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CASE REPORT

# Exogenous group G *Streptococcus* endophthalmitis following intravitreal ranibizumab injection



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**Abstract:** We report a case of group G *Streptococcus* endophthalmitis following an intravitreal ranibizumab injection for a choroidal neovascular membrane. Pars plana vitrectomy was applied for endophthalmitis and group G *Streptococcus* cultures were isolated in the vitreous samples taken from the patient. Twenty-four hours following pars plana vitrectomy the patient underwent myocardial infarction and cardiac arrest. To our knowledge this is the first reported case of group G *Streptococcus* endophthalmitis following an intravitreal injection.

**Keywords:** group G *Streptococcus*, endophthalmitis, intravitreal injection

## Introduction

In eyes with age-related macular degeneration (AMD) and choroidal neovascular membrane, intravitreal anti-vascular endothelial growth factor treatment is one of the most important treatment options.[1,2] The efficacy and safety of ranibizumab (an intravitreal anti-vascular endothelial growth factor injection) has been shown in many multi-centered studies, however endophthalmitis, vascular thromboembolic events and cardiovascular side effects are possible complications.[3–6] Group G beta hemolytic streptococci are members of the normal flora of the skin, pharynx, gastrointestinal tract and vagina but can also cause epidemic pharyngitis, bacteremia, puerperal sepsis, peritonitis, cellulitis, arthritis, wound infection, septicemia, and infective endocarditis.[7,8] Endogenous and exogenous endophthalmitis caused by group G *Streptococcus* is very rare with few reported cases.[8–10] We present a case of group G *Streptococcus* endophthalmitis in which myocardial infarction occurred following intravitreal ranibizumab injection.

## Case report

A 58-year-old male patient presented with progressive visual loss in both eyes over the last 2 years. His examination showed a best corrected visual acuity of 20/400 in his right and left eyes and the intraocular pressure was normal. Fundus examination findings were consistent with bilateral exudative-type AMD with edema and subretinal hemorrhage. Bilateral active choroidal neovascular membranes were detected with fundus fluorescein angiography and optical coherence tomography. The patient had no history of a systemic disease and his systemic examination was normal. Intravitreal ranibizumab was applied in both eyes (first right, then left) (0.5 mg/0.05 mL) in a sterile operating room on the same day consecutively. Twenty-four hours following the injection procedure, the patient returned with pain in his left eye, decreased

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visual acuity, and redness. On examination, his visual acuity was counting fingers at 2 meters, his eyelids and conjunctiva were hyperemic and edematous, and there were 4+ cells and flare in the anterior chamber. Ultrasonography of the posterior segment of the eye showed infiltrations in the vitreous cavity. The patient was hospitalized with a diagnosis of endophthalmitis. The patient's white blood cell count was 17,190, the percentage of neutrophils 92.2%, and lymphocytes 4.4%. An infectious disease consultation was held and a blood culture was taken.

Cefazolin 1 g intravenous (IV) 2 × 1, gentamicin 80 mg IV 2 × 1, topical fortified cefazolin (50 mg/mL), and gentamicin (14 mg/mL), and cyclopentolate were prescribed. The patient refused intravitreal antibiotics. Twelve hours later the light perception in his left eye disappeared. On examination, the anterior chamber was almost full with hypopyon and the posterior chamber could not be visualized. Pars plana vitrectomy (PPV) was applied immediately under local anesthesia (retrobulbar) and the vitreous material was sent to the microbiology laboratory. In the culture taken from the patient's vitreous material, beta hemolytic streptococci were isolated on blood agar and grouped as "G" using the Lancefield reference method. The blood culture was negative. Twenty-four hours after PPV, the patient's ocular pain decreased, and the eyelid, conjunctival edema, and hyperemia resolved. However, the patient then had sudden chest pain and an electrocardiogram was performed. A cardiology consultation was held and shortly after myocardial infarction was diagnosed according to the electrocardiography. Cardiac arrest followed but, despite active cardiopulmonary resuscitation and all further interventions, the patient died.

