The Role of Combined Therapy in the Treatment of Retinopathy and Optic Neuropathy Due to Radiotherapy in the Uveal Melanoma

Yasemin Benderli Cihan[1]

[1]Department of Radiation Oncology, Kayseri Education and Research Hospital, Kayseri, Turkey

Address for correspondence Yasemin Benderli Cihan, MD, Department of Radiation Oncology, Kayseri Education and Research Hospital, Sanayi District, Ataturk Boulevard, Hastane Street, No 78, 38010 Kocasinan, Kayseri, Turkey (e-mail: cihany@erciyes.edu.tr).

Asian J Oncol 2020;6:1–2

Abstract

Introduction Uveal melanoma has a relatively low incidence. Transpupillary thermotherapy (TTT), hypofractioned stereotactic radiotherapy (RT), stereotactic radiosurgery, plaque brachytherapy, charged particle radiation therapy, local tumor resection, enucleation, and exantation are applied in the treatment.

Methods The importance given to radiotherapy has increased to get more satisfactory results while treating the patient. However, it is the treatment of radiation retinopathy and optic neuropathy from complications.

Results Radiation retinopathy and optic neuropathy are the most important complications related to radiotherapy in the treatment of uveal melanoma. In recent years, many studies have been performed on the treatment of radiation retinopathy and optic neuropathy.

Conclusion The consecutive use of triamcinolone in combination with anti-VEGF supports that it may be a future therapeutic agent in the treatment of complications.

Keywords
- uveal melanoma
- radiotherapy
- retinopathy
- optic neuropathy

Introduction

Uveal melanoma is the most common primary intraocular tumor in adults. It accounts for ~3 to 5% of all melanomas seen in humans.[1-3] Iris develops from melanocytes of neural crest origin in ciliary body and choroid. According to cell types, epithelioid, spindle, and mixed groups are divided into three groups. Spindle cell–type melanomas are low risk tumors and have good prognosis. Epithelioid and mixed cell–type melanomas are high-risk tumors and are associated with poor prognosis. Treatment is done according to tumor size, location, and spread, presence of concomitant disease; general condition of the patient; and life expectancy. Transpupillary thermotherapy (TTT), hypofractioned stereotactic radiotherapy (RT), stereotactic radiosurgery, plaque brachytherapy, charged particle radiation therapy, local tumor resection, enucleation, and exantation are applied in the treatment.[2-5] Despite advances in diagnosis and treatment, survival rates of uvea melanoma have not improved over time. Five-year disease-related survival rate was found to be 81.6%.[2] The 2-, 5-, and 10-year metastasis rates were reported to be 10%, 25%, and 34%, respectively, regardless of tumor size.[3]

Methods

Until recently, enucleation was the only treatment option for uvea melanomas, and nowadays there is an increasing interest in alternative radiotherapy options for preservation of the eye and current vision. Plaque is preferred in small- and medium-sized tumors in which brachytherapy, stereotactic radiotherapy, stereotactic radiosurgery, and charged particle radiation treatment are aimed.[1,2,4,5] Although stereotactic radiotherapy has been reported to be successful with Gamma-Knife, it is not preferred because of high rates of radiation retinopathy and neovascular glaucoma.[2,5] Although the profit-loss ratio of RT treatment is very useful, it may cause some unwanted side effects due to the destructive effect of radiation on the retina. These side effects include lash loss,

DOI https://doi.org/10.1055/s-0040-1701391
ISSN 2454-6798.

retinal detachment, glaucoma, dry eye, cataract, retinopathy, and optic neuropathy. It is known that RT treatment options present in uveal melanomas have different side effects and development frequencies are variable.[1-5] Desjardins et al reported 5 and 10 years' local recurrence rate in patients with uvea melanoma with proton treatment as 4 and 10%, respectively, and the rate of metastases as 18.5 and 26.6%, respectively. Complications following 8 years of follow-up revealed 37% of the patients with maculopathy, 23.4% with glaucoma, 18% with optic neuropathy, 15% with cataract, 12% with eyelash loss, 8.5% with retinal detachment, and 6% with dry eye.[4]

Results

Radiation retinopathy and optic neuropathy are the most important complications related to radiotherapy in the treatment of uveal melanoma. Radiation retinopathy is a chronic, slowly progressive, occlusive vasculopathy of retinal capillaries due to endothelial damage in late-onset, slowly progressing vascular wall following radiation therapy. Although the pathogenesis of radiation optic neuropathy is not fully understood, it is considered as the radiation-induced necrosis of the optic nerve and chronicle. In particular, these complications can occur in 84% of cases after radiotherapy for cases with posterior uvea melanoma. The most important factors affecting the development of radiation retinopathy are radiation dose, radiation field, tumor location, diameter, spread, and presence of concomitant diseases (diabetes mellitus, hyperlipidemia, and hypertension). Currently, the optimal dose and number of fractions in the treatment of uveal melanoma is not clear. It is accepted that retinopathy will develop rarely under 35 Gy radiation dose and radiation retinopathy will develop in half of patients over 65 Gy. The time taken for the emergence of clinical findings with radiation therapy is variable. It can start at the earliest 3 months and at the latest 8 years.[5-11]

Discussion

In recent years, many studies have been performed on the treatment of radiation retinopathy and optic neuropathy. Systemic and intravitreal corticosteroids, focal or panretinal laser photocoagulation, photodynamic therapy, intravitreal anti-VEGF agents, intravitreal or periocular triamcinolone acetonide, and hyperbaric oxygen therapy have been tried in the treatment.[6-11] They applied intravitreal anti-VEGF for at least two injections to the choroidal melanoma case who developed radiation optic neuropathy after finger and chin plaque radiotherapy treatment. Decreased optic disc edema, reported a decrease in papillary hemorrhage.[6] Roelofs et al used intravitreal anti-VEGF and triamcinolone sequentially in patients with radiation papillopathy after plate brachytherapy for uveal melanoma and reported that combined use was effective.[9] Shah et al reported that triamcinolone plays a beneficial role in patients treated with refractory or progressive retinopathy.[11] In another study, it was reported that retinal bleeding, cotton-wool patches, and retinal edema decreased or resolved up to 10 years in patients receiving long-term intravitreal anti-VEGF therapy in patients with radiation retinopathy.[10]

Conclusion

Although uveal melanoma has a relatively low incidence, it has serious effects on quality of life and survival. Because of these reasons, the importance given to radiotherapy has increased to get more satisfactory results while treating the patient. However, it is the treatment of radiation retinopathy and optic neuropathy from complications. The consecutive use of triamcinolone in combination with anti-VEGF supports that it may be a future therapeutic agent in the treatment of complications.

Funding
None.

Conflict of Interest
None declared.

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