Safety of photodynamic therapy involving optic nerve head

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We present a case of large peripapillary polypoidal choroidal vasculopathy treated with standard-fluence photodynamic therapy (PDT) as other treatment options were unsuccessful or not justified. Due to large lesion size, treatment spot included part of optic disc also. PDT resulted in regression of polyp and visual improvement (from 20/300 to 20/20) without any collateral damage to optic nerve as evidenced by visual-field test and visual-evoked potential with a follow-up till 2 years. This case highlights the role of PDT as a safe alternative for treatment of large peripapillary lesion, even though the treatment spot encompasses part of the optic nerve head.

Key words: Optic nerve head, photodynamic therapy, polypoidal choroidal vasculopathy

Polypoidal choroidal vasculopathy (PCV), characterized by the presence of subretinal polypoidal vascular lesions, has various treatment options including focal laser photocoagulation, Verteporfin photodynamic therapy (PDT), intravitreal antivascular endothelial growth factor (anti-VEGF) injections and their combinations.[1,2] The actual treatment modality is decided based on the size and location of polyps as well as patient affordability. PDT in combination with anti-VEGF is recommended as initial therapy for subfoveal or juxtafoveal PCV, while anti-VEGF monotherapy is used as alternate treatment option where PDT is considered risky or unaffordable.[2] For peripapillary PCV, focal laser or anti-VEGF is usually preferred, as optic nerve head (ONH) safety is a concern with PDT.[3] There are very few reports showing safety of PDT for peripapillary choroidal neovascular membrane (CNVM) with treatment spot involving the ONH.[4]

We describe the first case of large peripapillary PCV continuous with ONH margin, treated with standard fluence PDT, with a long-term follow-up and documented safety.

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Case Report

A 60-year-old female presented with complaints of decreased vision in the left eye (LE) for 6 months. She had history of receiving four injections of ranibizumab in the LE without any visual improvement. She had no systemic illness. Her best-corrected visual acuity (BCVA) was 20/20 in the right eye (RE) and 20/300 in the LE. Anterior segment examination was unremarkable.

Fundus examination of RE was normal, whereas LE revealed a subretinal reddish lesion as shown in [Fig. 1]. Optical coherence tomography (OCT) of the LE showed the presence of a large serous macular detachment along with intraretinal hard exudates [Fig. 2]. Based on Fundus fluorescein angiography (FFA) and Indocyanine green angiography (ICG) features [Fig. 3], a diagnosis of peripapillary hemorrhagic PCV in the LE was made. As delineation of polyp area in early phase was not possible due to presence of subretinal pigment epithelial (RPE) hemorrhage, the greatest linear dimension, recorded as 4000 μ, was measured based on the late diffuse angiographic leakage seen on ICG.

A standard fluence PDT (SF-PDT) was performed using Verteporfin (Visudyne, Novartis Ophthalmics, Switzerland) at a dose of 6 mg/m^2 body in the LE. Zeiss Visulas II Laser (Zeiss, Germany) with an irradiance of 600 mW/cm^2 and 50 Joules, exposed for 83 s. The treatment spot (4000μ) was placed at the superior peripapillary region covering the angiographic leakage, which was continuous with and included the superior half of optic disc. 48 h after the PDT, she underwent intravitreal injection ranibizumab (Lucentis, Genentech, Switzerland). An informed consent was taken explaining the possibility of PDT-induced ONH damage and visual decline.

At 4-month posttreatment, LE BCVA improved to 20/20 with a superior peripapillary scar and a normal appearing ONH. The BCVA and fundus picture remained stable up to 2 years after PDT [Fig. 4].

Visually evoked potential (VEP) showed the amplitude and P100 latency to be within normal limits. Humphrey's visual fields (HFA 30-2) LE was normal except for a field defect inferior to the blind spot, corresponding to the peripapillary scar in the LE [Fig. 5].

