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Case report

Recurrent fungal endophthalmitis after intravitreal injections of bevacizumab

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ABSTRACT

Purpose: We intend to describe an uncommon case of recurrent post-cataract fungal endophthalmitis after intravitreal injections of Bevacizumab.

Observations: A 73-year-old male, who underwent an uncomplicated cataract surgery 8 months ago, presented to our department with postoperative endophthalmitis 5 days after his fifth intravitreal injection (IVI) of bevacizumab for treatment of cystoid macula edema caused by central retinal venous occlusion 6 months ago. The visual acuity (VA) was 0.1 (20/200). The patient underwent an emergency pars plana vitrectomy. Culture of vitreous tap was negative. Eight weeks later, the patient presented again with recurrent endophthalmitis 2 days after his sixth IVI of bevacizumab. VA was hand motion. The patient was treated with an emergency anterior and posterior segment washout with intracapsular posterior intraocular lens (pIOL) extraction. Culture of pIOL revealed **Saccharomyces cervisiae** fungi in the capsular bag. Six months later, clinical findings were stable with no signs of intraocular inflammation, VA was 0.3 (20/60).

Conclusions and Importance: we assume that this is a rare case of chronic late-onset post-cataract fungal endophthalmitis, which was activated by repeated intravitreal injections of Bevacizumab.

1. Introduction

Infectious endophthalmitis after intravitreal injections (IVI) is a devastating complication potentially leading to severe visual loss. The reported rate of endophthalmitis following intravitreal injection ranges from 0.038% to 0.065%.[1] We report an uncommon case of recurrent fungal endophthalmitis after intravitreal injections of bevacizumab, describing the clinical appearance and management.

1.1. Case report

A 73-year-old male, who underwent an uncomplicated phacoemulsification with implantation of a posterior chamber intraocular lens (pIOL) 8 months ago. The patient had high blood pressure without any immunological disease, malignancies or diabetes. He did not take any immunosuppression medications.

He presented to our department with postoperative endophthalmitis 5 days after his fifth intravitreal injection (IVI) of bevacizumab for treatment of cystoid macula edema (CME) caused by central retinal venous occlusion 6 months ago.

The visual acuity (VA) was 0.1 (20/200) and intraocular pressure (IOP) was 28 mmHg. Slit-lamp examinations demonstrated severe vitritis with infiltration. The ocular ultrasonography (Cine Scan A/B scan; Quantel Medical Inc., France) showed a complete involvement of the posterior segment of the eye (Fig. 1).

The patient underwent an emergency pars plana vitrectomy with intravitreal antibiotics (Vancomycin 2 mg in 0.1 mL, Ceftazidime 2 mg in 0.1 mL). Culture of vitreous tap was negative.

Four weeks after the vitrectomy, the VA increased to 0.5 (20/40) with recurrence of the CME. The patient underwent the sixth IVI of bevacizumab with the application of Ofloxacin eye drop as prophylaxis for three days before the injection and planned one week after the injection.

Furthermore and according to the rule for all IVIs in our department, an administration of polyhexanide eye drop was carried out 3 times; during the medical examination, in the preparation room and at the end of the IVI in the operation room. In addition, a disinfection of the conjunctival sac with povidone-iodine took place 3 minutes before the injection in the operation room.[2]

All bevacizumab injections were prepared as individual injection under sterile circumstances in the pharmacy of Saarland University Medical Center.

Two days after the sixth IVI, the patient presented again with recurrent endophthalmitis. VA was hand motion and IOP was 32 mmHg.

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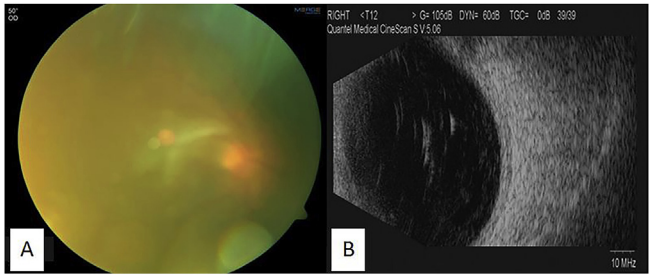

Fig. 1. Clinical and ultrasound findings at the first presentation showed a complete involvement of the posterior segment, Visual acuity 20/200; **A.** Vitreous haze and impaired fundus view, **B.** B-scan: dense vitreous opacities.

Slit-lamp examinations demonstrated intensive leukocytes in the anterior and posterior segment. The patient was treated with an emergency anterior and posterior segment washout with intravitreal antibiotics and antifungals (Vancomycin 2 mg in 0.1 mL, Ceftazidime 2 mg in 0.1 mL, Voriconazole 50 μg/0.1 mL and Amphotericin B 10 μg/0.1 mL) and intra-capsular pIOL extraction.

Culture of pIOL revealed **Saccharomyces cervisiae fungi in the capsular bag**, which is an ubiquitous yeast and a common colonizer of the human mucosae.

