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Case report

Treatment of juxtapapillary hemangioblastoma by intra-arterial (ophthalmic artery) chemotherapy with bevacizumab

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ABSTRACT

Purpose: To report on two cases of treatment-refractory juxtapapillary hemagioblastomas that were managed with intra-arterial bevacizumab delivered via the ophthalmic artery.

Observations: Case 1 is a 35 year-old man with juxtapapillary hemangioblastoma who continued to have progressive tractional retinal detachment, optic nerve neovascaularization and cystoid macula edema (CME) despite heavy prior treatment with intravitreal anti-vascular endothelial growth factor (VEGF) and steroid intravitreal injections and laser. Case 2 is a 41 year-old woman with juxtapapillary hemangioblastoma who had progressive tractional retinal detachment, CME and visually-threatening intraocular pressure elevation despite treatment with anti-VEGF injection and laser. Both cases were treated with three infusions of intra-arterial bevacizumab delivered via the ophthalmic artery. Both tumors demonstrated measurable decrease in height, stability of their secondary retinal changes and minimal requirement for additional treatment at 30 mos and 26 mos follow-up, respectively for cases 1 and 2.

Conclusions and importance: These cases suggest that higher-dose, targeted delivery of anti-VEGF to hemangioblastomas via ophthalmic artery injection may be useful in stabilizing the disease and abating the typical progression of secondary retinal pathology, at least in the first two years after treatment.

1. Introduction

Retinal hemangioblastomas are notoriously difficult to manage, often resulting in visual impairment. Many tumors are recalcitrant to treatment including intravitreous injections of steroids or anti-vasogenic endothelial growth factor (VEGF), cryotherapy, radiation and laser, including photodynamic therapy.[1–5] It is not uncommon for these eyes to progress to blindness due to exudation, tractional retinal changes, or neovascular glaucoma; and it has been predicted that 25% of eyes will be rendered permanently blind (vision less than 20/400).[2,6] An alternative form of management to halt the progression of disease, maintain vision and provide ocular salvage is explored in this case report.

2. Findings

Case 1: 35 year-old man with known Von Hippel Lindau (VHL) syndrome continued to be symptomatic with blurry vision despite prior treatment with 94 intravitreal anti-VEGF injections, photodynamic therapy and intravitreal steroids. At presentation he had a juxtapapillary hemangioblastoma in the left eye with progressive neovascularization of the disc, overlying tractional retinal detachment with fibrosis/gliosis and cystoid macula edema. The vision was 20/200.

The eye was treated with three monthly infusions of bevacizumab delivered via ophthalmic artery chemosurgery (to the ostium of the ophthalmic artery with a technique previously described[7]). The initial infusion delivered 515 mg bevacizumab followed by 1030 mg for the subsequent two infusions. One month following treatment, the hemangioblastoma decreased in height from 2.1 to 1.8 mm (Fig. 1). In addition over 30 months follow up, the hemangioblastoma remained stable, without progression of neovascularization, cystoid macula edema nor retinal detachment; and the hemangioblastoma has not required additional treatment. The vision was maintained at 20/200. There were no systemic side effects noted.

Case 2: 41 year-old woman (no known VHL syndrome and unknown genetics) with hemangioblastoma overlying the optic nerve of her left

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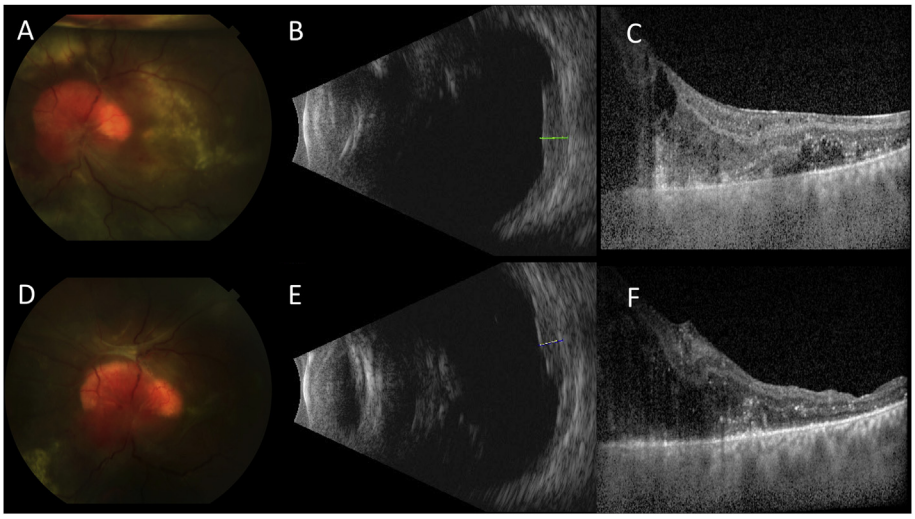

Fig. 1. Case 1. Fundus photography (A) demonstrating juxtapapillary hemangioblastoma with overlying fibrosis/gliotic retina, corresponding with elevated placoid mass on ultrasound measuring 2.1mm in height (B) and corresponding foveal optical coherence tomography (C). One-month following three infusions of bevacizumab devliered via ophthalmic artery chemosurgery, the fundus remained stable (D) and tumor height decreased to 1.8mm (E) with post-treatment foveal optical coherence tomography (F).

