



E-ISSN: 2663-8274
P-ISSN: 2663-8266
www.ophthalmoljournal.com
IJMO 2021; 3(1): 93-95
Received: 04-11-2020
Accepted: 12-12-2020

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Radiation retinopathy masquerading diabetic retinopathy

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DOI: <https://doi.org/10.33545/26638266.2021.v3.i1b.68>

Abstract

Background: Radiation retinopathy (RR) can occur years after irradiation as a chronic and progressive retinal micro-angiopathy. The presentations of RR are similar to other retinal vaso-occlusive disorders like diabetic retinopathy, hypertensive retinopathy. The patient was referred to us as a case of diabetic retinopathy who had received intravitreal injections for macular edema without any improvement. A thorough evaluation revealed it to be a case of Radiation retinopathy. RR treatment includes laser photocoagulation, intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections, intravitreal steroid injections, and surgery.

Case presentation: We report a case of a 47-year-old diabetic male patient in whom RR developed following 30Gy of radiation therapy for Ethmoidal sinus carcinoma masquerading as Diabetic retinopathy. FFA was showing extensive ischemia of the retina, and OCT showing Macular edema. He received Pan retinal photocoagulation in both eyes followed by multiple intravitreal Anti-VEGF injections on a PRN basis and underwent Pars plana vitrectomy in the right eye for non-resolving vitreous hemorrhage.

Conclusion: The patient's vision improved only after treating the retinal ischemia with photocoagulation and later treating the macular edema. This report emphasizes the importance of differentiating this disease entity from other vaso-occlusive retinopathy by eliciting a detailed patient history and planning further management accordingly.

Keywords: Radiation retinopathy, Diabetic Retinopathy, Masquerading, Macular edema, Capillary Nonperfusion, Pan retinal photocoagulation, Ethmoidal sinus carcinoma

Introduction

Radiation retinopathy (RR) is a chronic and progressive condition resulting from exposure to any source of radiation, including external beam radiation, plaque brachytherapy, proton beam radiation, helium ion, and gamma knife radiotherapy [1]. RR may be secondary to the treatment of intraocular tumors such as choroidal melanomas, retinoblastomas, or non-ocular tumors like cephalic, nasopharyngeal, orbital, and paranasal tumors [1]. The presentations of RR are similar to other retinal vaso-occlusive disorders like diabetic retinopathy, hypertensive retinopathy. It presents with intraretinal hemorrhages, cotton wool spots, hard exudates, macular edema, and late stages with vitreous hemorrhage due to neovascularization of the retina, disc, or iris.

Case presentation

A 47 years old male was referred to our hospital as a case of both eyes Severe Non-proliferative diabetic retinopathy (NPDR) with non-resolving macular edema following intravitreal injections for further evaluation and management. He was a known diabetic for 15 years on regular treatment. BCVA in both eyes was 6/60. On examination of both eyes, the anterior segment was normal, and the fundus showed multiple hemorrhages and cotton wool spots with macular edema mimicking Severe NPDR associated with macular edema (Fig. 1).

As there was no improvement with past injections, he revealed a history of 30 Gy radiation therapy for Ethmoidal sinus carcinoma operated 18 months ago on further probing. FFA was done, which showed extensive capillary nonperfusion areas and telangiectatic vessels around the macula but no neovascularization evidence, suggestive of Radiation Retinopathy (Fig. 2). The patient's SD-OCT showed macular edema with a neurosensory detachment in both eyes (Fig. 3a&b). Multiple intravitreal anti-VEGF injections followed Pan retinal photocoagulation in both eyes. Grid laser was done once macular thickness decreased (Fig.

3c&d).

Over the next 18 months, he received intravitreal anti-VEGF injections in both eyes on a PRN basis and maintained good vision. The patient later presented with vitreous hemorrhage in the right eye, which was non-resolving, for which Pars plana vitrectomy was done. During follow-up, the patient developed carcinoma of the larynx, for which radiation therapy was given again. He presented five months post-irradiation with vitreous hemorrhage in the left eye for which additional retinal photocoagulation (Fig. 4) was done. Since then, he is on regular follow-up. On the last follow up, the patient was maintaining BCVA of 6/18 in RE and 6/24 in LE with stable radiation retinopathy.

