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Case report

Circumferential iris lesions in a male with cirrhosis caused by Candida dublinensis endophthalmitis

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Introduction

Candida endophthalmitis (CE) is a subacute illness with presentation varying from an anterior uveitis to painful vitritis or pan inflammation. We are presenting a case of candida endophthalmitis in a 61-year-old male who presented with a vision change of 6 weeks in one eye. Diagnosis was confirmed with aqueous culture growing *Candida dubliniensis*. He was treated with intravenous, intravitreal and oral antifungal medications. His course was complicated by retinal detachment. *Candida dubliniensis* endophthalmitis is rare and the scattered numerous fluffy infiltrates on the iris is an unusual observation.

Case report

A 61-year-old male presented with a history of vision change for the previous six weeks in the right eye. His first symptom was as if he was seeing a spider web in his right eye and denied any prior ocular trauma, infection or surgeries. The past history was significant for alcohol and hepatitis C virus (HCV)-related cirrhosis and active intravenous methamphetamine abuse. Two years before, his HCV infection was successfully treated for 12 weeks with ribavirin, daclatasvir, and sofosbuvir. A referring ophthalmologist noted that visual acuity was limited to hand motion only in the right eye. There were anterior chamber cells, pupillary posterior synechiae and ultrasound showed mild vitreous echogenic debris. Left eye exam was normal with visual acuity of 20/20. He was prescribed topical steroids for acute anterior uveitis. He returned with worse symptoms including painful ocular movements, diminished visual acuity, photosensitivity, and right sided headache. On exam, the right eye showed worsening anterior chamber cells with a dense fibrinous membrane overlying the pupil and iris. Scattered numerous creamy fluffy infiltrates were seen on the iris (Fig. 1). A repeat ultrasound showed worsened vitreous debris. Anterior chamber paracentesis was performed and sent for bacterial, herpetic and fungal cultures.

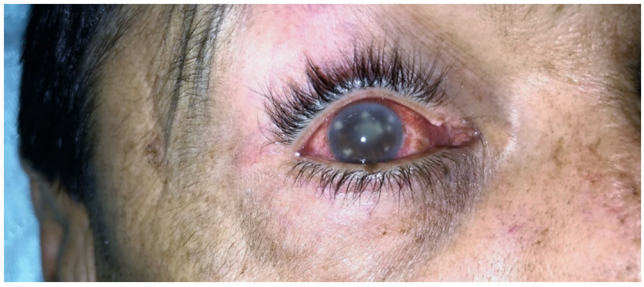

Fig. 1. Right eye of our patient showing circumferential scattered creamy iris infiltrates that are distributed in a clock-face pattern.

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Table 1
Types of Candidal Endophthalmitis (CE) and their proposed treatment [1,6].

Type of CE	Treatment
Exogenous endophthalmitis	Parsplana vitrectomy +/- intra-vitreal antifungal agent[a], removal of foreign materials and systemic antifungal agents[b].
Endogenous chorio-retinitis without significant macular involvement	Systemic antifungal agents[b]
Endogenous chorio-retinitis with significant macular involvement	Systemic antifungal agents[b], intra-vitreal antifungal injections[a]
Endogenous endophthalmitis with Vitritis	Systemic antifungal agents[b], intra-vitreal antifungal injections[a], vitrectomy.

[a] Amphotericin B or Voriconazole, rare reports of select Echinocandins as alternatives.
[b] Fluconazole or Voriconazole. Liposomal Amphotericin B should be used if azole resistant strain with or without Flucytosine.

The patient was admitted and Varicella Zoster Virus (VZV) and Herpes Simplex virus (HSV) polymerase chain reaction (PCR) from corneal swabs were sent. Intravenous acyclovir was started empirically. Human immunodeficiency virus (HIV) antigen-antibody assay, two sets of blood cultures and a transthoracic echocardiogram were ordered. Aqueous humor cultures grew *Candida dubliniensis*. HIV testing, VZV and HSV PCR and blood cultures were negative. A transthoracic echocardiogram was negative for vegetations. He was initially treated with intravenous and intra-vitreal amphotericin B and eventually changed to oral fluconazole based on species identification susceptibilities, for a total of six weeks. He thereafter underwent lensectomy and vitrectomy and was noted to have significantly ischemic retinal vasculature. His postoperative course was complicated by development of diffuse epi-retinal membranes with tractional retinal detachment and underwent additional vitrectomies. His final visual acuity on the right eye was 20/400.

