Transient reversal of macular ischemia with intravitreal steroid implant injection in a case of radiation maculopathy

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Diabetic retinopathy (DR) is a well-known risk factor in the development of radiation maculopathy (RM). Steroids have been shown to improve the vision and reduce the macular thickness in patients with RM. This observational case report highlights altered course of DR after a course of radiotherapy for orbital lymphoma, after a single dose of intravitreal dexamethasone implant showed a dramatic revascularization of the ischemic macula, with a significant reduction in the size of ischemic area. This appears to be the first case in literature corroborating the favorable effect on steroids on retinal vasculature, seen angiographically.

Key words: Fundus fluorescein angiogram, intravitreal steroid implant, ischemic maculopathy, radiation maculopathy

Radiation maculopathy (RM) is a known vision-threatening complication with poor outcomes following radiation therapy to the periocular area. Steroids in various forms have been tried (periocular route and intravitreal route) either

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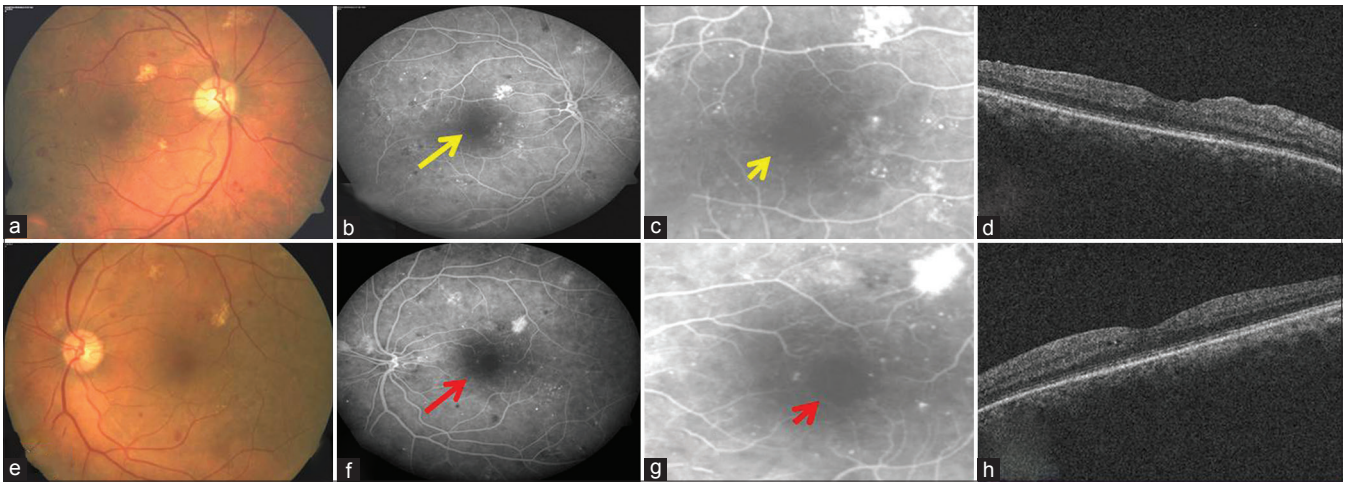

Figure 1: (a) Color fundus picture of the right eye showing neovascularization elsewhere. (b) and (c) Fundus fluorescein angiography showing neovascularization elsewhere with mildly distorted and irregular foveal avascular zone (yellow arrow). (d) The optical coherence tomography of the right eye showing a normal foveal contour with an epiretinal membrane. (e) Color fundus of the left eye showing proliferative diabetic retinopathy. (f and g) The fundus fluorescein angiography picture showing proliferative diabetic retinopathy and mildly irregular foveal avascular zone (red arrow). (h) The optical coherence tomography of the macula of the left eye showing a normal foveal contour

