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 hemangioblastomas 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 neovascularization 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 intravitreal 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 tractional retinal detachment, optic nerve neovascularization 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.

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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 neovascularization 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 bevacizumab 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. One treatment approach involves injecting anti-VEGF into the vitreous: which bathes the tumor in diluted anti-VEGF vitreous fluid. 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), 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 aberrations 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
blindness and possible ptosis 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.ajo.c.2018.05.007.

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