Discussion & Conclusion

Radiation retinopathy (RR) can occur years after irradiation as a chronic and progressive retinal micro-angiopathy. The first report describing RR's posterior segment complications was that of Stallard in 1933, who characterized it as slowly progressive occlusive vasculopathy with delayed onset post-irradiation [2].

External beam irradiation 30 Gy or more is usually necessary to cause retinal damage, and a marked increase in the incidence of retinopathy is noted when the dose exceeds 50 Gy [3]. With external beam irradiation, retinal changes have been seen as early as three weeks and as late as seven years, mostly within six months to three years after therapy [4]. Nakissa *et al.* described that RR changes occur after treatment for nasopharyngeal carcinoma and sinus carcinoma [5]. Similarly, our patient received 30 Gy of radiation during the treatment of Ethmoidal sinus carcinoma and developed ocular signs 1-year post-irradiation.

RR and diabetic retinopathy share similar clinical features, and both concurrently add to the retinal ischemia. In RR, the earliest damage is to the capillaries' endothelial cells, causing focal capillary closure leading to irregular dilation of perifoveal and parafoveal microvasculature, relatively sparing pericytes. As the damage increases, there is leakage from retinal vessels leading to macular edema, retinal hemorrhages, cotton wool spots, hard exudates, and neovascularisation. In patients with concurrent diabetes mellitus, there is early loss of pericytes, which along with RR induced endothelial damage, causes early severe capillary nonperfusion and inner and outer retinal atrophy. Concurrent chemotherapy seems to have an additive effect on vascular radiation damage to the posterior segment [6].

Macular edema is the earliest manifestation of RR. OCT is a sensitive tool for evaluating macular edema, which shows subtle changes in foveal thickness, subsequently progressing to macular edema and, in late stages, shows inner and outer retinal atrophy [6]. Horgan *et al.* demonstrated that macular edema could be found on OCT approximately five months earlier than clinically detectable radiation maculopathy [6]. The fluorescein angiographic hallmark of RR is retinal capillary non-perfusion, implicating vascular decompensation as the primary pathway responsible for radiation damage to the retina. Other findings are microaneurysms, irregular foveal avascular zone, telangiectasia, focal or diffuse macular edema, and leakage from neovascularisation [4]. In our patient, all FFA features of RR were present but clinically were mimicking diabetic retinopathy, which misleads the diagnosis.

The course of management of RR is usually complicated. In most forms of ischemic retinopathies, Retinal photocoagulation remains the gold standard treatment.

However, the beneficial effect of prophylactic photocoagulation in RR remains unjustified. In cases with severe capillary nonperfusion 360° laser photocoagulation is indicated along with grid laser for macular edema [1].

In the case of maculopathy, Finger *et al.* concluded anti-VEGF helps suppress and halt the progression; dosage and number of injections should be titrated according to the response [7]. Contrary to this, our case, anti-VEGF worked only after PRP was done. We postulated that the VEGF load in our case was very high due to extensive ischemia; therefore, the initial injection had minimal effect on macular edema. Shields *et al.* reported the beneficial effects of intravitreal triamcinolone in RR induced macular edema [8]. Pars Plana vitrectomy is advised only in cases of non-resolving vitreous hemorrhage and tractional retinal detachment. Photodynamic therapy in RR related macular edema is tried in a few studies with good results [9]. Oral pentoxifylline and hyperbaric oxygen have been tried, but more studies are required to prove their efficacy and safety [1]. Similarly, in our patient, multiple treatment options were tried before achieving stability in the ocular condition and most important factor is to treat the retinal ischemia.

Thus, this case report emphasizes that diabetic retinopathy must be differentiated from radiation retinopathy, and both can coexist in the same patient. Long-term follow-up is required as RR is progressive retinopathy, and complications can develop after initial treatment success. The most helpful factor in establishing RR diagnosis is eliciting previous irradiation history that patients do not reveal easily, especially when treated for non-ocular carcinoma.