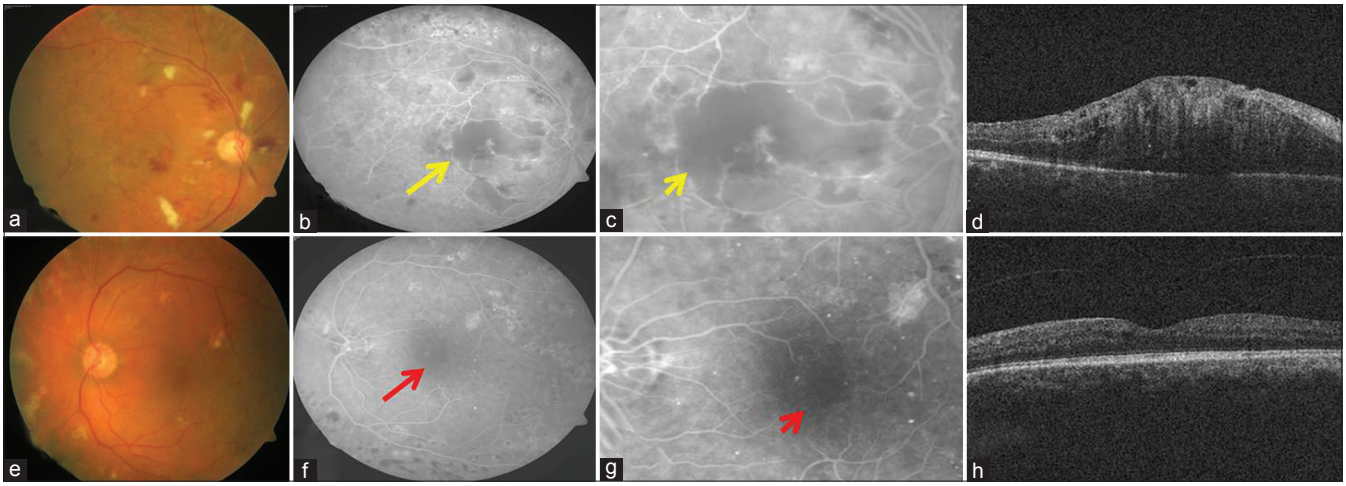

Figure 2: (a) Color fundus picture of the right eye taken 1 year after the radiation therapy, showing increased cotton wool spots and intraretinal hemorrhages over the posterior pole, suggesting radiation maculopathy. (b and c) Markedly enlarged and distorted foveal avascular zone (yellow arrow). (d) Increased central foveal thickness with macular edema and neurosensory detachment under the macula and ellipsoid zone disruption. (e-h) A stable left eye after the laser photocoagulation with resolving proliferative diabetic retinopathy and stable foveal avascular zone (red arrow)

prophylactically or therapeutically with partial success for the treatment of RM.[1,2] Recent introduction of the sustained release dexamethasone implant (Ozurdex®) for the treatment of RM has shown some promising results, with transient and long-term improvement in visual acuity and reduction in macular thickness.[3,4] The reduction in macular edema has been linked to the effect of steroids on regulating the capillary permeability and restoration of a compromised inner blood-retinal barrier. However, reperfusion of occluded perifoveal capillary network and a reversal of macular ischemia, albeit transient, as seen angiographically, has never been documented.

Case Report

A 66-year-old male with a history of diabetes mellitus, hypertension, and coronary artery disease was seen with chief complaint of floaters. On presentation, the visual acuity was 20/30, N6, and the intraocular pressure was 12 mmHg in both the eyes. The anterior segment evaluation was unremarkable. The dilated fundus evaluation showed the presence of proliferative diabetic retinopathy (DR) with few capillary dropout changes and mildly enlarged foveal avascular zone (FAZ) confirmed with fundus fluorescein angiography (FFA) [Fig. 1]. The optical coherence tomography (Cirrus HD-OCT 4000; Carl Zeiss Meditec Inc., Dublin, CA, USA, vertical raster scan through foveal center) at this stage showed a maintained foveal contour in both the eyes. The patient was advised panretinal photocoagulation in both the eyes. The condition remained stable for the next 2 years when he came with severe irritation and redness in the right eye. Examination showed dilated episcleral vessels. The patient was diagnosed with orbital lymphoma (non-Hodgkin's) on the right side, which was also confirmed with incisional biopsy. He was advised external beam radiotherapy, and a total of 4500 cGy was delivered to the right orbit in 25 fractionated doses. He presented 1 year

