# Bilateral endogenous fungal endophthalmitis

Endoftalmite fúngica bilateral endógena

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# Abstract

A 77 year-old female patient suffering from pyelonephritis developed bilateral endogenous endophthalmitis presumed by Candida after have been treated with global spectrum antibiotics. Early vitrectomy and intravitreal amphotericin B injection were performed, in addition to oral voriconazole. Clinical aspects of endogenous endophthalmitis are also pointed out by a literature review. **Keywords:** Endophthalmitis; Eye infections, fungal; Candida albicans; Voriconazole

# Resumo

É apresentado o caso de uma paciente do sexo feminino, 77 anos, internada por pielonefrite e tratada com antibóticos de amplo espectro, tendo desenvolvido endoftalmite endógena bilateral presumida por Candida. Foi submetida à vitrectomia via pars plana e injeção intravítrea de anfotericina B, além de voriconazol oral. São abordados, ainda, os aspectos clínicos da endoftalmite endógena por meio de revisão da literatura.

Descritores: Endoftalmite; Infecções oculares fúngicas; Candida albicans; Voriconazol

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# INTRODUCTION

ndophthalmitis is a severe intraocular infection involving aqueous humor, vitreous humor, or both, which severely threatens vision.<sup>(1)</sup>

Endogenous fungal endophthalmitis is a complication caused by outspread fungal infections, of intraocular involvement, potentially damaging to visual function.<sup>(2,3)</sup> It is often related to immunosuppression states, debilitating diseases and invasive procedures.

Recent studies have suggested that the incidence of endogenous fungal endophthalmitis is increasing,<sup>(4)</sup> mainly because most patients who develop it are immunocompromised hosts, which is an increasingly prevalent condition in our environment. The advancement of intensive therapies, the increasing use of broad-spectrum antibiotics and easier access to diagnostic means led to irrefutable increase in the number of endogenous fungal endophthalmitis cases, and it created a growing demand by professionals for its approach.

The aim of the current study was to report a bilateral endogenous fungal endophthalmitis case, whose early diagnosis and intervention were decisive to reach a satisfactory visual outcome.

#### **Case report**

Female patient, aged 77 years, with diabetes and 6-year high blood pressure history, went to the Ophthalmology Emergency Care reporting low visual acuity on both eyes, for 10 days. The patient had been hospitalized in ICU in the week before due to pyelonephritis, when she was treated with culture-guided antibiotic therapy, after Pseudomonas aeruginosa identification in the collected medium. The bacterium showed sensitivity to Polymyxin B, which was the chosen medication.

The patient reported visual acuity (VA) in both eyes in the ophthalmologic examination by counting fingers at 4 meters. She reported anterior chamber reaction (ACR) 2+ and 18mmHg intraocular pressure (IOP) in both eyes in the biomicroscopy exam. Funduscopy showed vitreitis, with whitish plaques on the posterior pole of the right eye (RE) and in the foveal region of the left eye (LE). OCT evidenced inflammation involving the choroid with extension to the retina and vitreous opacity (Figure 1).

Pars plana posterior vitrectomy (PPV) was conducted in the left eye to collect material for further exams; balanced saline solution was used as vitreous substitute. Amikacin (400  $\mu$ g/0.1 ml) and amphotericin B (5 mcg/0.1 ml) intravitreal injection was performed in both eyes, in addition to dexamethasone (400  $\mu$ g/0.1 ml), at the end of the surgical procedure. Oral prednisone (20 mg on a daily basis) was not allowed to the patient, who was treated with moxifloxacin eye drops (5 mg/ml) added with dexamethasone 1 mg/ml every 4 hours in the postoperative period. The assistant expert in infectious diseases evaluated the patient and suggested using voriconazole 6 mg/kg every 12 hours (orally) in the first 24 hours and 4 mg/ kg every 12 hours for 4 weeks.

The patient reported 14mmHg IOP in both eyes, absence of ACR, and progressive reduction in vitreous opacity and in the size of funduscopic lesions 10 days after surgery (Figure 2). Direct bacterioscopic and mycological examinations results and collected vitreous cultures were negative.

