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Recurrent Radiation Retinopathy and Optic Neuropathy after Cranial Irradiation Therapy Treated by Intravitreal Bevacizumab

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Authors' contributions

This work was carried out in collaboration between all authors. Author SO designed the study, wrote the protocol and wrote the first draft of the manuscript. Author MS managed the literature searches. Author MC revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Purpose: To report a case of radiation retinopathy and optic neuropathy after head irradiation therapy treated by intravitreal triamcinolone and bevacizumab
Methods: Case report.
Case: A 38 year old woman presented with visual acuity impairment. She received cranial radiation therapy (dose: 35Gy) for brain metastasis 1 year ago. The best-corrected visual acuity (BCVA) was 16/20 in the right and 4/20 in the left eye. Fundus examination showed hard exudate, retinal hemorrhage, and macular edema in both eyes. Triamcinolone acetonide was injected into the vitreous of both eyes. BCVA improved to 20/20 in the right and 12/20 in the left eye after 4 weeks. Both eyes showed recurrence of macular edema 3 months after the injection. BCVA was 2/20 in the right and 6/20 in the left eye. Fundus examination showed retinal exudation and hemorrhage around the optic nerve and blurring of the optic nerve head borders was established. Three scheduled monthly injections of Bevacizumab were administered intravitrealy. After 3 injection, BCVA was 16/20 and 18/20 in her right and left eyes respectively.

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Conclusion: Intravitreal bevacizumab was well tolerated, improved vision, and reduced retinal edema. No ocular or systemic side effects were noted.

Keywords: Bevacizumab; optic neuropathy; radiation retinopathy; recurrence; triamcinolone.

1. INTRODUCTION

Radiation retinopathy is one of the most common causes of visual morbidity in patients receiving irradiation for malignancies. The first radiation retinopathy case was reported by Stallard in 1933 as a clinic manifestation with exudates, hemorrhages, macular edema and optic disc edema similar to diabetic retinopathy [1]. Since then, radiation retinopathy remains its importance being a devastating complication.

2. CASE REPORT

A 38 year old woman presented to our hospital with bilateral visual acuity impairment. Tracing back her history, she was diagnosed with metastatic breast cancer nine years ago. She received several chemotherapy and radiotherapy achieving complete remission. One year ago she was diagnosed with brain metastases. She received total dose of 35 Gy cranial radiation therapies in fractions. Last fraction was received one year before the onset of radiation retinopathy and no radiation therapy was administered during follow up. She had no other history of systemic and ocular disease.

The best-corrected visual acuity (BCVA) was 10/20 in the right eye and 4/20 in the left eye. Intraocular pressures (IOP) were 15 mmHg OD and 17 mmHg OS respectively. Anterior segment examinations of both eyes were completely normal and no cataract formation was observed. Fundus examination showed hard exudates, cotton wool spots, intraretinal hemorrhages and macular edema in both eyes (Fig. 1). Fluorescein angiography (FA) revealed microaneurysms in the subfoveal area and no capillary perfusion in the areas corresponding to cotton wool spots. Optical coherence tomography (OCT) showed bilateral increase in foveal thickness, retinal cystic changes and subretinal fluid in localized areas of macula in both eyes (Fig. 2).

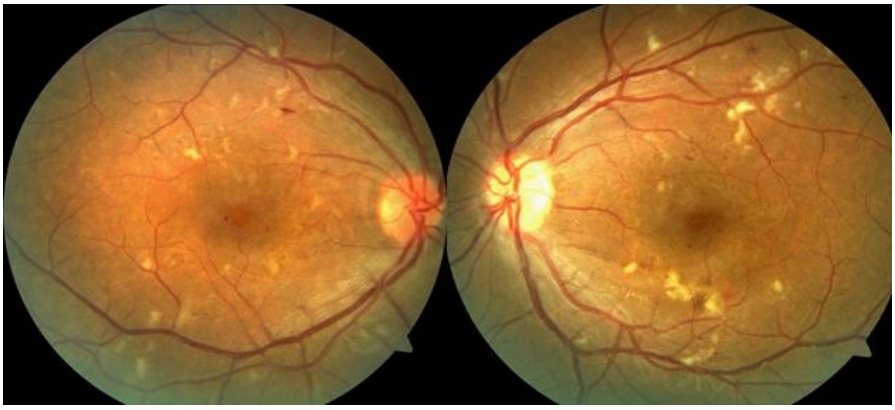

Fig. 1. Fundus examination revealed hard exudates, cotton wool spots, intraretinal hemorrhages and macular edema before IVT injection

