Rate of Endophthalmitis After Anti-VEGF Intravitreal Injection

The rate of endophthalmitis was low in a series of almost 20,000 intravitreal injections of anti-VEGF agents.

BY ANDREW A. MOSHFEGHI, MD

The availability of vascular endothelial growth factor (VEGF) inhibitors has revolutionized the care of patients with age-related macular degeneration (AMD). Beginning with the introduction of pegaptanib sodium (Macugen, OSI/Eyetech) in 2004,[1] followed by reports of off-label use of bevacizumab (Avastin, Genentech),[2] and most recently the approval of ranibizumab (Lucentis, Genentech) in 2006,[3,4] retina specialists have gained access to a new set of tools for the treatment of choroidal neovascularization (CNV) in AMD.

In this "anti-VEGF era" that began only a few years ago, the number of intravitreal injections has rapidly increased at centers around the country. At the Bascom Palmer Eye Institute and its satellite clinics, approximately 4,000 intravitreal injections of anti-VEGF agents were performed in 2005, more than 7,100 in 2006, and close to 9,000 in the first 10 months of 2007.[5]

Exudative AMD is overwhelming the primary indication for these injections, although there are numerous other indications for which off-label intravitreal bevacizumab is used at our institution. These indications include branch and central retinal vein occlusions (CRVO), diabetic macular edema, proliferative diabetic retinopathy, cystoid macular edema (CME), and neovascular glaucoma.

In light of the rapid increase in the frequency of these procedures at our institution, we performed a study to identify the rate of culture proven endophthalmitis after intravitreal injections of pegaptanib, bevacizumab or ranibizumab.[5] In this retrospective, noncomparative case series we sought to characterize the cases of treated endophthalmitis after intravitreal injection that were encountered at Bascom Palmer during this period.

We examined the records of all patients treated for endophthalmitis following an intravitreal injection of any of the three VEGF inhibitors between Jan. 1, 2005, and Nov. 1, 2007. A review of the logs for anti-VEGF intravitreal injections provided the denominator for our calculation.

Patients receiving anti-VEGF intravitreal injections received topical povidone-iodine application before injection and topical antibiotics immediately after injection as infection prophylaxis.

RESULTS AND CASE REPORTS

In this period of almost 3 years, in 19,830 intravitreal injections, three cases of clinically suspected and treated endophthalmitis were recorded. Two cases were culture-proven, and there was one culture-negative vitreous tap.

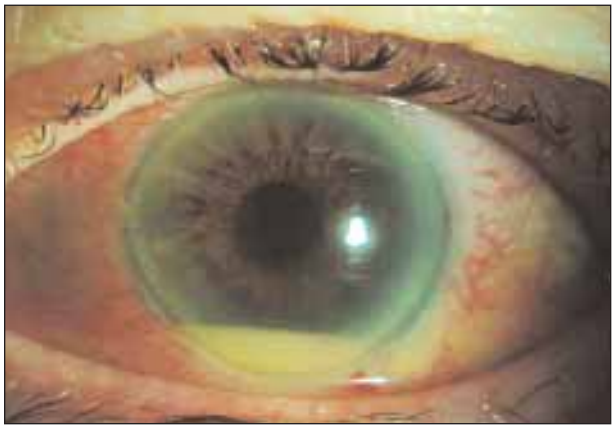

Figure. A separate case of culture-negative endophthalmitis presenting 2 days after an intravitreal bevacizumab injection for neovascular AMD (several previous bevacizumab injections were administered without a problem). The patient was treated with intravitreal ceftazadime and vancomycin with good visual outcome.

The percentage of treated cases was 0.015% (3/19,830), and the percentage of culture-positive endophthalmitis cases was 0.010% (2/19,830).

Case 1. The patient with suspected endophthalmitis was an 81-year-old man who presented with a red, painful eye and visual acuity of hand motions 3 days after a ranibizumab injection. He had previously undergone multiple injections of pegaptanib, bevacizumab, and ranibizumab in the same eye without adverse outcomes. It came to light that this patient had mistakenly used a medicated ear drop for his pet dog, instead of the prescribed fluoroquinolone antibiotic drops, in his eye after the injection. He was treated with intravitreal vancomycin, ceftazidime, and dexamethasone. Vitreous cultures were negative. Visual acuity improved to baseline by 6 months follow-up and to 20/80 by 1-year follow-up. The patient has undergone subsequent ranibizumab injections without adverse outcomes.

Case 2. A 59-year-old man with a CRVO and visual acuity of 20/400 was treated with off-label bevacizumab injection. He was re-treated for persistent CME with a visual acuity of 20/80. On day 1 after this injection, he presented with swelling, redness, and hypopyon, and these conditions continued to worsen on postinjection days 2 and 4.

Vitreous culture was positive for *Streptococcus sanguinis/gordoni*, and the strain was identified as resistant to erythromycin and sensitive to penicillin, vancomycin, ceftriaxone, and levofloxacin. Despite aggressive treatment, the patient experienced rapid deterioration of visual acuity to no light perception with a 360° ciliochoroidal detachment and retinal detachment.

Case 3. An 83-year-old man with diabetes mellitus, wet AMD and visual acuity of 20/100 was treated with intravitreal ranibizumab injection. On day 1 after his second ranibizumab injection, he presented with floaters, pain, and decreased visual acuity in the right eye. Vitreous culture was positive for *Staphylococcus epidermidis*, which was found to be resistant to fluoroquinolones but sensitive to vancomycin. With treatment, the eye returned to the baseline visual acuity of 20/100 at 6 months' follow-up.

DISCUSSION AND CONCLUSIONS

A review of the literature identified a number of reports of endophthalmitis rates after large series of intravitreal injections. Ferrone and colleagues,[6] reviewing data from several large studies of ranibizumab injection, reported an endophthalmitis rate of 0.07% in 19,254 injections. In cumulative data from the MARINA (Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular AMD), ANCHOR (Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in AMD) and PIER (Phase IIIb Study of the Efficacy and Safety of Ranibizumab) studies of ranibizumab injection,[3,4,6] the endophthalmitis rate was 0.05% in 17,065 injections. In the VISION study of pegaptanib injection,[1] the rate was 0.16% in 7,545 injections. A retrospective study by Jager and colleagues[7] found an endophthalmitis rate of 0.3% in 14,866 injections of triamcinolone acetonide.

Our low endophthalmitis rate of 0.01% in almost 20,000 intravitreal anti-VEGF injections compares well with the published literature. This is encouraging, as the frequency of intravitreal injections for treatment of numerous retinal pathologies is likely to continue to rise in the coming years of the anti-VEGF era.

The organisms identified in our review of endophthalmitis incidence after intravitreal injection at Bascom Palmer were primarily gram positive, but the rate of endophthalmitis was too low to draw any meaningful general conclusions about the characteristics of responsible organisms.

With prompt, proper and aggressive treatment of suspected or confirmed endophthalmitis after intravitreal anti-VEGF injection, good visual outcomes can be seen. ■

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