

# Endogenous *Candida albicans* endophthalmitis in a patient with chronic renal failure on hemodialysis

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**Dear Editor,**

We report a rare case of endogenous endophthalmitis caused by *Candida albicans* in a patient with chronic renal failure concomitant hemodialysis. A 71-year-old man with a history of hypertension and 2-year chronic renal failure on hemodialysis via a native arteriovenous fistula (AVF) was presented to the local hospital due to fever 3wk ago. No pathogens were detected through blood culture on admission, and his fever gradually subsided with intravenous ceftriaxone sodium. After a week of fever, he experienced progressive blurred vision in both eyes, accompanied by pain and headaches. Subsequent magnetic resonance imaging (MRI) of the brain revealed sinusitis. He had not undergone any previous eye surgeries or trauma.

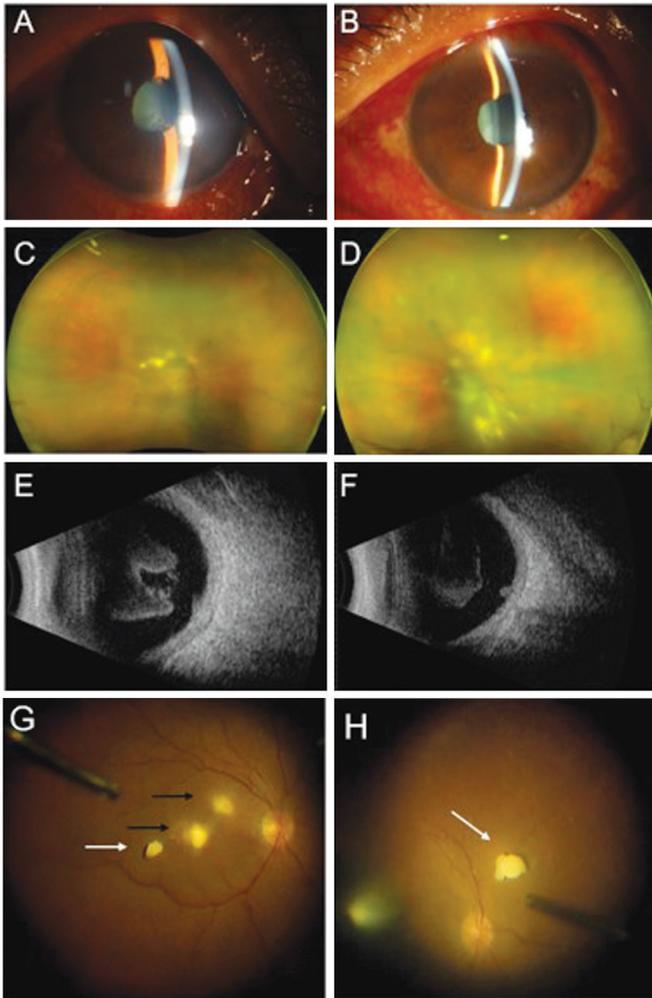
This work was approved by the Ethics Committee of Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences). The approval number is KY2023-085-01. The informed consents were obtained from this patient.

When he entered our hospital, his visual acuity was counting fingers at 40 cm in the right eye and hand movements at 50 cm in the left eye, accompanied by low bilateral intraocular pressure (7.9 and 7.4 mm Hg). In both eyes, there was a mixed congestion of the conjunctiva, mild anterior chamber cells, partial posterior

synechia of the iris, and opacified lens (Figure 1A, 1B). The vitreous bodies were gray-white floccular turbidities, meanwhile yellowish-white lesions were indistinctly observed on the retinal surface and underneath the retina (Figure 1C, 1D). Ocular B ultrasound showed dense vitreous echoes, together with small clump-like hyperechoic shadows in front of the retina and eyeball wall thickening in both eyes (Figure 1E, 1F). The results of laboratory tests upon admission showed an increase in serum procalcitonin (1.67 ng/mL), plasma 1-3- $\beta$ -D glucan (191.4 pg/mL), serum C-reactive protein (5.29 mg/L), blood urea (12.62 mmol/L), serum creatinine (766.85  $\mu$ mol/L), and urine white blood cell (2437.00  $\mu$ L), while hemoglobin decreased to 110 g/L. Midstream urine culture indicated mixed bacteria with a small amount of yeast growth. No positive findings were observed in blood culture. Based on the patient's clinical manifestations and the findings of paranasal sinus computed tomography (CT), MRI and nasal endoscopy, the otolaryngologist ruled out sinus infection.

