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Letter to the Editor

Radiation-Induced Neovascular Glaucoma: Dose and Volume Issues

Dear Editor:
I read with great interest the article by Jeon et al., titled 'Neovascular glaucoma following stereotactic radiosurgery for an optic nerve glioma: a case report' [1]. Eight months after the patient underwent radiosurgery in the affected orbit, the intraglobular mass regressed to a partially residual retroglobular nodule; however, neovascular glaucoma (NVG) developed in the same eye. The authors stated that the stereotactic image-guided robotic radiosurgery using the Cyberknife system for the treatment of optic nerve glioma (ONG) might cause NVG and should be selectively utilized. Although there seems to be a causal relationship between radiosurgery and the development of NVG, some issues need to be clarified.

First, the authors suggested the post-radiation development of cataract in the affected eye supports their speculation that radiation effects may be the most likely causative factor of NVG in their case. To demonstrate that a complication is radiation-induced, the radiation dose must be taken into account. The radiobiologic model of acute and late effects on normal human organs according to the radiation dose and volume has been well established through *in vivo* and *in vitro* studies, and it is true that radiotherapy can affect the retina, lens, conjunctiva, lacriminal apparatus, optic nerve, and eyelids. However, retinitis and optic neuropathy are found to occur following only high doses of radiation greater than 50 to 65 Gy, whereas cataracts are reported to develop following small radiation doses as low as 10 to 18 Gy, due to the differences in the sensitivities of the normal organs [2]. In the present case, the total irradiated dose of 16 Gy in four fractions was sufficiently high to cause lens opacity but was too low to have any effects on the retina or the optic nerve (16 Gy of four fractions equals 25 Gy with 2 Gy per fraction according to the biologically effective dose calculation, $\alpha/\beta=3$). In the uveal melanoma cases, which the authors referred to as "NVG after stereotactic radiosurgery for intraocular tumors," the target dose for the tumor apex was set at greater than 100 Gy. Moreover, plaque brachytherapy was used in those melanoma cases, instead of stereotactic radiosurgery [3].

Second, the volume irradiated is also an important factor in the development of NVG. Recently, Hirasawa et al. [4] found radiation damage to the anterior segment of the eye and the optic disk to be a risk factor for NVG based on a dose–volume histogram analysis. In their study, both the dose to the anterior segment of the eye and the optic disc and the volume irradiated with greater than 50 Gy were statistically significant factors contributing to the development of NVG. Current advances in planning techniques for stereotactic radiosurgery aimed to minimize the dose to the anterior segment and the disc can reduce the risk of this complication. One of these new instruments, the CyberKnife robotic radiosurgery system (Accuray, Sunnyvale, CA, USA), used in this case, enables delivery of high radiation doses to the target with a much steeper dose gradient outside the tumor volume compared with those of other treatment systems that have been reported to produce NVG [5]. Using the Cyberknife system, far less than 50% of the total dose generally affects the anterior segment of the eye. Dose and volume issues need to be carefully considered when determining the cause-and-effect relationships between radiation therapy and its associated complications.

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Author reply

Dear Editor:

We hypothesized that the target tissue is an important issue in this case. Kline et al. [1] included patients with pituitary lesion, and the radiation effect focused on the pituitary gland would be attenuated in ocular tissue. The radiation plan for melanoma would be localized to the specific retinal lesion [2,3] and would have an effect on the adjacent vitreous and optic disc. Radiation to the entire intraconal optic nerve and optic nerve head will show distinct responses because they contain the central retinal artery and veins. If the central retinal artery and veins are damaged, whether by the destroyed adjacent tissue or from the radiation itself, the ocular blood flow will be severely disturbed, and various cytokine levels, such as vascular endothelial growth factor, will be elevated, a condition which is known to cause neovascular glaucoma (NVG) [4,5]. In this case, NVG developed after low-dose radiation to the optic nerve, and we believe that this illustrates the need for careful planning of radiation therapy on the optic nerve.

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