Discussion

This case highlights the management of a massive recalcitrant peripapillary PCV treated with PDT involving a part of ONH in the treatment zone and showed safety of the procedure in such a setting. For the management of this case we had four options including observation, anti-VEGF therapy, focal thermal laser and PDT. We were not in favor of observing this lesion due to

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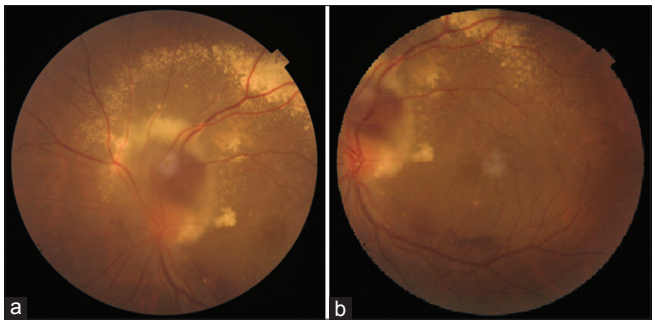

Figure 1: (a) Baseline color fundus appearance of the LE showing orange red elevated lesion three disc diameters in size superior and continuous with ONH with surrounding concentric hard exudates with foveal involvement. (b) Fundus color picture of the same patient showing the inferior subretinal hemorrhage

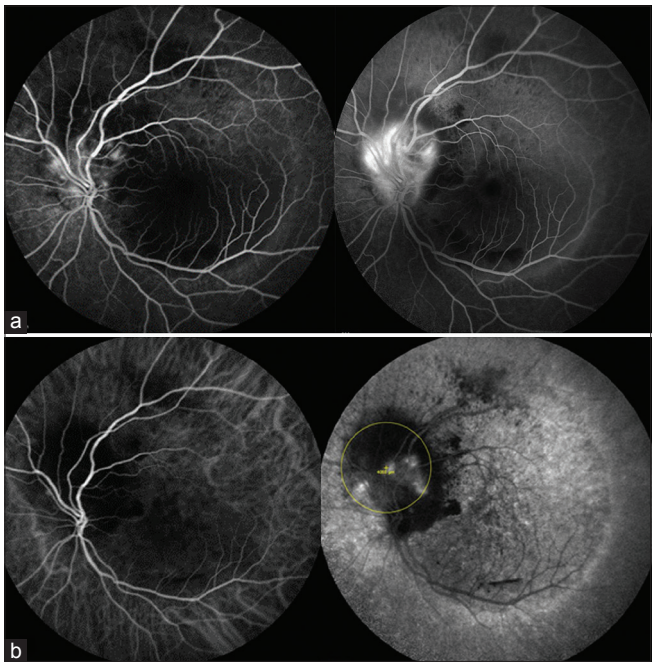

Figure 3: (a) FFA early phase showing blocked fluorescence and late diffuse hyperfluorescence continuous with superior half of ONH. Blocked fluorescence at inferior macula corresponding to the subretinal hemorrhage. (b) ICG angiography early phase showing nasal ill-defined hyperfluorescence and late diffuse hyperfluorescence suggestive of hemorrhagic PED of a PCV. Treatment spot size was 4000μ involving ONH

progressive visual decline. Multiple anti-VEGF injections were already attempted with poor response. Aflibercept injection was not freely available in India in 2016 and also the cost of such multiple injections was prohibitively expensive for the patient to afford. The lesion size being 4000 microns was very large and elevated to be treated with focal thermal laser. This led us to go ahead with SF-PDT despite the explicit label warning.

Though PDT is considered as a safe treatment modality with rare visually significant complications, its effect on the ONH is not well studied. The verteporfin package information states that the spot size should be at least 200 μ from the ONH border. This prohibition arises from the exclusion criteria of the treatment of age related macular degeneration with photodynamic therapy (TAP) study that led to approval for

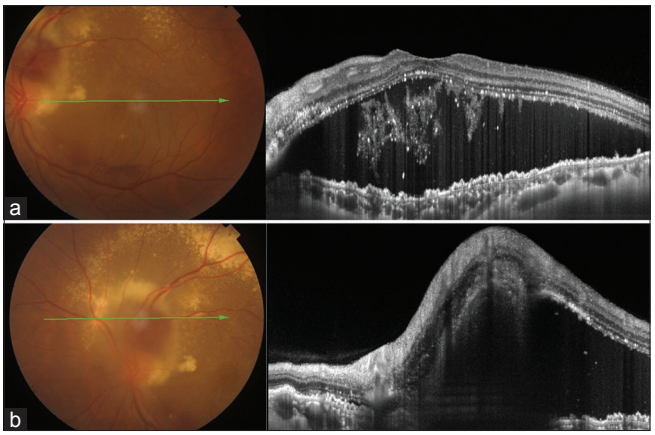

Figure 2: (a) Baseline OCT showing large serous macular detachment with intraretinal hard exudates and drusenoid drusenoid pigment epithelial detachments (PEDs). (b) OCT of superior peripapillary region showing the large hyperreflective subretinal lesion continuous with the ONH margin

clinical use of verteporfin PDT. In literature, there are very few studies describing about the effect of PDT to the ONH. In an experimental study, Min *et al*. used PDT over ONH to induce anterior ischemic optic neuropathy in mice eyes, and described the morphological and histopathological changes.[3] However, in another study conducted in monkey eyes, PDT conducted with verteporfin dose of 6 mg/m^2 was found well tolerated over the normal retina, choroid as well as ONH.[5]