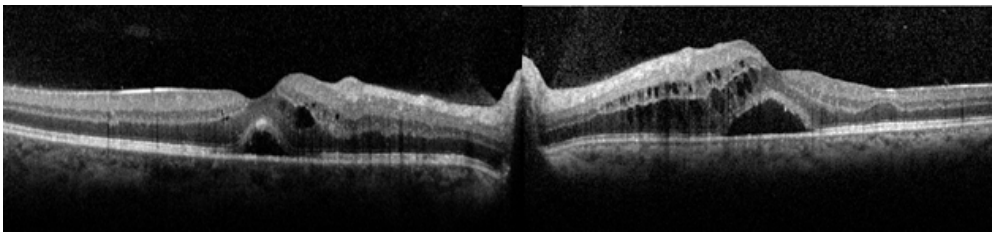

Fig. 2. OCT showed bilateral increase in foveal thickness, retinal cystic changes and subretinal fluid before IVT injection

Triamcinolone acetonide (0.1 cc of 40 mg/mL) was injected into the vitreous of both eyes. 4 weeks after intravitreal injections, BVCA improved to 20/20 in the right and 12/20 in the left eye. OCT disclosed regression of macular edema in the right eye and parafoveal intraretinal cystic changes in the left eye.

Both eyes showed recurrence of macular edema 3 months after the injection. BCVA was 2/20 in the right eye 6/20 in the left eye. Fundus examination showed cotton wool spots, macular edema, blurring of the optic nerve head borders and swelling of optic disc in both eyes (Fig. 3). FA showed widespread dye leakage and peripapillary hyperfluorescence. OCT demonstrated significant subfoveal fluid in the right eye and moderate subfoveal fluid in the left eye as well as cystoid macular edema in both eyes (Fig. 4). Three scheduled injections of Bevacizumab were administered intravitrealy in the dose of 1.25 mg/0.05 ml at monthly intervals. After 3 injections, BCVA was 16/20 in the right and 18/20 in the left eye respectively. Anterior segment examinations of both eyes were normal and lenses were clear. Decrement in macular edema and significant reduction in retinal hemorrhages, exudates, cotton wool spots and microangiopathy were documented (Fig. 5). No recurrence of macular edema noted since the third intravitreal injection.

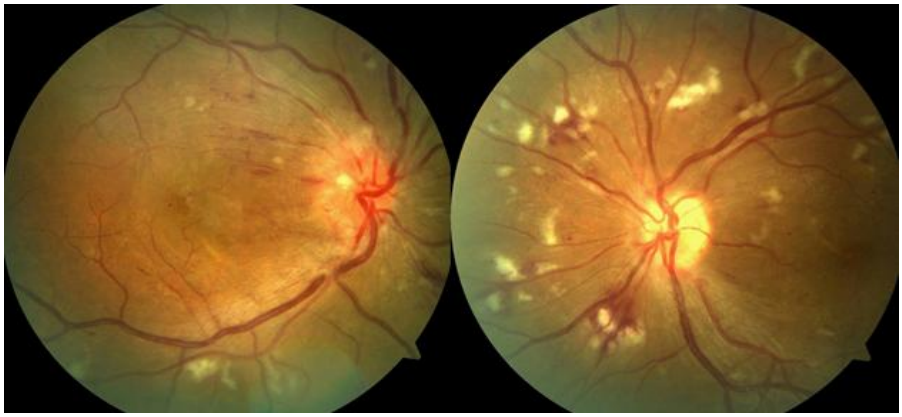

Fig. 3. Fundus examination showed cotton wool spots, macular edema, blurring of the optic nerve head borders and swelling of optic disc three months after IVT injection

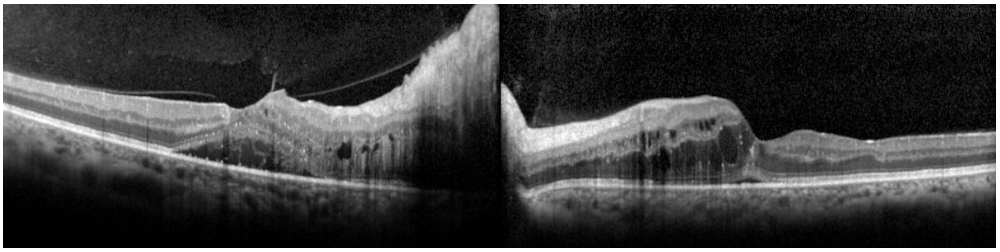

Fig. 4. OCT revealed significant subfoveal fluid in the right eye, moderate subfoveal fluid in the left eye and cystoid macular edema in both eyes before IVB injections

