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Confirmed *Candida albicans* endogenous fungal endophthalmitis in a patient with chronic candidiasis

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ABSTRACT

We present a case of a confirmed *Candida albicans* endogenous endophthalmitis in a 35-year-old diabetic white female patient with a long standing history of severe chronic vaginal *C. albicans* infection. The patient had recently undergone ureteric stenting and received intravenous broad-spectrum antibiotics for renal stones complicated by urinary sepsis. Pan-fungal polymerase chain reaction (PCR) analysis of vitreous aspirate confirmed the presence of *C. albicans*. Samples showed no microbial growth.

1. Introduction

Endophthalmitis is an inflammation of the intraocular tissues of the aqueous and vitreous cavities. It is most commonly caused by microbial pathogens. However, sterile cases have been described in the literature [1].

Endogenous endophthalmitis is a rare but potentially blinding infection of the inner eye. It results from haematogenous spread of the microorganism from an infected site into the eye. Predisposing factors make this infection more likely.

Fungal organisms are commonly responsible for endogenous endophthalmitis [2] and in the western world *Candida albicans* is the most common fungal pathogen [3]. The majority of cases of endogenous fungal endophthalmitis (EFE) have been shown to occur in patients with debilitating disease, immunosuppression and recent hospitalisation [4].

In order to disseminate the fungal pathogen it must reach the bloodstream. Yeasts can originate either from a primary fungal infection leading to a candidaemia or alternatively spread from an indwelling central venous catheter. Although rare, EFE has been reported in immunocompetent individuals [5]; in this group IV drug abuse is the most common inoculation risk factor [6] (Table. 1).

2. Case

A 35-year-old female presented with loss of vision affecting her right eye, she reported initially experiencing visual floaters with a subsequent rapid visual deterioration over 48 h. This was on a 1 week background of right sided frontal and retro-orbital pain associated with photophobia, visual floaters and decreasing vision affecting the right eye.

Past medical history was significant for Type 2 Diabetes mellitus, Asthma, Chronic sinusitis, pneumococcal meningitis, urinary tract infections and a 1 year history of chronic vaginal candidiasis. No allergies were reported and regular medications comprised of Metformin, Salbutamol, Paracetamol and Tramadol.

The week prior to presentation this patient had been admitted at a different hospital with renal stones complicated by urinary sepsis. She had received intravenous broad-spectrum antibiotics including Vancomycin and Meropenem and underwent right-sided ureteric stenting. Blood and urinary cultures at the time showed no growth of bacterial or fungal organisms. During this admission she complained of floaters and photophobia, ophthalmic review at the time diagnosed iritis and commenced Dexamethasone 0.1% twice daily, Cyclopentolate 1% twice daily, and Hypromellose 0.3% as required.

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Table 1
Risk factors for endogenous fungal endophthalmitis [7–9].

Host	Inoculation
Corticosteroid use	Intravenous catheters
Chemotherapy	Bowel surgery
Immunosuppression	Intravenous drug abuse
Antibiotic use	

Table 2
Summary of examination findings.

Right eye		Left eye
PL	**Visual Acuity**	6/5
N	**Lids**	N
Injected ++	**Conjunctiva**	N
Clear	**Cornea**	Clear
1 mm hypopyon		Small hypopyon
360° posterior synechia	**Anterior chamber**	
No view—vitreous haze	**Fundus**	'Fluffy' vitreous abscesses
14	**Intraocular pressure**	11

Baseline clinical observations were within normal limits and the patient was afebrile. Best corrected visual acuities were perception of light (PL) in the right eye and 6/5 in the left. Both lids were normal (*N*) and her right eye had a marked diffuse conjunctival injection and there was a 1 mm hypopyon in the right anterior chamber and 360° posterior synechiae. The left conjunctiva was white however there was a small hypopyon in the left anterior chamber. Both corneas were clear. Intraocular pressure was 14 mm Hg in the right eye and 10 mm Hg in the left. Right eye fundal view was not possible due to extensive vitreous haze, the left fundus showed several small patches of fluffy vitreous condensation. A diagnosis of bilateral endogenous endophthalmitis was made (Table. 2).

The patient was admitted (day 0) and promptly underwent right, then left vitreous aspiration with intravitreal injection of Ceftazidime 1 mg in 0.05 ml, Vancomycin 1 mg in 0.05 ml and Amphotericin 0.005 mg in 0.1 ml. In addition oral Fluconazole 400 mg once daily and intravenous Ceftriaxone 2 g twice daily and guttae Atropine 1% twice daily, Cyclopentolate 1% twice daily and guttae Prednisolne were commenced.

Blood and urinary cultures were negative and a HIV test was negative. A vaginal swab cultured *C. albicans*. Microscopy of both right and left vitreous aspirates showed the presence of leucocytes but no organisms were seen on gram-stain or cultured.

