Intravitreal ranibizumab, photodynamic therapy, and vitreous surgery for the treatment of juxtapapillary retinal capillary hemangioma

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Dear Editor,

Retinal capillary hemangiomas (RCH) are capillary angiomatosus hamartomas of the retina and optic nerve head. The median age of diagnosing the disease is 31 years old [1]. Although most RCH is isolated, 10–30% in the 31–40 age group are associated with Von Hippel Lindau disease (VHL). Up to 15% of RCHs are juxtapapillary, where most are located temporally [2]. They are often associated with epiretinal membrane (ERM) formation and serous and tractional retinal detachment of the macula, which leads to a poor prognosis [1].

We report a typical case of isolated juxtapapillary RCH that underwent successful combined therapy with intravitreal ranibizumab injection and photodynamic therapy (PDT) 1 week before PPV and ERM peeling surgery.

A 32-year-old woman presented with reduced right eye vision and metamorphopsia for 3 months. At presentation, her best-corrected visual acuity was 20/50 and 20/25 for the right and left eyes, respectively. Right eye fundus examination revealed a reddish mass measuring 2.0 × 1.5 mm in the inferotemporal juxtapapillary region associated with macular subretinal fluid and ERM (Fig. 1a).

Fundus fluorescein angiogram (FFA) showed early filling of the lesion with late leakage into the subretinal space. Anomalous vascular channels were seen sprouting from the lesion (Fig. 1b). Optical coherence tomography (OCT) confirmed serous detachment of the macula with vitreomacular traction (Fig. 1c). Central foveal thickness was increased to 570 µm (normal values=≤315 µm) [3].

A diagnosis of juxtapapillary retinal capillary hemangioma was made. Systemic workup for Von Hippel Lindau (VHL) disease did not reveal any other tumors. Her visual acuity continued to deteriorate to 20/100 in the subsequent 2 months. She was treated once with PDT using standard fluence at that time, with reduced diameter laser spot centering on the lesion avoiding the optic disc. There was no clinical response and her vision continued to deteriorate to 20/200 3 months after the initial PDT. Combined therapy, using standard fluence PDT and intravitreal injection of ranibizumab were performed 2 months later (7 months since presentation). Reduction of lesion size (1.5 × 1.5 mm) and vascularity was noted 1 day after the combined therapy (Fig. 2a). One week later, PPV and ERM peel were carried out and intravitreal triamcinolone injection (2 mg in 0.05 ml) was given at the conclusion of surgery.

The patient's visual acuity improved to 20/25 after successful surgery and the lesion remained stable for 12 months, up to the latest follow-up (Fig. 2b). The central foveal thickness remained reduced within normal limits at 324 µm. FFA showed hyperfluorescence in the late phase (Fig. 2c). A small superotemporal branch retinal vein...
occlusion developed secondary to an iatrogenic break resolved spontaneously.

**Discussion**

To date, no single modality in the treatment of juxtapapillary RCH has been particularly effective [1]. Laser photocoagulation applied to the neural tissue surrounding the tumor can cause permanent scotomas [2]. Use of cryotherapy is limited due to the posterior location of the lesion.

Anti-vascular endothelial growth factor (anti-VEGF) therapy has been reported to reduce vascular permeability by altering the balance of vaso-active cytokines like nitric oxide.
oxide and endothelin-1 [4] or by directly altering endothelial tight junction proteins [5]. It is postulated that excessive accumulation of hypoxic induced factor (HIF) in the neoplastic stromal cells of RCH leads to the production of other angiogenic factors that are able to maintain and promote the growth of primary hemangiomas [6].

PDT is shown to be effective in causing fibrosis and involution of the primary angioma, but its use on peripapillary area is limited by vaso-occlusive effects [2, 7]. For larger tumors, verteporfin may only be activated on the surface of the tumor, and the reactive oxygen species may not cause closure of deeper tumor vessels. By combining anti-VEGF with reduced fluence PDT, the outline of the primary angioma can be better delineated and may thus reduce the energy and the treatment area, thereby minimizing the damage to the neurological tissues [8]. Recent reports of combined therapy with anti-VEGF therapy and PDT have shown promising results in these lesions [7].

Anti-VEGF agents, like bevacizumab, have been reported as a useful pre-operative adjunct in the surgical treatment of proliferative diabetic retinopathy, with significant reduction in neovascularization, bleeding, and adherence of fibrovascular complex to the retina [9]. We found that ranibizumab is useful in the present case. Combined treatment with anti-VEGF and PDT 1 week before surgery caused a reduction in macular edema, which reduced the risk of retinal cyst rupture during peeling procedure [10]. Reduced tumor vascularization may have lowered the risk of intraoperative bleeding.

In summary, pre-operative combination therapy with an anti-VEGF agent and PDT, PPV, and ERM followed by intravitreal triamcinolone at the conclusion of surgery led to improvement in visual outcome. The use of triple therapy was recently shown to be effective in the treatment of age-related macular degeneration and our case may suggest that a multi-faceted approach could be beneficial in cases of juxtapapillary RCH [11].

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