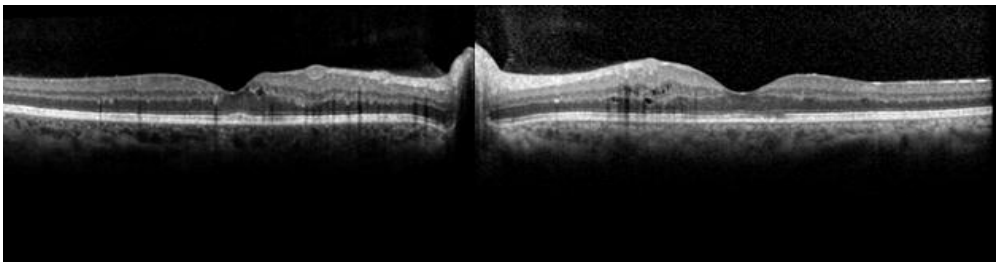

Fig. 5. OCT showed significant decrement in macular edema after three scheduled IVB injections

3. DISCUSSION

Radiation retinopathy (RR) is a common, over threshold ionizing radiation dose dependent, progressive retinal and papillary occlusive vasculopathy and the most common sight limiting complication of radiation treatment.

The risk factors of RR are effective (cumulative) radiation dose, accompanying systemic diseases like diabetes mellitus and receiving chemotherapy [2]. Pregnancy is also associated with increase of RR risk [3,4]. Our patient had metastatic breast cancer and received chemotherapy.

Cumulative radiation dose that causes RR is different in each patient due to patient's tolerance, hyper fractionation of radiation therapy, chemotherapy and systemic diseases. [5]. Risk of retinopathy increases steadily at cumulative doses more than 45 Gy [6]. Delivering radiation in fractions decreases the risk of retinopathy if received fraction sizes do not exceed 1,8 - 2 Gy [5]. Although previous studies stated that RR risk increases at cumulative doses more than 45 Gy, our patient received total dose of 35 Gy in fractions. In our case, development of RR at lesser dose may be due to receiving several chemotherapies before cranial irradiation.

RR has a delay onset, typically after months or years of radiation therapy, and is slowly progressive [7]. In general; RR is seen around 18 months after treatment. The time of onset of RR may vary from 6 months to 3 years [4]. In our case initial symptoms of RR came along, 1 year after receiving cranial irradiation, consistent with previous studies and reviews.

Exposure of ionizing radiation has a destructive effect on endothelial cells of blood vessels due to DNA damage of direct exposure or free radicals' damage to cell membrane [4,8]. All underlying mechanisms lead to vascular inflammation and occlusive vasculopathy that causes ischemia [3]. Ischemia may cause retinal edema, neovascularization, rubeosis iridis, vitreous hemorrhage, tractional retinal detachment, optic neuropathy, papillopathy and optic atrophy [4]. In our case, findings like hard exudates, cotton wool spots, intraretinal hemorrhages, total blurring of the optic nerve head margin, widespread dye leakage, peripapillary hyperfluorescence and macular edema, are consistent with previous studies in literature.

There is no consensus about the treatment of RR. Developed treatment strategies have been had limited effect. Patients still utilize some treatment strategies including intravitreal bevacizumab (IVB), intravitreal triamcinolone acetonide (IVTA), intravitreal dexamethasone implant and laser photocoagulation. Shields et al. [5] reported that after IVTA injection (4 mg/0.1 mL) for macular edema due to RR, visual acuity was stable or improved in 91% (20/22) of patients by 1 month and 45% (14/31) by 6 months. Shah et al. [5] reported a case series of 81 patients who developed RR and received IVB 81 of 159 (50.9%) demonstrated 20/50 or better vision at mean follow up of 34.6 months [9]. IVB and IVTA have variable effects on the reduction of macular edema due to RR. The combination of IVB and IVTA may resolve macular edema in cases of severe RR or cases refractory to IVB monotherpay alone. The reason for this may be due to their different therapeutic mechanisms of action [10]. IVTA may utilize as consolidation treatment for patients with recalcitrant radiation maculopathy or as an adjuvant to IVB for refractory macular edema [10]. In our case, we preferred IVTA administration because of anti-inflammatory and edema resolving effect. After administration of 3 months, IVTA had a limited effect. Although IVB is not an on-label therapy for RR in our country, authorities gives special permission for the usage of IVB for recalcitrant RR. Due to recurrence of macular edema, IVB (1.25 mg/0.05 ml) were administered at monthly intervals for 3 months. Significant decrement in macular edema noted after scheduled IVB injections.

4. CONCLUSION

Scheduled intravitreal bevasizumab administration is an effective treatment in patients with recurrent radiation retinopathy.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this paper and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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