PDT is known to cause collateral damage, which depends on the light intensity and duration of the exposure, concentration of the photosensitizer, and the time interval between administration of the dye and the laser. In a study of human eyes with choroidal melanoma destined for enucleation, PDT-induced damaging effects were found to be confined only to the choroid and RPE, and were dose dependent (seen at 100 J/cm^2, but not at 50 J/cm^2). However, no damage to the capillaries of the optic disc was noted, irrespective of the light dose.[6]

Vilaplana *et al*. treated a case of peripapillary PCV at the papillomacular bundle using PDT with 1000μ spot size, but avoiding ONH. Good visual acuity was noted at 2 year follow-up; however, no visual field test or VEP was done to assess optic nerve function.[7]

Bernstein and Horn retrospectively evaluated seven patients with peripapillary CNVM who underwent SF-PDT with treatment zone including part of the ONH. All seven patients showed angiographic resolution of CNVM without ONH pallor, hemorrhage, edema, or afferent pupillary defect. The authors concluded that despite the label warnings to keep the laser spot at least 200 μ away from the ONH, treatment with PDT was safe and effective even if some or all of the ONH falls in the treatment field.[4] There are few other case reports, where PDT has been used successfully to treat optic disc hemangiomas; however, none of them have elucidated regarding safety of the procedure over the ONH.[8-10]

This is the first documented report of successful management of large peripapillary PCV with PDT, with proven long-term functional and anatomical safety of optic nerve, despite the involvement of the ONH in the treatment area. In spite of the label warnings of PDT to keep the laser spot at least 200 μ from

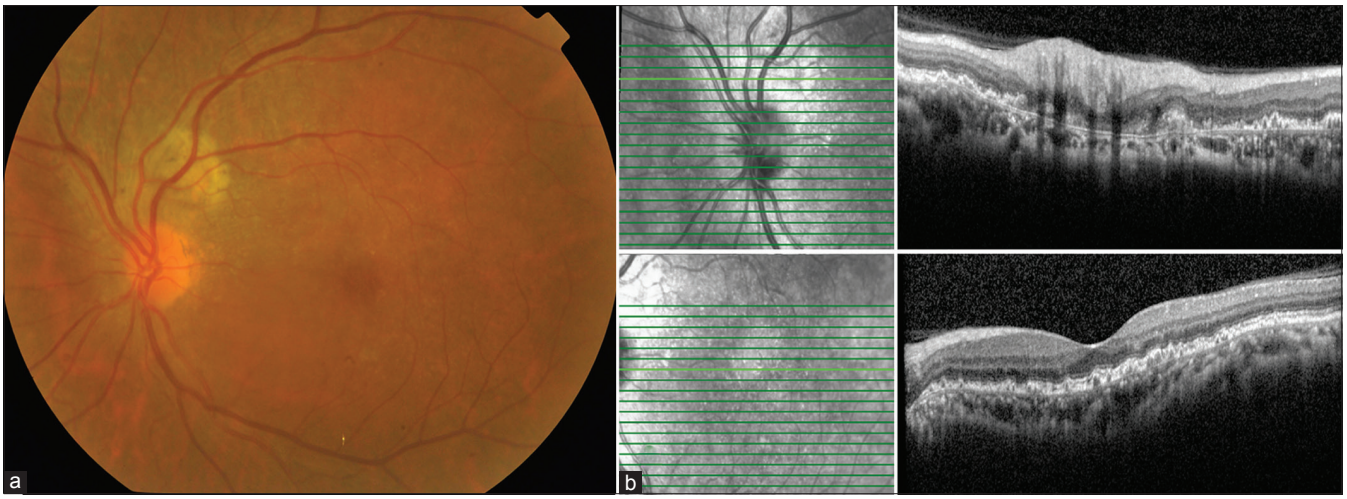

Figure 4: (a) Fundus picture at 2 years post-PDT shows a normal ONH with a superior peripapillary scar. (b) OCT picture at 2 years post-PDT showing normal foveal contour with drusenoid PEDs and peripapillary scar