The patient reported corrected VA of 20/200 RE and 20/40 LE 30 days after the surgical procedure in the left eye and





**Figure 1-A:** Color fundus photography - when the patient was hospitalized - showing multiple white infiltrative lesions with vitreous extension (cotton balls colony) in both eyes. It is possible noticing several intraretinal hemorrhages in the right eye. **Figure 1 – B:** OCT - when the patient was hospitalized - showing increased retinal thickness and a lesion involving the choroid, with extension to the intraretinal layers in both eyes and apparent extraretinal migration to the vitreous



**Figure 2:** Color fundus photography - taken ten days after LE PPV and at the beginning of the systemic therapy - showing progressive vitreous opacity and funduscopic lesion size reduction in both eyes



Figure 3: OCT after 30-day evolution. A: Right eye shows perifoveal intraretinal edema. B: Left eye evidenced full edema regression.

was prescribed for intravitreal antibiotic therapy in both eyes. Funduscopy showed moderate vitreous opacity and papillary hemorrhage in RE, in addition to upper perifoveal atrophic scar in LE. Optical coherence tomography (Figure 3) evidenced macular edema in RE; PPV and intravitreal dexamethasone injection were administered in this eye. LE OCT showed full edema regression.

The patient did not show any change in visual acuity and in funduscopic examinations from the previous examination (Figure



**Figure 4:** Exams after 78-day evolution. A – Right eye with foveal scar lesion and peripapillary intraretinal hemorrhages and left eye with perifoveal atrophic superior lesion. B – Hypo-autofluorescence areas corresponding to the atrophic regions of both eyes. C – Right eye OCT showing important macular edema reduction, structural disorganization of the internal retinal layers and subretinal hyper-reflective lesion. Left eye remained similar to the previous exam; it showed small, hyper-reflective, peripheral subretinal lesion with intraretinal hyper-reflective points.

4) at the 22nd day after surgical procedure - PPV RE, 78 days after symptoms had began. She remains under follow-up.

## DISCUSSION

Endophthalmitis is one of the most severe complications among ophthalmic disorders; it accounts for the worst functional outcomes.<sup>(5)</sup> Endogenous endophthalmitis responds for 2% to 15% of all endophthalmitis cases and is the cause of hematogenous spread of distant focus.<sup>(6)</sup>

Candida albicans is the most common etiologic agent related to endogenous fungal endophthalmitis. <sup>(2, 7-9)</sup> With respect to the here described case, endophthalmitis is assumed as a candidemia complication, since the patient was previously hospitalized because of pyelonephritis and treated with broad-spectrum antibiotics. She had a central venous catheter during hospitalization, a fact that corroborates the emergence of endogenous endophthalmitis. <sup>(2)</sup>

Classic findings on chorioretinal involvement through funduscopy consist in focal, white, infiltrative, mostly "mound-like" lesions in the retina. In case of vitreous extension, one can observe vitreous haze; "fluffy white balls", "snowballs" or "string of pearls" in the vitreous.<sup>(10-12)</sup>

Ocular ultrasound is a useful method to help the diagnosis, treatment and follow-up of media-opacity endophthalmitis cases, whose detailed posterior segment evaluation is not possible.<sup>(13)</sup> Clinical suspicion alone justifies starting the optimized therapy; however, ultrasound findings end up minimizing complication rates - resulting from possibly unforeseen and undetected conditions - by predicting the involvement degree of ocular structures.<sup>(14)</sup>

Endophthalmitis diagnosis is clinical and confirmed through positive aqueous or vitreous culture. However, negative culture does not exclude the diagnosis because this outcome can happen in up to 30% of cases.<sup>(15)</sup> As for the current case report, the presumptive diagnosis of endogenous fungal endophthalmitis by Candida was based on the patients' previous pathological history, on ocular clinical case and on classical retinal manifestation. Empirical treatment was promptly prescribed: intravitreal amphotericin B injection, systemic antifungal with oral voriconazole and pars plana vitrectomy.

The choice for oral antifungal therapy lied on the fact that the patient had reduced renal function. Intravenous therapy is preferable in cases of similar severity; however, this formulation contains the excipient sulfobutyl ether-beta-cyclodextrin, which accumulates in patients with renal failure. Therefore, oral therapy is safer for patients with renal failure.<sup>(16)</sup>

PPV was initially performed in the left eye because it showed possibly better final visual prognosis. The right eye had important lesions in the foveal region; therefore, priority was given to vitrectomy of the eye with the best prognosis. approach of the contralateral eye was left for a moment when the patient reported clinical improvement compatible to a new surgical procedure.

Another important factor was the use of intravitreal steroids; they seem to have promoted faster inflammation elimination.<sup>(17)</sup> We chose to use intravitreal dexamethasone from the beginning of the treatment due to the severity of the evidenced uveitis.