A further vitreous aspiration was taken (day +7) from the right eye with a repeat intravitreal injection of Ceftazidime 1 mg in 0.05 ml, Vancomycin 1 mg in 0.05 ml and Amphotericin 0.005 mg in 0.1 ml. Microscopy of this sample again showed the presence of leucocytes but no organisms were seen on gram-stain or cultured. The visual acuity and vitreous haze in the right eye did not improve over the following seven days so the patient underwent a right pars plana vitrectomy with phacoemulsification and intraocular lens implantation (day +14). Further intravitreal Ceftazidime 1 mg, Vancomycin 1 mg and Amphotericin 0.005 mg were administered intra-operatively. Microbiological examination of vitreous material collected at operation showed no microscopical abnormalities and again was culture negative.

The vitreous abscesses seen in the left eye responded well to the intravitreal antimicrobial treatment. The patient was discharged (day +17) following the right pars plana vitrectomy with visual acuities of hand movement in the right eye and 6/9 in the left. The vitrectomy sample (day +14) was sent to the Health Protection Agencies, Microbiological services, Colindale for pan-bacterial polymerase chain reaction (PCR) and the HPA Mycology Reference Laboratory, Bristol for pan-fungal (PCR) analysis. Pan-bacterial PCR based on 16S rRNA gene amplification was negative. For pan-fungal PCR the vitrectomy sample was first subjected to bead beating for 1 min (MP FastPrep 24 using 710-1,180 μm glass beads, Sigma) to break the walls of any fungal cells present in the sample. The DNA was then purified using the QIAamp DNA mini-blood DNA purification kit (Qiagen) according to the manufacturer's instructions. 5 μl of extracted DNA was added to the pan-fungal PCR targeting the Internal transcribed spacer region 1 (ITS1) using primers and amplification conditions described previously [11]. The resulting positive PCR product was sequenced and a Basic local alignment search tool (BLAST) search of the resulting sequence showed a 98% match with *C. albicans*.

3. Discussion

This is a case of bilateral endogenous endophthalmitis in which *C. albicans* was identified following PCR analysis of the right vitrectomy sample.

At presentation the right eye vitreous was completely hazy with only perception of light possible, this did not improve with two intravitreal Amphotericin B injections alongside systemic antifungal therapy using the triazole, Fluconazole. The patient underwent right pars plana vitrectomy with phacoemulsification and intraocular lens implantation. Visual acuity in the right eye, on discharge, was perception of hand movements. The left fundal view initially showed classical fluffy vitreous abscesses, these improved with intravitreal Amphotericin B; best corrected visual acuity on admission was 6/5 in the left eye, this reduced to 6/9 at discharge. At 3 months visual acuities were counting fingers in the right eye and 6/5 in the left.

This patient had a number of systemic risk factors for developing EFE; these included acute illness with hospitalisation, usage of broad spectrum antibiotics including intravenous Meropenem and Vancomycin and longstanding Type 2 Diabetes mellitus. Locally guttae dexamethasone into the right eye will have caused immunosuppression and may have resulted in the more advanced infection in the right eye.

The precise method and timing of *C. albicans* inoculation and spread to the eye is difficult to determine although first onset of ocular symptoms correlates with the acute admission for renal stones and urinary sepsis. At the time the patient received intravenous Meropenem and Vancomycin. The broad spectrum systemic antibiotics would have reduced the patient's normal bacterial flora; this may have increased the microbial load of the infecting *C. albicans*.

A number of routes for yeast inoculation are possible in this case; percutaneous inoculation of fungus is a possibility and has been previously described in an immunocompromised patient [12]. During the acute admission this patient had undergone intravenous cannulation and urethral catheterisation both of which may have served as routes for microbial inoculation. The patient had also undergone ureteric stenting; this invasive procedure involves cystoscopy with endoscopic insertion of a stent which may have introduced the cutaneous *C. albicans* from the groin into the blood stream.

Microscopy of the vitreous aspirate samples identified leucocytes; however no microbial pathogens were cultured. Pan-fungal PCR on the right vitrectomy sample identified *C. albicans*. PCR sequencing of the ITS region has previously been used to successfully identify fungal pathogens causing ocular infection [13–15]. The only other confirmed *C. albicans* infection in this patient was

from her vaginal swab. Blood and urinary cultures collected on admission all revealed no growth.

4. Conclusions

This was a serious case of bilateral endogenous fungal endophthalmitis; at presentation the infection in the right eye was advanced and did not respond to combined intravitreal and systemic antifungal therapy, this eye eventually required pars plana vitrectomy. The left eye infection was less advanced at presentation and responded fully to intravitreal and systemic antifungal therapy. The right vitrectomy sample was sent for pan-bacterial and pan-fungal polymerase chain reaction (PCR) analysis which confirmed the presence of *C. albicans*. All three vitreous aspirate samples showed no microbial growth.

There has been no previous case reported in the literature of confirmed *C. albicans* endophthalmitis in a patient with chronic vaginal candidiasis. This case highlights that there may be additional risk involved when performing invasive procedures which may breach an area of active cutaneous *Candida* infection. This is of particular importance in patients with additional immunosuppressive risk factors. This raises questions about the need to carefully monitor patient's eyes or administer antifungal prophylaxis in patients with active genital candidiasis undergoing invasive urological procedures.

In this case conventional microbiology laboratory diagnostics were negative and EFE was only confirmed with molecular techniques. This highlights the need to utilise DNA diagnostics in the early identifications of at-risk patients.

Conflict of interest

No competing interests. Not submitted for publication elsewhere.

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