Letters to the Editor

Endophthalmitis After Anti-VEGF Injections

Dear Editor:

Intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents have become the standard of care for the treatment of neovascular age-related macular degeneration. They are increasingly being used to treat other types of choroidal neovascularization and retinal vascular diseases. Endophthalmitis is the most dreaded complication of intravitreal injection. Several studies have reported on the incidence of endophthalmitis after intravitreal injection.[1–5] Unfortunately, little data exist regarding outcomes of endophthalmitis after intravitreal injection of anti-VEGF agents.

We have examined a cohort of 30,736 injections–128 pegaptanib, 8039 bevacizumab, and 22,579 ranibizumab–performed in 5 community-based retinal practices around the country between August 1, 2006 and July 31, 2007. We identified 15 cases of presumed endophthalmitis (Table 1, available online at http://aaojournal.org) from these 30,736 injections (0.049%; 0.03–0.08% 95% confidence interval [CI]). Five of these cases followed injections of bevacizumab (5/8039 = 0.062%; 0.02–0.15% 95% CI), 10 followed injections of ranibizumab (10/22579 = 0.044%; 0.02-0.08% 95% CI), and none followed injections of pegaptanib (0.00%; 0.00–2.31% 95% CI). Endophthalmitis rates for these 3 types of intravitreal injections did not differ significantly. As assessed by survey, physicians in our practices used various intravitreal injection techniques, e.g., some used preinjection topical antibiotics, whereas some did not. A lid speculum was used in 14 of the 15 incident cases. All used 5%–10% povidone iodine to cleanse the eye before injection.

Fourteen of 15 endophthalmitis patients were tapped and injected intravitreally with vancomycin and ceftazidime. One of the 15 patients was tapped then injected intravitreally with vancomycin only. Four patients also received a subtenons injection of triamcinolone acetonide. One patient was placed on oral ciprofloxacin, and 2 were placed on oral moxifloxacin. Four patients subsequently had vitrectomies.

Thirteen of these 15 cases were diagnosed within 4 days of the intravitreal injection. Mean time to diagnosis was 3.5 days (range, 1–8 days). Three cases were diagnosed just 1 day after injection; 2 of these cases were culture positive.

Six of 13 (46%) cases were culture positive. Culture data were not available for 2 of the cases. Only gram positive organisms were isolated: *Staphylococcus epidermidis* × 3, coagulase-negative staphylococcus × 1 (not speciated), *Streptococcus salivarius* × 1, and *S. viridans* × 1.

Ten of the 15 patients returned to baseline vision (±1 line). Two patients lost between 3 and 5 lines of vision. One patient dropped from 20/30 to hand motions vision and was pre-phthisical. Two patients lost all vision (no light perception), and 1 of these patients developed phthisis bulbi.

Of note, 20% of our patients were diagnosed with presumed endophthalmitis on the first post-injection day. Two of those 3 patients were culture positive. Additionally, 87% of our cases of endophthalmitis were diagnosed within 4 days of anti-VEGF injection. Therefore, a high index of suspicion for endophthalmitis is necessary in regarding patient complaints, especially in the first 1 to 4 days after intravitreal injection.

Anti-VEGF drugs have greatly enhanced our abilities to treat neovascular AMD, as well as a host of other retinal conditions. Unlike previous treatments such as verteporforin photodynamic therapy, anti-VEGF therapy involves injecting medication directly into the vitreous, thus putting the eye at risk for endophthalmitis. We have found an incidence of presumed endophthalmitis similar to previous studies.[3,5] Given that we have amassed the largest series (based on a recent PubMed search) of endophthalmitis cases after intravitreal anti-VEGF injections, we are in a unique position to additionally comment on outcomes of these endophthalmitis patients. Some earlier reports[4,5] had suggested that patients with endophthalmitis following anti-VEGF agents do well, typically with a return to baseline vision. Unfortunately, this does not seem to be the case in our series, in which 2/3 of patients returned to baseline vision at last follow-up, but 20% of patients had very poor outcomes.

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Table 1. Presumed Endophthalmitis after Intravitreal Anti-VEGF Injection Patient Data

Pt	Medication	Dz	Time to Presentation	Culture	PPV	Pre-Rx VA	Final VA	F/U
1	bevacizumab	AMD	2 days	No growth	No	20/40	20/40	1 mo
2	bevacizumab	AMD	2 days	No growth	No	20/50	20/60	1 mo
3	bevacizumab	AMD	1 day	*S. salivarius*	Yes	10/200	5/200	1 mo
4	ranibizumab	AMD	1 day	No growth	No	20/160	20/160	1 mo
5	bevacizumab	AMD	1 day	*S. viridans*	Yes	20/30	HM	6 wk
6	ranibizumab	AMD	2 days	*S. epi*	No	CF	CF	2 mo
7	bevacizumab	Myopic CNV	3 days	*S. epi*	No	20/30	20/60	6 mo
8	ranibizumab	AMD	8 days	*S. epi*	No	20/40	20/40	1 wk
9	ranibizumab	AMD	5 days	No growth	No	20/400	20/200	3 wk
10	ranibizumab	AMD	3 days	Coag neg staph	No	20/50	20/60	1 y
11	ranibizumab	AMD	4 days	N/A	No	20/60	20/200	3 mo
12	ranibizumab	AMD	4 days	No growth	Yes	20/150	20/200	7 mo
13	ranibizumab	AMD	4 days	No growth	No	20/200	20/400	11 mo
14	ranibizumab	AMD	2 days	N/A	No	20/400	NLP	6 mo
15	ranibizumab	AMD	2 days	No growth	Yes	20/150	NLP	1 mo

AMD = age-related macular degeneration; CF = counting fingers; CNV = choroidal neovascularization; Coag neg staph = coagulase-negative staphylococcus; Dz = disease; F/U = follow-up; HM = hand motions; N/A = not available; NLP = no light perception; PPV = pars plana vitrectomy; Pre-Rx = pretreatment; Pt = patient; S. salivarius = Strep salivarius; S. viridians = Strep viridans; S. epi = Staph epidermidis; VA = visual acuity.