Fungal endophthalmitis treatment remains an important challenge to Ophthalmology because it still shows unsatisfactory outcomes in a considerable number of cases. The early detection and immediate management of endophthalmitis seem to be the most important clinical factors influencing prognosis;<sup>(18)</sup> therefore, the full clinical domain of this condition by ophthalmologists is mandatory in order to get to satisfactory visual outcomes.

## Referências

- 1. Kim CH, Chen MF, Coleman AL. Adjunctive steroid therapy versus antibiotics alone for acute endophthalmitis after intraocular procedure. Cochrane Database Syst Rev. 2017 Feb 22;2:CD012131.
- Essman TF, Flynn HW Jr, Smiddy WE, Brod RD, Murray TG, Davis JL, Rubsamen PE. Treatment outcomes in a 10-year study of endogenous fungal endophthalmitis. Ophthalmic Surg Lasers. 1997;28(3):185-94.
- Feman SS, Nichols JC, Chung SM, Theobald TA. Endophthalmitis in patients with disseminated fungal disease. Trans Am Ophthalmol Soc. 2002;100:67-70; discussion 70-1.
- Takebayashi H, Mizota A, Tanaka M. Relation between stage of endogenous fungal endophthalmitis and prognosis. Graefes Arch Clin Exp Ophthalmol. 2006;244(7):816-20.
- 5. Schirmbeck T, Romão E, Rodrigues MLV, Figueiredo JFC. Endoftalmite: uma análise de 58 casos. Arq Bras Oftalmol. 2000;63(1):39-44.

- Keynan Y, Finkelman Y, Lagacé-Wiens P. The microbiology of endophthalmitis: global trends and a local perspective. Eur J Clin Microbiol Infect Dis. 2012;31(11):2879-86.
- 7. Clinch TE, Duker JS, Eagle RC Jr, Calhoun JH, Augsburger JJ, Fischer DH. Infantile endogenous Candida endophthalmitis presenting as a cataract. Surv Ophthalmol. 1989;34(2):107-12.
- Neves RA, Rigueiro MP, Bordon AF, Burnier M Jr. Endoftalmite micótica endógena: aspectos clínicos e histopatológicos de 3 casos. Arq Bras Oftalmol. 1990;53(1):20-2.
- Heinemann MH, Bloom AF, Horowitz J. Candida albicans endophthalmitis in a patient with AIDS: Case report. Arch Ophthalmol. 1987;105(9):1172-3.
- Griffin JR, Pettit TH, Fishman LS, Foos RY. Blood-borne Candida endophthalmitis. A clinical and pathologic study of 21 cases. Arch Ophthalmol. 1973; 89(6):450-6.
- Edwards JE Jr, Foos RY, Montgomerie JZ, Guze LB. Ocular manifestations of Candida septicemia: review of seventy-six cases of hematogenous Candida endophthalmitis. Medicine (Baltimore). 1974; 53(1):47-75.
- 12. Donahue SP, Greven CM, Zuravleff JJ, Eller AW, Nguyen MH, Peacock JE Jr, et al. Intraocular candidiasis in patients with candidemia. Clinical implications derived from a prospective multicenter study. Ophthalmology. 1994;101(7):1302-9.

- Adan CB, Blay D, Yu MC, Freitas DD, Allemann N. Ultra-sonografia ocular em suspeita clínica de endoftalmite. Arq Bras Oftalmol. 2001; 64(5):423-8.
- Kohanim S, Daniels AB, Huynh N, Eliott D, Chodosh J. Utility of ocular ultrasonography in diagnosing infectious endophthalmitis in patients with media opacities. Semin Ophthalmol. 2012;27(5-6):242-5.
- 15. Durand ML. Endophthalmitis. Clin Microbiol Infect. 2013;19(3):227-34.
- Neofytos D, Lombardi LR, Shields RK, Ostrander D, Warren L, Nguyen MH, et al. Administration of voriconazole in patients with renal dysfunction. Clin Infect Dis. 2012;54(7):913-21.
- Akler ME, Vellend H, McNeely DM, Walmsley SL, Gold WL. Use of fluconazole in the treatment of candidal endophthalmitis. Clin Infect Dis. 1995;20(3):657-64. Review.
- Bhoomibunchoo C, Ratanapakorn T, Sinawat S, Sanguansak T, Moontawee K, Yospaiboon Y. Infectious endophthalmitis: review of 420 cases. Clin Ophthalmol. 2013;7:247-52.

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