

Ocular Candidiasis: Presented at FA Conference November 2016

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Case 1: 13 yo boy

- 13 yo boy being treated for B cell ALL following induction therapy and subsequently developed a FUO
- CT imaging found lesions concerning for candidiasis
- Started on IV Caspofungin for presumed candidiasis
- Seen by local eye doctor who saw several concerning retinal lesions and subsequently referred to the Moran

Initial Examination

- VA: 20/25 OU
- IOP: 16 OU
- No RAPD, no field loss, and EOM full OU
- Anterior segment unremarkable
- Rare vitreous cell OU
- Dilated Exam:





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Plan

- Elected to **observe** with **close follow up**
- Presumed leukemic retinopathy OD and endogenous fungal endophthalmitis OS

Update: 4 days later

- VA: 20/40, 20/30; OD and OS respectively
- No positive microbiology
- Continued to observe as no changes on exam

Update: 1 week later

- IV caspofungin stopped and started on oral fluconazole (400mg)
- VA: 20/20 OU

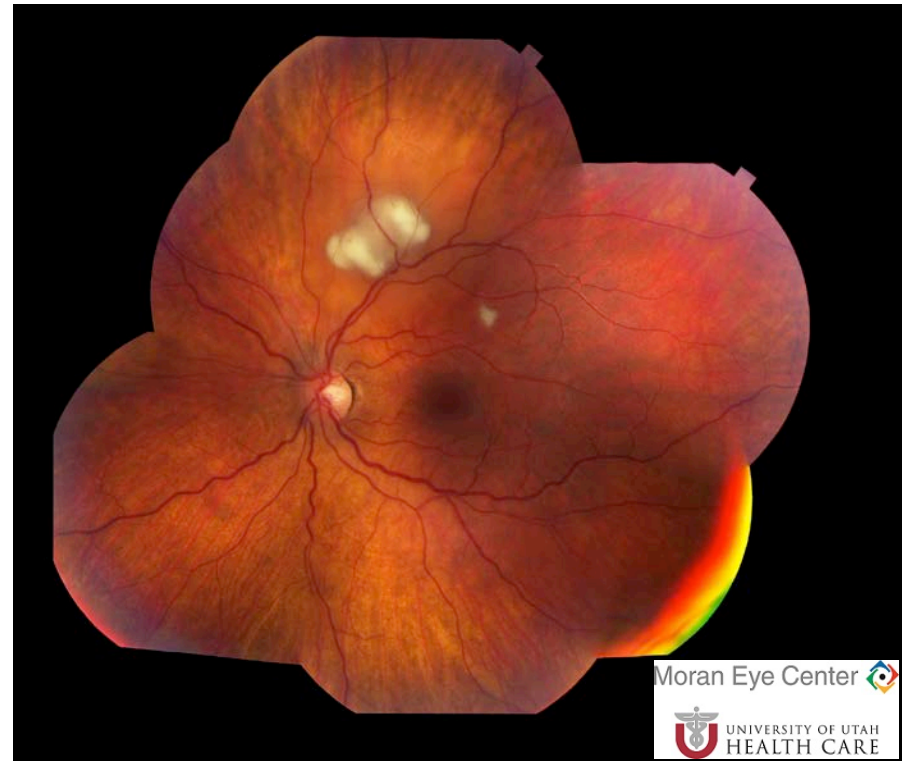


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Comparison



- Due to enlarging lesion, an intravitreal injection of voriconazole was performed
- Remained on fluconazole

10 days later...

- “Enlarging blurry spot”
- No positive microbiology, presumed candidiasis diagnosis from imaging and elevated Beta-D-glucan
- VA: 20/20, 20/150

