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CASE SERIES

Acute endophthalmitis following intravitreal bevacizumab (Avastin) injection

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Abstract

***Purpose*: To report two cases of acute endophthalmitis following intravitreal bevacizumab injection.**
***Methods*: Two patients with exudative age-related macular degeneration were treated sequentially with an intravitreal injection of bevacizumab and developed signs of severe but painless infectious endophthalmitis 2 days later. Vitreous samples were obtained, followed by the injection of vancomycin 1 mg/0.1 ml and ceftazidime 2.25 mg/0.1 ml. Pulsed-field gel electrophoresis (PFGE) was used to determine whether the isolated microorganisms were the same.**
***Results*: Coagulase-negative staphylococci were identified and isolated from the vitreous specimen of both patients. PFGE revealed different patterns of banding, excluding that interpatient contamination occured.**
***Conclusions*: Infectious endophthalmitis is a potential complication of intravitreal bevacizumab injection.**
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Keywords: intravitreal bevacizumab; endophthalmitis; ocular inflammation; VEGF

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Introduction

Bevacizumab, a full-length recombinant humanized monoclonal antibody directed against vascular endothelial growth factor (VEGF), has been recently used for neovascular age-related macular degeneration (AMD) with encouraging results.[1,2] Herein, we report two cases in which infectious endophthalmitis occurred 2 days following intravitreal bevacizumab (IVB, 1.25 mg/0.1 ml) injections performed sequentially. Both patients had subfoveal occult choroidal neovascularization owing to AMD, with signs of recent progression despite treatment with photodynamic therapy with verteporfin. The contents of one vial of bevacizumab (100 mg/4 ml) were previously aliquoted into 0.1 ml (2.5 mg) single-use vials by a compounding pharmacy using aseptic techniques, which were stored in the refrigerator for up to 2 months. After informed consent was obtained, the drug was injected through the pars plana using a 30-gauge needle in the operating room with topical and subconjunctival anaesthesia, sterile lid speculum, and topical 5% povidone–iodine under aseptic conditions. The surgeon used sterile gloves and surgical clothing. Ciprofloxacin 0.3%, one drop four times a day, was prescribed for 5 days after the procedure.

Case reports

Case 1

Case 1 is an 80-year-old woman, right eye. Best-corrected visual acuity (BCVA): 20/160. Two days after IVB injection, the visual acuity had dropped to hand movement. There was mild corneal oedema, 2+ cells in the anterior chamber, 3+ vitreous cells, focal accumulations of whitish material within the vitreous, and scattered intraretinal haemorrhage in the posterior pole. The macular region could not be well observed. Pars plana vitrectomy and a vitreous aspiration biopsy were performed followed by an injection of vancomycin 1 mg/0.1 ml and ceftazidime 2.25 mg/0.1 ml. Numerous Gram-positive cocci were identified

in the smears from the centrifuged vitreous aspirate and the cultures were positive for coagulase-negative staphylococci. BCVA was counting fingers at 1 m 4 weeks later. No intraretinal haemorrhage was then observed. There was macular subretinal fibrosis with no evidence of exudation and diffuse retinal pigment epithelium atrophy OD.

Case 2

Case 2 is an 83-year-old man, left eye. BCVA: 20/200. Two days after IVB injection, BCVA was light perception. There was mild corneal oedema, hypopion, and a diffuse vitreous haze obscuring any view of the fundus. Pars plana vitrectomy and a vitreous aspiration biopsy were performed followed by an injection of vancomycin 1 mg/0.1 ml and ceftazidime 2.25 mg/0.1 ml. No microorganisms were identified in the smears from the centrifuged vitreous aspirate and the cultures were positive for coagulase-negative staphylococci. BCVA was hand movement 4 weeks later. Fundoscopy revealed diffuse retinal pigment epithelium atrophy and optic disc pallor OS. Disciform scarring of the right macula was seen.

Discussion

The vitreous specimen from both patients was submitted to PFGE analysis, revealing different patterns of banding. PFGE is a reliable method, based on the digestion of bacterial DNA with restriction endonucleases that recognize few sites along the chromosome, with the orientation of the electric field across the gel being periodically changed, allowing DNA fragments to be separated according to size.[3–5] The rest of the unused drug in the vial was sent for culture, which was negative. These results exclude the possibility of interpatient and drug contamination. In both cases, no pain, eyelid oedema, or increased conjunctival injection were noted. On the other hand, an aggressive process led to severe retinal damage as well as irreversible visual loss. This severe but painless course was similar to that of infectious endophthalmitis following intravitreal triamcinolone.[6] VEGF is an important signal in the dialogue between the tissues and the immune system and its inhibition may affect the evolution of the inflammation that accompanies an infectious process.[6,7]

There was no change in bevacizumab injection policy or method at our service after these complications, because the procedures were performed under sterile conditions in the operating room. Besides, infectious endophthalmitis has been described in association with any intravitreal drug injection. In a recent study, infectious endophthalmitis rate after IVB was 0.01% (one out of 7113 injections).[8]

In summary, infectious endophthalmitis is a potential complication of intravitreal bevacizumab injection and the physician should be able to recognize it and treat it promptly, bearing in mind that some of the signs and symptoms associated with endophthalmitis in the eyes without intraocular steroids or VEGF inhibitors may be lacking.

The authors have no commercial interests.

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