of bevacizumab at the end of the surgery to treat the neovascularization.

One month following surgery, her vision had improved to 20/200 on the left. Dilated fundus examination revealed a clear vitreous cavity. The swelling of the left optic nerve had resolved and the disc now appeared pale. Her retinopathy had resolved and the neovascularization had regressed.

The patient provided written consent for publication of personal information including medical record details and photographs.

3. Discussion

Our case demonstrates the importance of considering not just the cumulative radiation dose that the optic nerves can tolerate but also the size of each fraction to minimize the risk of RON. Previous studies of external beam radiotherapy involving the anterior visual pathway have demonstrated that single doses of 1.9 Gy or less are typically safe. The single-dose tolerance with stereotactic radiosurgery is estimated to be 8–12 Gy.

The single dose threshold for RON in proton beam treatment has yet to be defined, though one would expect it to be near that of photon radiation once adjusted for the increased relative biological effectiveness. A study of 577 patients receiving proton beam radiotherapy for intraocular tumors identified a cumulative threshold dose of 30 cobalt Gy equivalents (CGE, 27.3 proton Gy × 1.1 relative biologic effectiveness) below which the risk of RON was minimal. Beyond this dose, there was a sharp upturn in the RON incidence curve with the risk approaching 100% at a cumulative dose of 70 CGE. In this study, treatments were delivered in 5 equal fractions, suggesting that single doses to the optic nerve of 6 CGE or less were well tolerated.

Fig. 3. Magnetic resonance imaging of the brain. A. Axial T1-weighted image (pre-contrast). B. Axial T1-weighted image (post-contrast), showing enhancement of the left optic nerve head. C. Coronal T1-weighted image (post-contrast), showing enhancement of the left optic nerve.
4. Conclusion

Our patient received proton beam radiotherapy to a uveal metastasis in the left macula and subsequently developed RON. Though the cumulative radiation dose was relatively low, the treatment was administered in two 10 Gy fractions. While larger scale studies are needed, this case suggests that smaller fractionated doses of proton beam radiation should be considered when treating intraocular tumors, particularly in patients receiving concurrent chemotherapy.

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