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Candida auris and endogenous panophthalmitis: clinical and histopathological features

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ABSTRACT

Purpose: To report an unusual case of endogenous panophthalmitis involving *Candida auris* and describe its clinical and histopathological features.

Findings: A 30 year-old man with history of human immunodeficiency virus, polysubstance abuse, syphilis, and recently treated pneumonia presented with polymicrobial endogenous panophthalmitis. Two separate ocular specimens confirmed simultaneous *Pseudomonas aeruginosa* and *Candida auris* involvement. Histopathological analysis demonstrated fulminant polymorphonuclear infiltration of all ocular tissue layers. Despite aggressive management including two intravitreal injections and enucleation, the patient died, ultimately after receiving care at four neighboring urban medical centers.

Conclusions and importance: Candida auris has been a recently and increasingly described pathogen leading to mortality in metropolitan hospitals worldwide. To the authors' knowledge, *Candida auris* has not previously been reported with endophthalmitis or panophthalmitis. Future cases may be expected with the reported rise in *Candida auris*. A high suspicion of its contribution to panophthalmitis could be warranted early in the evaluation and management of profoundly immunocompromised patients, particularly those who have had sequential care at multiple neighboring metropolitan hospitals.

Disclosures

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1. Introduction

Candida auris is a new, increasingly endemic, and multi-drug resistant fungal pathogen reported in metropolitan hospitals worldwide. We demonstrate the first clinical and histopathological features of polymicrobial endogenous panophthalmitis involving *Candida auris*.

2. Methods

Case study with clinical and histopathological analysis.

3. Results

A 30 year-old man with human immunodeficiency virus (HIV) and polysubstance abuse presented with painful right eye vision loss over one day. Three weeks elsewhere, he was treated for syphilis and pneumonia of unknown etiology.

Examination revealed a normal left eye, and no light perception in the right eye. There was proptosis, chemosis, mucopurulent corneal discharge, haze, and hypopyon (Fig. 1). Vitreous opacities limited posterior visualization. Extraocular motility was absent. Treatment included intravenous vancomycin, metronidazole, ganciclovir, and

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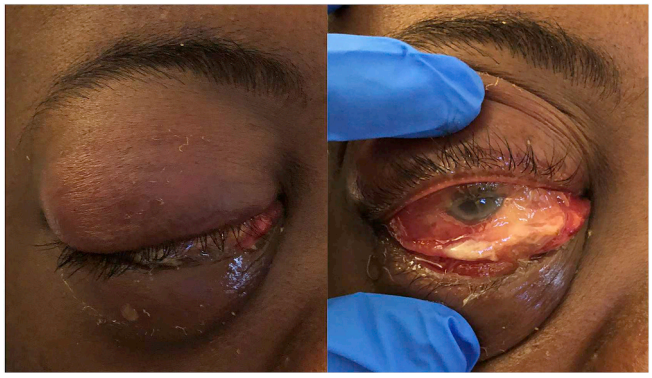

Fig. 1. Clinical photographs of affected eye, without (left) and with assisted lid retraction (right). Marked ptosis, proptosis, chemosis, purulence, corneal haze and opacification, and hypopyon are consistent with florid endophthalmitis and orbital cellulitis (panophthalmitis).

cefepime. Blood cultures were negative, but urine culture showed pansensitive *Pseudomonas aeruginosa.* Intravitreal vancomycin and ceftazidime were injected.

Orbital edema worsened over 5 days. Neuroimaging confirmed lack of intracranial involvement. Intravenous penicillin and amphotericin B, oral moxifloxacin, and topical ofloxacin, atropine, and prednisolone were added. Vitreous aspiration was performed with intravitreal amphotericin B and additional ceftazidime and vancomycin injections. After previous refusals, enucleation was finally elected. Enucleation specimen demonstrated fulminant inflammation with profound polymorphonuclear infiltration in all tissue layers (Fig. 2, H&E). Special histochemical staining for organisms (Gram, PAS, GMS, and AFB) revealed no morphologic evidence of etiologic agents. Vitreous and enucleation cultures both demonstrated *Pseudomonas aeruginosa* and *Candida auris*. Clinical improvement prompted initiation of highly active anti-retroviral therapy and eventual discharge with systemic ciprofloxacin and micafungin.

Poor compliance and return to recreational drug use preceded a fall and admission elsewhere. Identification of cerebral hematoma with midline shift and mycotic aneurysm prompted glue embolization. Pseudomonal meningitis with multiple brain lesions, spinal infection, respiratory failure, hydrocephalus, and ultimately, herniation followed. Supportive care was withdrawn, and the patient expired.

4. Discussion

Endogenous panophthalmitis results from blood-ocular barrier violation with intraocular seeding from bloodstream organisms.[1,2] Risk factors here include HIV and polysubstance usage. Polymicrobial endogenous endophthalmitis is exceedingly rare and occurs with different bacteria.[3] However, reporting of simultaneous bacterial and fungal involvement is unique. Another unusual aspect of this case is the isolation of *Candida auris* which has not previously been found to cause panophthlamitis. While some aspects of this case have recently been published,[4] the missing follow-up, clinical photography, and histopathologic analysis are now presented.

