Sustained Elevation in Intraocular Pressure Associated With Intravitreal Bevacizumab Injections

Malik Y. Kahook, MD  
Alan E. Kimura, MD  
Lisa J. Wong, MD  
David A. Ammar, PhD  
Marco A. Maycotte, MD  
Naresh Mandava, MD

ABSTRACT
This retrospective case series reports sustained elevation of intraocular pressure (IOP) after single or repeated intravitreal injections of bevacizumab (Avastin; Genentech, San Francisco, CA) for wet age-related macular degeneration (AMD). All six cases experienced significant and sustained elevation in IOP after single or repeated intravitreal injections of bevacizumab. Initiation or advancement of IOP-lowering therapy was required in all cases. The results support the need for further studies investigating the incidence of this potential side effect and the need for close long-term surveillance of IOP after injection of bevacizumab, particularly in patients with glaucoma or suspected glaucoma. Future in vitro and in vivo studies are needed to better understand the reasons for this observed phenomenon. [Ophthalmic Surg Lasers Imaging 2009;40:293-295.]

INTRODUCTION
Bevacizumab (Avastin; Genentech, San Francisco, CA) is an anti-vascular endothelial growth factor (anti-VEGF) agent used for retinal and choroidal neovascular diseases, with few reported side effects.1-3 Although transient intraocular pressure (IOP) elevations have been documented, we could only find one report of sustained elevation in IOP after intravitreal injection of bevacizumab.4,5 In this chart review, we report six cases of sustained elevation in IOP after single or repeated intravitreal injections of 1.25 mg/0.05 mL of bevacizumab. Institutional Review Board approval was obtained for this retrospective review.

CASE REPORTS
Case 1
A 77-year-old man with new-onset wet age-related macular degeneration (AMD) in his left pseudophakic eye underwent intravitreal injection of bevacizumab. Documented IOP measurements were in the range of 14 to 17 mm Hg in the 2 years prior to injection. He had been diagnosed 2 years previously as having suspected glaucoma due to bilateral increased cup-to-disc ratio. Prior to the initial bevacizumab injection, IOP was 16 and 15 mm Hg in the right and left eyes, respectively. He received a second injection 8 weeks later with IOP measurements recorded as 18 and 22 mm Hg in the right and left eyes, respectively. Six weeks later, IOP measurements were 17 mm Hg in the right eye and 27 mm Hg in the left eye. The optic nerve examination at that time revealed thinning of the optic nerve head rim inferiorly in both eyes, more severe on the left. IOP measurement at the subsequent presentation to the glaucoma service was 18 mm Hg in the right
eye and 28 mm Hg in the left eye. Topical glaucoma therapy was started in both eyes.

Case 2
A 54-year-old woman with bilateral pseudophakia and a history of high myopia presented with high IOP after injection of bevacizumab in the left eye for myopic choroidal neovascular membrane. IOP measurements ranging from 9 to 13 mm Hg and a cup-to-disc ratio of 0.4 in both eyes were noted during the 5 years prior to the diagnosis of choroidal neovascular membrane. During a course of five injections of bevacizumab over 6 months, IOP measurements in the left eye increased gradually from 15 to 42 mm Hg, whereas IOP in the right eye remained stable. IOP elevation did not respond to topical therapy and trabeculectomy with mitomycin C was recommended due to a left-sided inferior optic nerve head notch and superior arcuate scotoma on visual field testing.

Case 3
A 77-year-old phakic woman with dry AMD and primary open-angle glaucoma was noted to have a new choroidal neovascular membrane in the right eye. Her IOP was stable in both eyes with pressures below 14 mm Hg with latanoprost monotherapy. After a single right-sided injection of bevacizumab, IOP in the right eye increased gradually over 5 months from 11 to 24 mm Hg while remaining in the low teens in the left eye. Subsequent visits over the next 3 months revealed pressures of 30 and 31 mm Hg in the right eye despite the addition of brinzolamide. The patient refused further interventions.

Case 4
An 83-year-old woman with a history of chronic angle-closure glaucoma in the pseudophakic right eye, treated with latanoprost, had been observed for suspected glaucoma in the phakic left eye without treatment for 6 years. She was noted to have a choroidal neovascular membrane in the left eye in 2006 and was treated with 8 consecutive injections of bevacizumab with consistent improvement in macular edema and vision. The IOP in the right eye remained stable, whereas the IOP in the left eye steadily increased from a baseline of 14 mm Hg prior to injection to the mid 30s post-injection. Latanoprost treatment was recommended for the left eye. At last follow-up with the retina service, the IOP was 33 mm Hg in the left eye and she was referred for glaucoma consultation, at which time brimonidine therapy was initiated twice daily.

Case 5
A 93-year-old woman with bilateral pseudophakia and a 5-year history of choroidal neovascular membrane in the right eye was treated with 8 injections of bevacizumab over 14 months. She had no known history of glaucoma and no history of optic nerve head cupping. The IOP in the right eye remained stable until after the seventh bevacizumab injection, when it increased to 30 mm Hg. The IOP in the left eye remained stable in the mid-teens. She was prescribed timolol and latanoprost and referred for management of her topical glaucoma therapy.

Case 6
An 85-year-old woman with right-sided choroidal neovascular membrane was referred to our glaucoma service for management of elevated IOP in the right eye after 10 intravitreal injections of bevacizumab over 2 years. She did not have glaucoma and was bilaterally phakic. On presentation to our service, she was noted to have an IOP of 12 mm Hg in the left eye and 25 mm Hg in the right eye. She began taking brimonidine three times per day and the IOP remained in the upper teens at 4 weeks of follow-up.

DISCUSSION

The low cost and clinical efficacy of intravitreal bevacizumab has led to widespread off-label use for wet AMD and many other choroidal and retinal neovascular diseases. We describe six separate cases of increased IOP after intravitreal bevacizumab. Bevacizumab, a 149 kDa full-length antibody, diffuses into the anterior chamber and clears slowly from the vitreous cavity. Jalil et al. hypothesized that bevacizumab may accumulate in the trabecular meshwork, thereby blocking aqueous outflow and leading to increased IOP. The presence of a proinflammatory Fc portion and the potential for large antibodies to have a longer serum and vitreous half-life may all be factors that would lead to increased outflow resistance and IOP after intravitreal bevacizumab injection. Elevations in IOP may be more likely to occur in patients with glaucoma due to compromised outflow facility. Close post-injection surveillance may be warranted in these patients.
REFERENCES