Hazy borders, enlarged in size

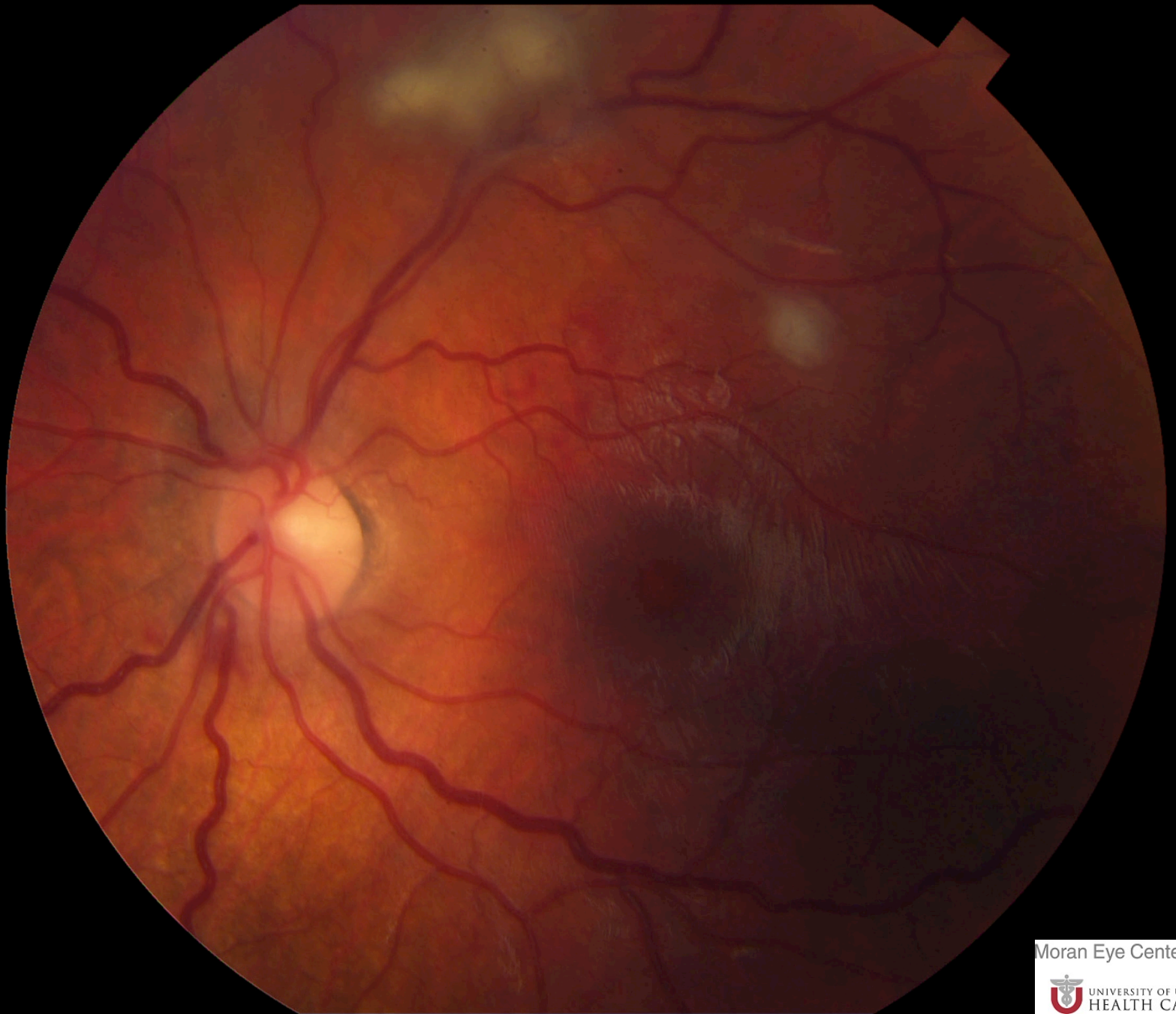


Add on...

- Underwent PPV and intravitreal voriconazole and amphotericin B

7 days later...

- No changes in vision
- VA: 20/20, **20/25**



Fungal endophthalmitis

- Endogenous (systemic dissemination) vs. exogenous
- Most common cause: *Candida albicans*
- 10 year outcome study from 1997: marked vitreous infiltrates should warrant PPV, systemic antifungals, and intravitreal amphotericin
- Prospective studies: 9-37% of hospitalized patients with candidemia develop endophthalmitis
 - Prompt treatment lowers rates to 3-9%
 - Candida prognosis better than Aspergillus
 - Risk factors: Indwelling catheters, total parental nutrition, broad spectrum antibiotics, neutropenia, and steroid therapy
 - Prospective study of 125 cases of candidemia places numbers for chorioretinitis at 5.6% and endophthalmitis at 1.6%