eye and hand motion vision presented with cystoid macula edema, retinal fibrosis with overlying tractional retinal detachment. She developed intermittent episodes of elevated intraocular pressure in this phakic eye despite three laser iridotomies. The exact nature of the pressure elevations was unknown (narrow angles with synechiae and no neovascualtization of the angle was noted on gonioscopy), but suspected to be related to vasculogenic factors associated with the hemangioblastoma, as well as possible uveal thickening leading to angle closure. In an effort to reduce the vasculogenic activity of the tumor in preparation for cataract surgery, the eye was treated with three monthly infusions of bevacizumab delivered via ophthalmic artery chemosurgery. The first two infusions delivered 835 mg bevacizumb followed by 1000 mg for the third infusion. There were no systemic side effects noted.

Following treatment, the tumor reduced in height from 5.9 to 3.8 mm with reduced reflectivity on ultrasonography (Fig. 2). Uncomplicated cataract surgery was performed without disturbance of the hemangioblastoma (no bleeding was observed). The tumor and retinal findings have remained stable without further elevations in intraocular pressure and without requiring additional hemangioblastoma treatment at 26 months follow up. The vision improved to 20/200.

3. Discussion

Eyes with hemangioblastomas are often recalcitrant to treatment, and despite all efforts, often have dismal outcomes including blindness.[2] One treatment approach involves injecting anti-VEGF into the vitreous: which bathes the tumor in diluted anti-VEGF vitreous fluid.[3] Alternatively, ophthalmic artery chemosurgery may provide an advantage by: 1. delivering almost 1000 times the dose of anti-VEGF agent compared to an intravitreous injection; and 2. delivering drug to the ophthalmic artery which presumably feeds directly into the aberrant blood vessels of the hemangioblastoma.

Modeled after the dosing used for intra-arterial bevacizumab delivery to glioblastomas (15mg/Kg),[8] we treated two recalcitrant hemangioblastomas with intra-arterial bevacizumab. In each case there was measurable regression of the hemangioblastoma, with decrease in height. And more importantly, the tumors stabilized and required minimal additional treatment.

Future treatments may include additional targeted agents that address other potential aberations in the VHL pathway. Given the recognition of constitutive activation of HIF in VHL {Haase:2009vo}, the utility of concomitant HIF-inhibitor may want to be explored in the future.

4. Conclusion

These cases suggest that high-dose, targeted delivery of anti-VEGF to hemangioblastomas via ophthalmic artery chemosurgery may be useful in tempering the disease and abating the typical progression to

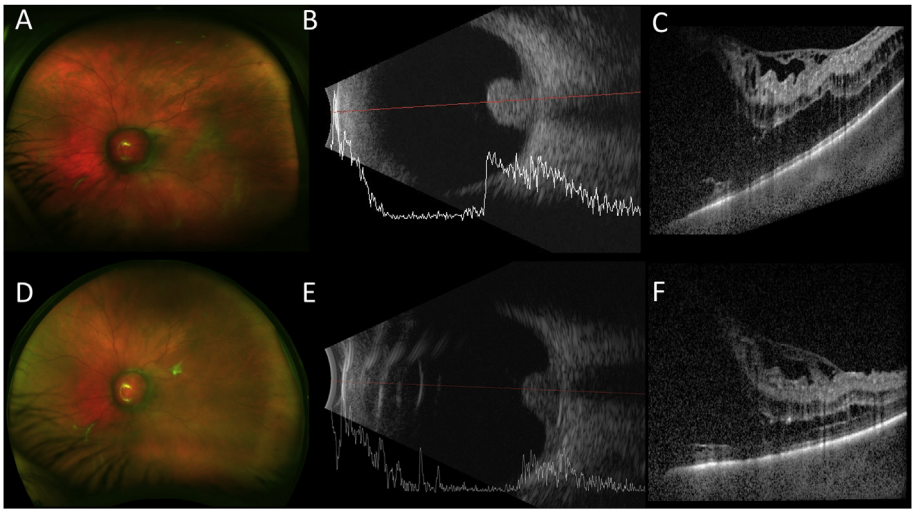

Fig. 2. Case 2: Fundus photography (A) demonstrating juxtapapillary hemangioblastoma with overlying fibros/gliotic retina, corresponding with elevated mushroom-shaped mass on ultrasound measuring 5.9mm in height (B) and corresponding foveal optical coherence tomography (C). Note contraction of the tumor one-month following three infusions of bevacizumab delivered via ophthalmic artery chemosurgery (D): with decreasing reflectivity and height to 3.8mm on ultrasonography (E) with post-treatment foveal optical coherence tomography (F).

blindness and possible pthisis or enucleation. The follow up of these two cases was over two years, but the long-term effects of intra-arterial bevacizumab and the impact on peripheral tumors are still to be determined.

Patient consent

Written consent to publish personal information and case details has been obtained from the patients.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajoc.2018.05.007.

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