Discussion

Candida endophthalmitis (CE) is a subacute illness with presentation varying from an anterior uveitis to painful vitritis or pan inflammation [1–3]. Blood cultures can be negative at diagnosis if the antecedent candidemia was transient. Culture of intraocular fluids often confirms the diagnosis. Risk factors include intravenous drug abuse, presence of a central venous catheter (CVC), total parenteral nutrition, administration of broad-spectrum antimicrobials, recent abdominal surgery, neutropenia, glucocorticoid therapy and diabetes [1]. In our case, intravenous drug use is probably the risk factor [4]. *C. albicans* has been the predominant species isolated and *C. dubliniensis* is a rare cause [5]. *C. dublinensis* had been generally considered less virulent than *C. albicans* as it is susceptible to environmental stressors and produces less hyphae in-vitro than *C. albicans* [6,7]. Disputing this are increasing reports on infections caused by *C. dubliniensis* that have hypothesized increased neutrophil migration, phagocytosis, cytokine release and ineffective interleukin-17A production by peripheral blood mononuclear cells as possible reasons [4,8]. Newer methods such as matrix assisted laser desorption ionization – time of flight (MALDI-ToF) and polymerase chain reaction (PCR) have enabled differentiation of closely related species and this could be another reason [8].

Early diagnosis and rapid aggressive antifungal therapy are important to reduce ocular complications such as blindness. Diagnosis is often based on clinical findings documented by dilated eye exam and work up should be directed to identify the source [1,2,6]. The intraocular inflammation in fungal endophthalmitis tends to occur in “clumps” within the aqueous and/or vitreous (Fig. 1) which differentiates it from bacterial endophthalmitis where the intraocular inflammation is typically diffuse [1]. At diagnosis, blood cultures are often negative because the candidemia was antecedent (days or weeks earlier) and often transient. Hence, culture of intraocular fluids is often required at presentation to confirm the diagnosis. A suggested method of follow up on visual recovery is optical coherence tomography (OCT) which is a noninvasive imaging study that uses light waves to take cross-sectional pictures of the retina [1,9]. Outcome depends on disease severity at presentation and the choice and duration of treatment. In one series, most patients were active intravenous drug abusers with hepatitis C infection and 30% developed retinal detachment despite treatment [6]. Table 1 lists the treatment options for exogenous and endogenous CE [1].

For *C. albicans*, fluconazole is the drug of choice. For non-*albicans Candida* either fluconazole or voriconazole can be used based on susceptibility results. For azole resistant strains such as *C. glabrata*, both intra-venous liposomal amphotericin B and intra-vitreal amphotericin B should be used with or without 5-flucytosine [1,10]. In general, the azoles achieve better intra-ocular concentrations with systemic administration than amphotericin B. Among the newer azoles, voriconazole shows the most promise and can be used for both systemic and intra-vitreal administration. As the choroidal retina is highly vascular, systemic therapy alone may be sufficient, but if sight-threatening macular involvement and vitritis are present, initial intra-vitreal amphotericin B or voriconazole in addition to systemic therapy is recommended in order to quickly achieve a high local concentration in the posterior segment of the eye [1,10,11]. Posaconazole is not recommended because it fails to achieve good intra-ocular concentrations by systemic administration, moreover, intra-vitreal preparations are unavailable [10,11]. A few recently published reports of anidulafungin and caspofungin as intra-vitreal injections exist, but it is very important to remember that systemic administration of echinocandins should never be used alone as they fail to achieve adequate intra-vitreal concentrations [12,13]. The Infectious Diseases Society of America (IDSA) recommends at least four to six weeks or longer as the duration of systemic therapy depending on the clinical course and recovery determined by serial ophthalmological exam [11].

Conclusion

Candida endophthalmitis poses diagnostic and therapeutic challenges. An antecedent fungemia often goes undetected due to delayed development of appreciable ocular symptoms. Hence, knowledge of known risk factors such as intravenous drug abuse and cirrhosis, coupled with high index of suspicion is needed for earlier diagnosis and treatment. Intra-ocular sample cultures are often needed to pin-point diagnosis. Delays in diagnosis have devastating ocular consequences such as retinal detachment and permanent blindness, even with appropriate treatment.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request

CRediT authorship contribution statement

Suha Abu-Khalaf : Conceptualization, Writing - original draft. **Ahmed Elkeeb:** Visualization, Writing - review & editing. **William Salzer:** Supervision, Writing - review & editing. **Hariharan Regunath:** Supervision, Writing - review & editing.

Declaration of Competing Interest

Regunath received honoraria from Getinge. Other authors have no financial disclosures or conflicts of interest.

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