Candida auris was first isolated in Japan in 2009[5] and has obtained widespread media attention for lethality. While reported mortality occurs in approximately 4% with endogenous endophthalmitis,[1] it approaches 60% for systemic *Candida auris* infections.[5] As in this patient, most affected by endogenous fungal endophthalmitis typically present with ocular symptoms despite no growth from fungal blood cultures.[6] Nonetheless, fear of missing endogenous endophthalmitis has led to routine ophthalmologic screening for patients with fungal bloodstream infections, but without proven benefit.[2] Even when identified, fungal endophthalmitis has relatively poorer outcomes compared to other endophthalmitis causes.[6]

Challenges in managing systemic fungal infections involve delays from slow culture growth. Additional difficulty, as seen here despite empiric antifungal coverage, is possibly attributable to known *Candida auris* multi-drug resistance.[4] Ultimately, it is impossible to determine the individual contribution of *Candida auris* and its virulence given concurrent *Pseudomonas aeruginosa* infection with the fulminant intraocular inflammation. Indeed, the histologic feature of inflammation floridly extending into the orbit (panophthalmitis) has been described only in a paucity of endogenous cases; namely, from *Pseudomonas aeruginosa,*[7] *Escherichia coli,*[8] or *Serratia marcescens*.[9] It is therefore challenging to discern from this case whether *Candida auris* alone can cause this fulminant panophthalmitis. A limitation here is the absence of both identifiable organisms histologically, despite their microbiologic isolation from two different ocular specimens. However, the multi-system bacterial infections and treatments during prior hospitalization predisposing to fungal infection, relatively high virulence of *Candida auris* (including production of phospholipases and proteinases),[10] and absence of systemic or local antifungal coverage upon initial recognition of panophthalmitis (while still covering for *Pseudomonas aeruginosa*) favors the contribution of *Candida auris*. To our knowledge, the literature is scant regarding cases of endogenous cases with simultaneous bacterial and fungal organisms. Given the uniqueness of this case and multiple variables, it is impossible to know with certainty whether recognizing or addressing the fungal etiology sooner would have changed the ultimate clinical outcome.

Candida auris has recently been reported in densely-populated cities such as New York.[5] Risk factors for mortality with endophthalmitis include large center hospitalization, lack of insurance, septicemia, and pneumonia,[1] all playing a role here. In total, this patient received care at four neighboring hospitals. Geography and interconnectedness of metropolitan facilities have contributed to *Candida auris* emergence.[5] High suspicion for polymicrobial disease for similar cases involving this fungus is warranted, particularly upon initial evaluation in a profoundly immunocompromised patient within a dense urban setting and recently extensive systemic antimicrobial treatment.

In summary, this is the first described isolation of *Candida auris* as a pathogen in the setting of histologically demonstrated panophthalmitis. As this microbe gains more notoriety in metropolitan areas, future investigations are needed to assess its clinical behavior in the eye. In select cases that otherwise receive antimicrobial agents limited to bacterial coverage with a known bacterial source, additional empiric coverage for fungal organisms like *Candida auris* may be warranted with initial management.

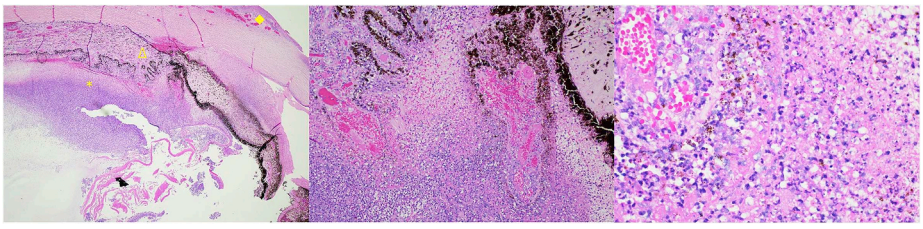

Fig. 2. Histopathologic imaging of enucleated eye with panophthalmitis (H&E). All layers of and around the eye including vitreous (*), uvea (Δ) and extra-scleral tissue (◆) demonstrate inflammation (Left panel, 2x). Medium power shows dense polymorphonuclear infiltration with hemorrhage within vitreous and uvea (Middle panel, 10x). High power demonstrates intense necrosis and liberation of pigment (Right panel, 40x).

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Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

Written consent to publish potentially identifying information, such as details or the case and photographs, was obtained from the patient(s) or their legal guardian(s).

Contributions

Each author contributed to the manuscript as follows: design and conduct of the study (M.P.B., A.A.T., K.J.G., C.E.I.); collection, management, analysis, and interpretation of the data (M.P.B., A.A.T., K.J.G., C.E.I., N.A.Y., H.W.F.); preparation, review, or approval of the manuscript and decision to submit for publication (M.P.B., A.A.T., K.J.G., C.E.I., N.A.Y., H.W.F.). All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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