List of abbreviations

1. Radiation Retinopathy – RR.
2. Vascular endothelial growthfactor – VEGF.
3. Optical Coherence tomography – OCT.
4. Fundus Fluorescein Angiography – FFA.

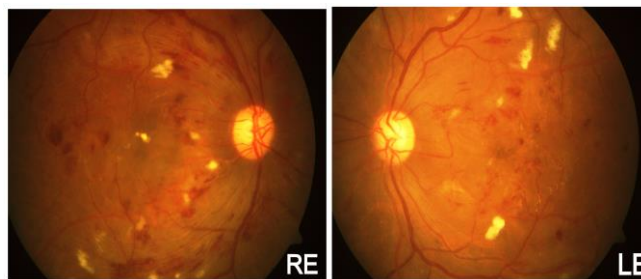


Fig 1: Colour fundus photograph of both eyes showing retinal hemorrhages, cotton wool spots, hard exudates, and macular edema.

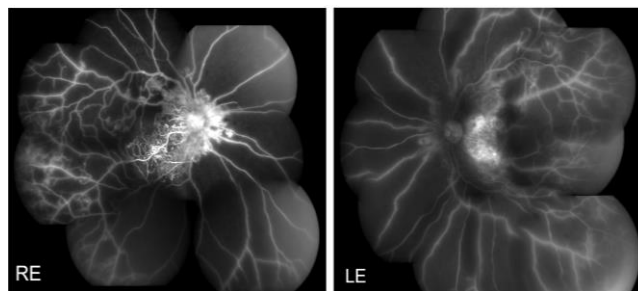


Fig 2: FFA montage picture of both the eyes showing microaneurysms, telangiectasia in the parafoveal area with macular edema, and extensive capillary nonperfusion areas in the periphery.

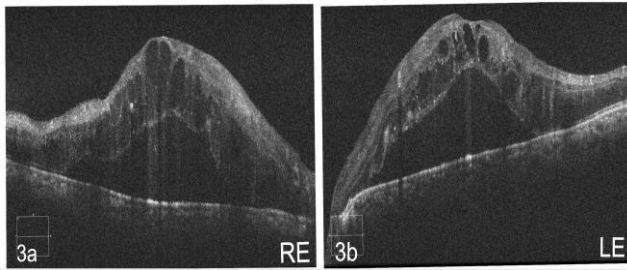


Fig 3a, 3b: SD-OCT at presentation, showing cystoid macular edema with a neurosensory detachment in both eyes.

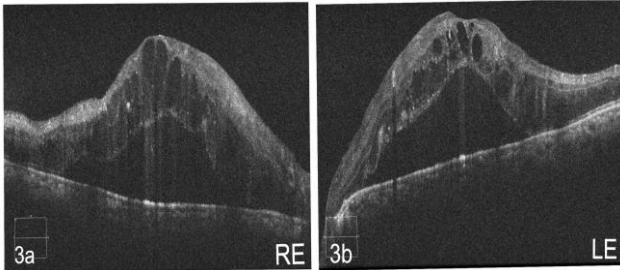


Fig 3c, 3d: SD-OCT at the last visit showing inner and outer retinal atrophy in both eyes.

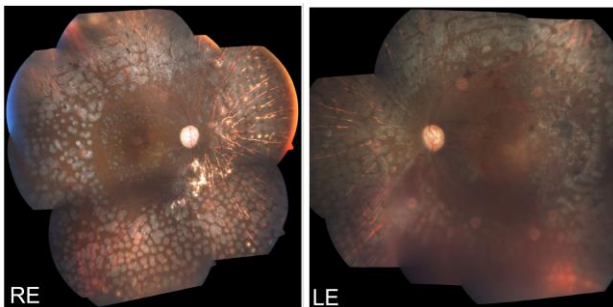


Fig 4: Colour montage of both the eyes at last visit; RE showed stable RR with PRP marks and grid laser marks. LE shows Stabilising RR post PRP with mild vitreous hemorrhage

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