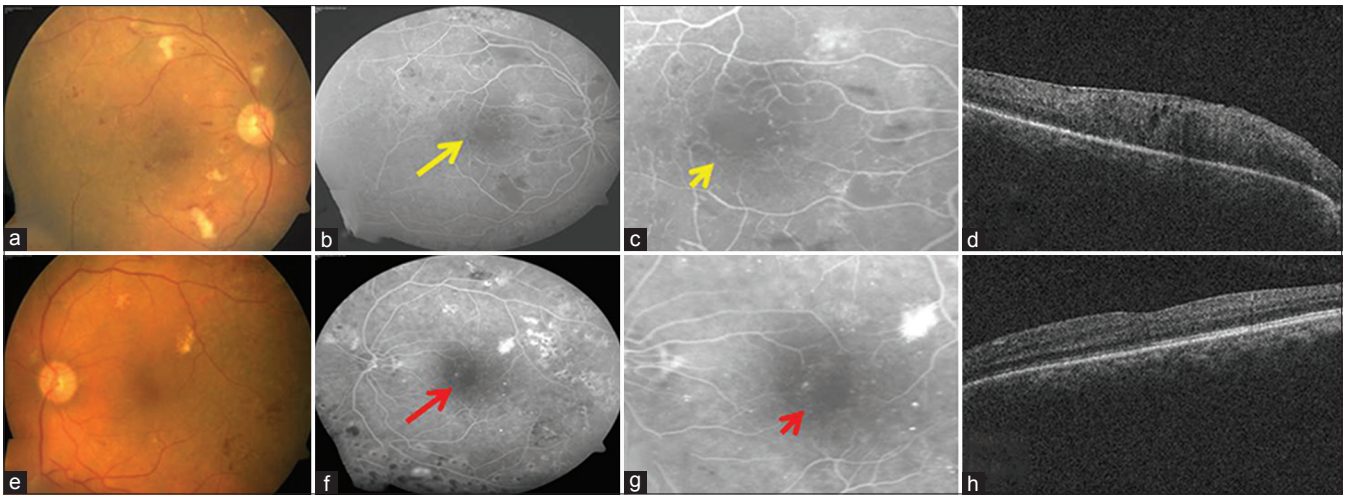

Figure 3: (a) The color fundus picture of the right eye 2 months after dexamethasone implant injection showing resolving cotton wool spots and retinal hemorrhages, (b and c) Partial but significant revascularization of the macular capillary network with reduced size of the ischemic extent of foveal avascular zone (yellow arrow). (d) Optical coherence tomography image showing reduction in macular edema with reduced central foveal thickness. (e-h) A stable course of diabetic retinopathy in the left eye with a stable macular ischemia (red arrow, stable foveal avascular zone)