Current ID Recommendations

- Non-neutropenic patients with candidemia should have a dilated exam within 1 week of initiation of therapy; most would recommend 2 dilated exams even in asymptomatic patients
 - Neutropenic pts: Delay examination until neutrophil recovery
- Chorioretinitis WITHOUT vitritis (candida chorioretinitis)
 - No macular involvement: systemic antifungals
 - WITH macular involvement: +/- intravitreal injections
 - Duration of therapy at least 4-6 weeks
- Chorioretinitis with vitritis (candida endophthalmitis)
 - As above +/- vitrectomy to reduce fungal burden

Ocular penetration of antifungals

- Amphotericin B – poor ocular penetration
 - Has been used as sole intravitreal agent to treat endophthalmitis to reduce systemic toxicity
- Flucytosine
 - Synergistic with Amphotericin B and achieves high levels in the intraocular compartment
- Fluconazole
 - Experiments in rabbits: vitreous levels 50% of peak plasma levels
 - In humans: ~70% of plasma levels
 - Response rates of >90% (some patients included had additional treatments)
- Voriconazole
 - Broad spectrum
 - Levels 38% of plasma levels in humans
 - Added activity against *Aspergillus* and *Candida glabrata*
- Little information on Posaconazole and Echinocandins (poor penetration)

Case 2: 10 yo boy with ALL



**Elected to
monitor
peripheral
lesions

- Case #2 outcome: peripheral lesions remained stable on IV and then oral antifungals in the left eye
- No imaging to who but the patient's right eye had a foveal-splitting lesion requiring multiple intravitreal injections and eventually recovered vision to 20/40
- Final VA OS 20/20

What we learned...

- These two cases highlight the use of intravitreal injections in conjunction with systemic therapy and when observation of chorioretinal lesions in the setting of systemic therapy can be utilized.

Citations

- Brod RD, Flynn HW Jr., Clarkson JG, Pflugfelder SC, Culbertson WW, Miller D. Endogenous *Candida* endophthalmitis: management without intravenous amphotericin B. *Ophthalmology* 1990;97:666-72.
- Essman TF, Flynn HW Jr, Smiddy WE, Brod RD, Murray TG, Davis JL. Treatment outcomes in a 10-year study of endogenous fungal endophthalmitis. *Ophthalmic Surg Lasers*. 1997 Mar. 28(3):185-94.
- Hariprasad SM, Mieler WF, Holz ER, et al. Determination of vitreous, aqueous, and plasma concentration of orally administered voriconazole in humans. *Arch Ophthalmol* 2004;122:42-7.
- O'Day DM, Head WS, Robinson RD, Stern WH, Freeman JM. Intraocular penetration of systemically administered antifungal agents. *Curr Eye Res* 1985;4:131-4.
- Paulus YM, Cheng S, Karth PA, Leng T. PROSPECTIVE TRIAL OF ENDOGENOUS FUNGAL ENDOPHTHALMITIS AND CHORIORETINITIS RATES, CLINICAL COURSE, AND OUTCOMES IN PATIENTS WITH FUNGEMIA. *Retina*. 2015 Dec 11.
- Riddell et al., Treatment of Endogenous Fungal Endophthalmitis: Focus on New Antifungal Agents. *Clinic Inf Dis*. 2011.
- Schmid S, Martenet AC, Oelz O. *Candida* endophthalmitis: clinical presentation, treatment and outcome in 23 patients. *Infection* 1991;19:21-4.
- Sridhar J, Flynn HW Jr, Kuriyan AE, Miller D, Albin T. Endogenous fungal endophthalmitis: risk factors, clinical features, and treatment outcomes in mold and yeast infections. *J Ophthalmic Inflamm Infect*. 2013 Sep 20. 3 (1):60.
- Tod M, Lortholary O, Padoin, Chaine G. Intravitreal penetration of fluconazole during endophthalmitis. *Clin Microbiol Infect* 1997;3:379A.
- Walsh TJ, Foulds G, Pizzo PA. Pharmacokinetics and tissue penetration of fluconazole in rabbits. *Antimicrob Agents Chemother* 1989;33:467-9.