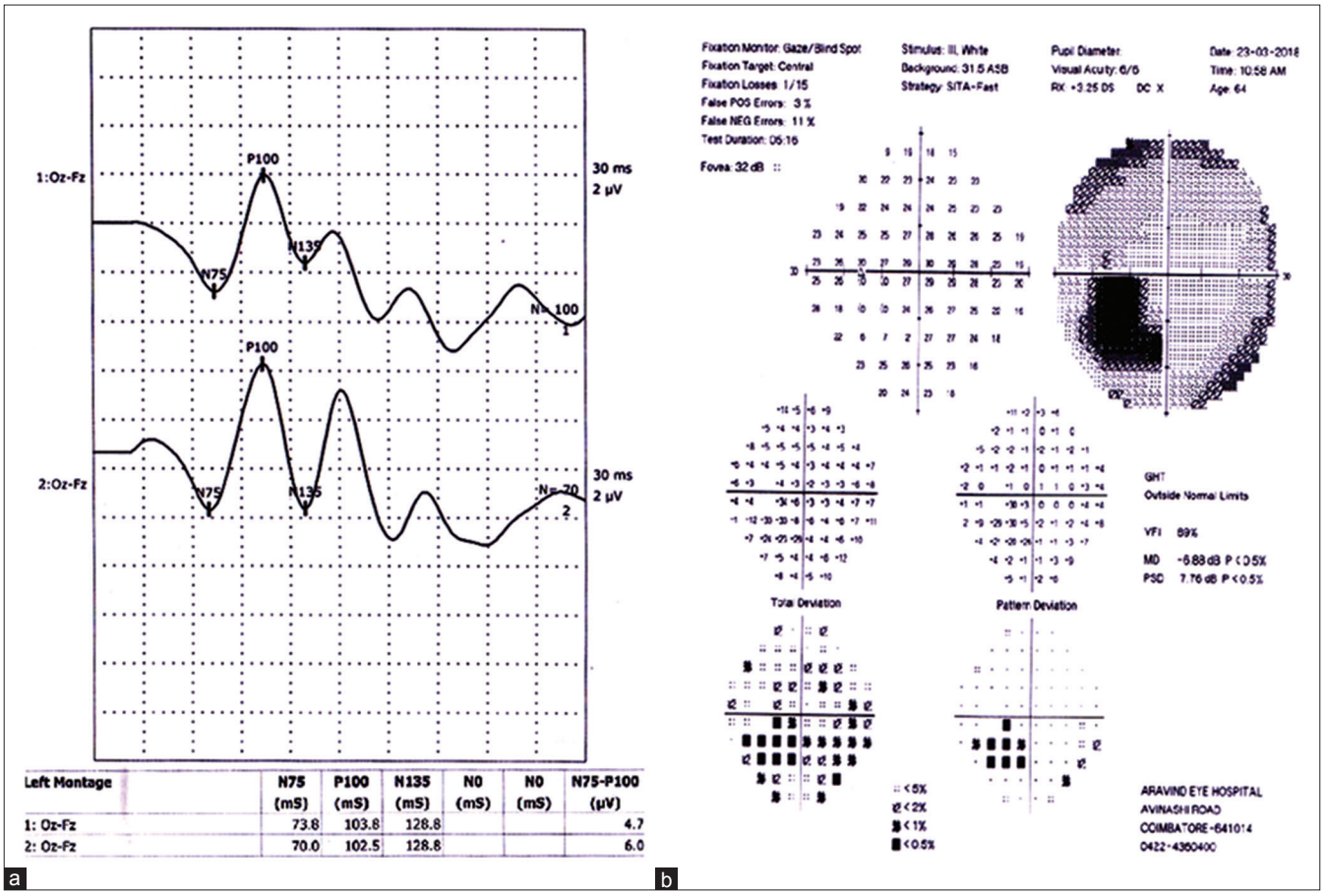

Figure 5: (a) LE VEP showing a normal amplitude and P100 latency. (b) LE HFA 30-2 showing a scotoma inferior to the blind spot corresponding to the superior peripapillary scar

the temporal edge of the ONH, we proceeded with PDT for the reason as described earlier. At 2-year follow-up, visual fields and VEP showed the absence of any structural or functional ONH damage. Documented functional safety based on visual field and VEP tests, as well as a long follow-up period was lacking in previous reports.

Conclusion

This case shows that SF-PDT is an effective and safe modality for the treatment of large peripapillary PCV abutting ONH. Therefore, PDT may be considered as an alternative treatment modality in such cases where other treatment options are not justifiable.

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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