1.2. The patient underwent an intensive treatment

- Four times intravitreal Vancomycin 2 mg in 0.1 mL, Ceftazidime 2 mg in 0.1 mL Voriconazole 50 μg/0.1 mL and Amphotericin B 10 μg/0.1 ml, every 2 days in the first week.
- Topical: Voriconazole 1% eye drop 8 times daily, Prednisolone acetate 10 mg/ml 8 times daily (both tapered over 3 months) and Moxifloxacin hydrochloride 0.5% 8 times daily for 2 weeks.
- Systemic: Vancomycin 1g intravenous 2 times daily, Ceftazidim 2g intravenous 3 times daily (both for one week) and Fluconazol tab 200 mg 2 times daily for 2 months.

After three weeks, VA was 0.3 (20/60). The slit lamp biomicroscopy and the ocular ultrasonography showed no signs of intraocular inflammation (Fig. 2).

Six months later, clinical findings were stable with no signs of intraocular inflammation, VA was 0.3 (20/60). A secondary retroiridal implantation of a Verisyse iris-claw IOL (AMO) is planned. However, the patient died of heart attack seven months after the last vitrectomy.

2. Discussion

Saccharomyces organisms, also known as “baker's yeast” or “brewer's yeast”, are increasingly reported causes for invasive infections.[3] They are common in nature and can be found on plants in soil or included in some health foods.[4]

While *Saccharomyces cerevisiae* is a common colonizer of the human mucosa, it has been isolated since the 1980s as a cause of invasive fungal infections in patients with hematologic diseases.[5] Furthermore, its incidence has significantly increased in the last 25 years.[3]

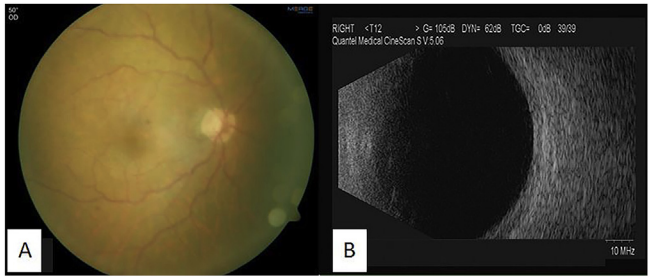

Fig. 2. Clinical and ultrasound findings, three weeks after intensive treatment, showed no signs of intraocular inflammation, Visual acuity 20/60; **A.** clear fundus view, **B.** clear B-scan image.

The choice of initial treatment for endophthalmitis is based on the clinical suspicion. Our patient was treated initially with vitrectomy and intravitreal antibiotics for a presumed acute bacterial endophthalmitis following IVI.

The most common causative organisms of acute endophthalmitis after IVIs of anti-vascular endothelial growth factor are coagulase-negative Staphylococcus species. This can also result from infection with other bacteria, viruses, fungi, protozoa, or algae.[1,6–8]

The **acute fungal endophthalmitis following IVIs** is uncommon and very much less common than bacterial endophthalmitis.[1]

According to the source of infection, endophthalmitis is divided into exogenous and endogenous.[9,10] The main feature of the exogenous fungal endophthalmitis is the exogenous introduction of fungal species from environmental sources into the eye by trauma or after surgery in apparently healthy individuals.[11] The exogenous fungal endophthalmitis can develop within the first 2 weeks postoperatively or can take several weeks.[12] The most common species causing exogenous fungal endophthalmitis are Aspergillus, Acremonium, Paecilomyces, and Prototheca. Uncommon cases were attributed to other fungi like the Saccharomyces species.[11] In general, some clinical records reported better prognosis in infection with yeast compared to infection with molds.[13]

However, the presence of Saccharomyces organism in the capsuler bag in our case raises also the possibility of a **chronic late onset post-cataract endophthalmitis**.

Post-cataract endophthalmitis is usually caused by Propionibacterium acnes, but also can rarely be caused by fungi. It usually manifests as a persistent low-grade inflammation in the anterior chamber with negative intra-ocular cultures, although the culture of the capsular bag is often positive. It is supposed that there is a 40–50% relapse rate in treatment regimens that leave the original IOL in place.[14] Some intraocular procedure like Nd:YAG laser capsulotomay may cause a mechanical reactivation pathomechanism by releasing the organism from the capsular bag and activate a late onset infection months or years after cataract surgery.[15]

Some clinical studies reported a few cases of fungal endophthalmitis after intravitreal injection of steroids,[13,16] this could be associated with the immunosuppression which might be caused by steroids. However, clinical studies have not described any correlation between anti-VEGF-drugs and immunosuppression.

In our clinical case, we may assume a mechanical reactivation pathomechanism. That could be related to the potential traumatic effect of the IVI due to the rapid elevation of the intraocular pressure after injection, which might activate the existed Saccharomyces fungi in the capsular bag leading to a late onset infection 8 months after cataract surgery.

After recurrence, our patient was treated with the intracapsular removal of the IOL, vitrectomy and intravitreal antibiotics in combination with intensive topical, systemic and intravitreal anti-fungal treatment according to culture results, which was a successful approach.

3. Conclusions

According to the clinical and microbiological courses and the uncommon occurrence of fungal endophthalmitis after IVI, we assume that this is a rare case of chronic late-onset fungal endophthalmitis after cataract operation, which was activated by repeated intravitreal injections of bevacizumab.

Patient consent

Consent to publish the case report was not obtained. This report

does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

All authors have no financial disclosures.

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