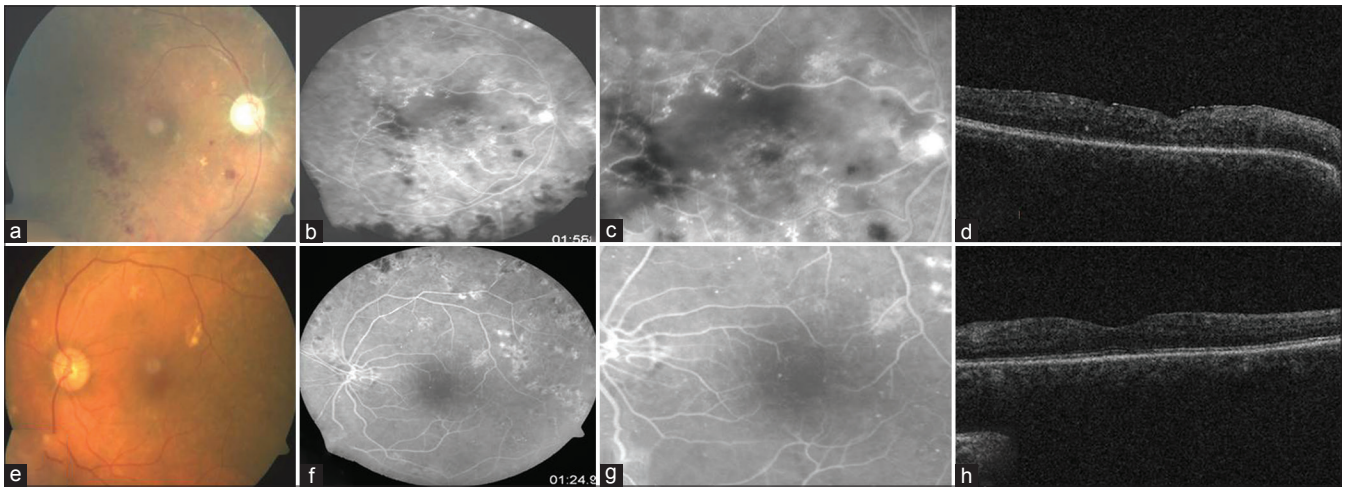

Figure 4: (a) Color fundus picture showing severe disc pallor and retinal vascular sclerosis, and a pale and atrophic looking retina over the posterior pole. (b and c) The development of neovascularization at the disk with marked distortion and enlargement of foveal avascular zone (yellow arrow). (d) Reduction in the central foveal thickness and stable macular contour on optical coherence tomography. (e-h) A stable course of diabetic retinopathy in the left eye after laser photocoagulation (red arrow, stable foveal avascular zone)

later with decreased vision in the right eye and was diagnosed with radiation-induced blepharitis, keratopathy, and RM in the right eye. The visual acuity in the right eye was 20/120, N36, at this stage. The fundus in the right eye showed new lesions in the form of multiple retinal hemorrhages and cotton wool spots over the posterior pole, whereas the left eye was stable. He was started on lubricant eye drops topically and was advised FFA and OCT [Fig. 2]. The FFA showed a markedly enlarged and distorted FAZ corresponding to ischemic maculopathy secondary to RM, and the OCT showed increased central foveal thickness with ellipsoid zone disruption. The patient was advised intravitreal injection of dexamethasone implant (Ozurdex®) in the right eye. Two months later, the patient presented with an improved vision of 6/24, N12, in the right eye. The FFA done at this stage showed a partial but significant revascularization of the macular capillary network, with a dramatic decrease in the irregularity and size of ischemic zone in FAZ [Fig. 3]. OCT also showed a significant reduction in macular edema with reduced central foveal thickness.

The patient was lost to follow-up for further 2 years, when he presented with markedly reduced vision in the right eye (counting fingers at 3 M, <N36), with a dense cataract, pale optic disc, and sclerosed vessels over the posterior pole [Fig. 4]. The left eye was stable. The FFA at this stage showed markedly enlarged FAZ with neovascularization at the disc in the right eye for which patient was advised additional laser. Two months later, the patient underwent cataract surgery in the right eye, and the vision stabilized at 6/60, N24. The left eye remained stable with a vision of 20/40, N6, and a stable DR.

Discussion

Retina and optic nerve are relatively resistant tissues to the ionizing radiation, but the vascular supply may get compromised

with resultant ischemic changes.[5] The resultant RM is a delayed onset, slowly progressive vaso-occlusive event with a resultant loss of vision. The pathophysiology of DR and RM has been found to be similar, i.e. destruction of the endothelial cells and capillary closure with resultant tissue hypoxia and proliferative changes later.[6-8] This also explains the exaggerated damage due to RM in the presence of DR. The right eye of our patient also showed marked RM changes with visual loss and macular ischemia after the radiotherapy for the orbital lymphoma.

Steroids, either periocular or intravitreal, have been shown to be effective in reducing the visual loss and in treating the macular edema associated with RM.[1,2] The use of intravitreal dexamethasone implant has been associated with long-term improvement of vision and reduction of macular edema.[3,9]

Even though the histological effects of ionizing radiation on the retinal vasculature and the reversal with steroids have been proposed, i.e., thickening of arteriolar and capillary walls and loss of endothelial cells resulting in vaso-occlusion, the same have not been studied *in vivo* in a living retinal tissue.[7,8]

Conclusion

Our case showed a transient but significant reopening of the capillary network after the steroid injection with a resultant markedly reduced size of ischemic zone at the macula. Lack of follow-up was a major limitation. Since the effect of steroid would have waned off after 4–5 months, the ischemic maculopathy showed a corresponding progressive damage with a resultant loss of vision. Similarly, OCT angiography, if available, would have shown the exact level of capillary bed alteration.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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