## Discussion

Intravitreal ranibizumab injection, an efficient treatment method often used for neovascular AMD, is associated with ocular and systemic adverse events. Serious ocular adverse events related to the injection procedure include intraocular inflammation, endophthalmitis, retinal detachment, retinal pigment epithelium tear, vitreous hemorrhage, and iatrogenic cataract.[3–6]

The incidence of endophthalmitis following intravitreal ranibizumab has been reported as 0.02%–0.3% in the literature.[3,4,11–13] Although the risk of endophthalmitis following intravitreal injection is low, the number of injections has increased dramatically, the morbidity of this complication giving this risk more importance. Thus, proper aseptic conditions are required to minimize the risk of endophthalmitis. Cleaning the periorbital skin, eyelids, eyelashes, and injection site with povidone iodine is the most accepted method to reduce the rate of endophthalmitis.[14] Further recommendations include performing the injection in an operating room; use of a sterile ophthalmic drape; use of preoperative and postoperative topical antibiotics; and scheduling of staggered injections instead of bilateral same-day injections. However, no clear consensus regarding these suggestions has yet been reached.[15]

In this case, we performed the injections in a sterile operating room using a sterile ophthalmic drape. Our patient received bilateral injections drawn from a single vial using separate needles on the same day consecutively. There are some publications regarding bilateral same-day injection procedures. Woo et al suggested the safety profile of bilateral same-day injections to be equivalent to that of unilateral injections;[16] Mahajan et al also claimed that bilateral same-day injection procedures did not increase the rate of adverse events.[17] In addition, Davis et al reported bilateral same-day injections to be preferred over staggered injections by their patients.[18] When performing bilateral same-day injections, care must be taken for adverse ocular events, in particular endophthalmitis. To minimize the risk of endophthalmitis, a separate needle must be used when performing the second injection.

In this case, a group G *Streptococcus* was the causative organism of endophthalmitis. Eye infection due to group G *Streptococcus* is very rare. It can cause endophthalmitis endogenously, the secondary bacteremia it causes accounting for 0.3%–0.4% of all bacteremias.[8,11–13,19] It is a pathogen that more often causes infection in cases of malignancy, alcoholism, and drug abuse. In the literature, group G *Streptococcus* has been shown to cause endogenous endophthalmitis following endocarditis and dental procedures,[20–23] and has also been reported as the cause of exogenous endophthalmitis due to bleb-associated cases,[9,24] facial trauma,[25] cataract surgery,[26,27] and penetrating keratoplasty.[27] To our knowledge, this is the first reported case of group G *Streptococcus* endophthalmitis following an intravitreal injection.

Endophthalmitis treatment modalities vary from intraocular antibiotic injection with or without PPV according to the severity of the signs and symptoms. The choice of antibiotics depends on the suspected microorganism. At the time of first intravitreal antibiotic injection the causative microorganism is usually unknown. When fungal infections are excluded, intravitreal vancomycin (1 mg/0.1 mL) is the empiric treatment of choice for endophthalmitis, as it is a

broad spectrum antibiotic and in most cases, therapy has to be initiated before the culture results are known. Cephalosporins (eg, ceftazidime 2.25 mg/0.1 mL) and aminoglycosides (eg, amikacin 0.4 mg/0.1 mL) have Gram-negative coverage; however, aminoglycosides may also cause retinal toxicity. In our case, our patient refused intravitreal antibiotic injection, so we used IV antibiotics and fortified eye drops before PPV. The benefits of systemic and topical antibiotics are controversial. Broad-spectrum IV antibiotics including third generation cephalosporins can be used. Cycloplegic drops may be administrated and sometimes topical steroids may be considered.[28,29]

In our case, after the endophthalmitis started to heal, the patient underwent acute myocardial infarction presenting with chest pain and, despite all our efforts, died from cardiac arrest. Hypertension, arterial thromboembolic events, myocardial infarction, stroke, and death are known systemic adverse events that may occur following intravitreal ranibizumab injection.[3–6,11–13] Our case was a patient who was healthy and had no systemic risk factors. In addition, vascular events such as arterial thromboembolism and fatal or nonfatal myocardial infarction have been reported in cases in which intravitreal ranibizumab was given.[3,4] This case is important, as a person healthy in all manners developed group G *Streptococcus* endophthalmitis and myocardial infarction following intravitreal ranizumab injection.

Although adverse events following intravitreal injections are rare, before performing intravitreal injection, the physician must inform the patient concerning ocular and systemic adverse effects of the injection procedure and gain informed consent. Proper aseptic conditions must be utilized during the procedure and the physician must be rigorous.

## Disclosure

The authors report no conflicts of interest in this work.

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