A diagnosis of endogenous endophthalmitis affecting both eyes, was made. The clinical manifestation indicated a possible fungal infection, although a bacterial infection could not be ruled out. In response, oral voriconazole was prescribed. Both eyes were given gatifloxacin, tobramycin and dexamethasone eye drops. The operations, including vitreous humor collection, pars plana vitrectomy, silicone oil filling and intravitreal voriconazole and vancomycin, were performed successively in both eyes, respectively. During vitrectomy, the vitreous bodies were distinctly gray-white floccular turbidities, with dense yellowish-white globular lesions in the vitreous adhered to the retina (Figure 1G, 1H, white arrows), and yellowish-white inflammatory foci were found beneath the retina (Figure 1G, black arrows).

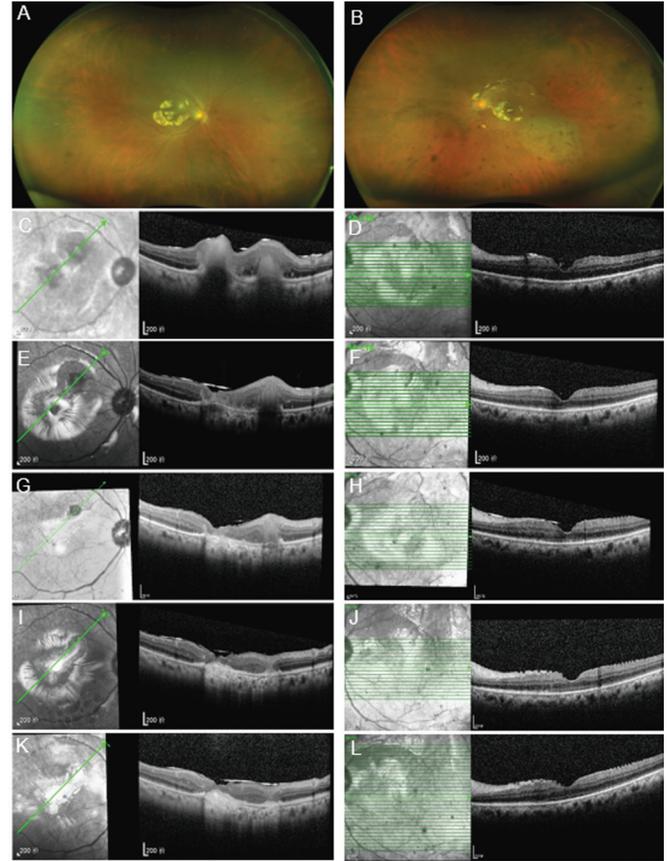
The results of metagenomic next-generation sequencing (mNGS) of vitreous humor displayed a relative abundance of *Candida albicans* was 6.14%, with 7 sequences, and the relative abundance of *Propionibacterium acnes* was 19.05%, with 18 sequences. Oral voriconazole treatment coupled with metronidazole was performed although only *Candida albicans* was subsequently demonstrated by vitreous humor culture. Plasma 1-3- $\beta$ -D glucan returned to the normal level of 97.3 pg/mL, and serum procalcitonin decreased to 0.58 ng/mL



**Figure 1** Clinical manifestations before surgery in the right (A, C, E) and left (B, D, F) eyes, and the retinal lesions in the right (G) and left (H) eyes during the vitrectomy.

after 5d of systemic medication. The best corrected visual acuity (BCVA) improved to 0.05 (Snellen 20/400) in the right eye and 0.12 (Snellen 20/166) in the left eye at 2-week follow-up after surgeries. In the subsequent follow-up, the patient's BCVA improved to 0.1 (Snellen 20/200) in the right eye and 0.5 (Snellen 20/40) in the left eye. Additionally, at 3mo after the surgeries, the subretinal inflammatory foci showed a gradual reduction (Figure 2).

Patients with endogenous endophthalmitis generally experience fever, particularly high fever, but bacteremia or fungemia may be transient and not exhibit symptoms of a systemic infection. mNGS, a novel high-throughput DNA sequencing methodology, can detect any pathogen present in a sample of intraocular fluid without bias<sup>[1]</sup>. Therefore, mNGS is a promising tool for patients who are difficult to be diagnosed with endophthalmitis. It has shown significant advantages in clinical diagnosis, with its characteristics of higher sensitivity, faster speed and reduced specimen volume requirements, especially for rare, new, and mixed infections<sup>[2]</sup>. However, there are two issues concerning the practical application of



**Figure 2** SLO and OCT showed a decrease of the subretinal invasive lesions after surgeries in the right (A, C, E, G, I, K) and left (B, D, F, H, J, L) eyes. A, B: SLO images at 2wk after surgeries. C-L: OCT images at 1d (C, D), 2wk (E, F), 1mo (G, H), 2mo (I, J), and 3mo (K, L) after surgeries. SLO: Scanning laser ophthalmoscopy; OCT: Optical coherence tomography.

mNGS. One issue is the possibility of an excessive amount of unexpected pathogen information resulting from testing. Another problem is the possibility of contamination leading to spurious results. In this case, *Candida albicans* was detected using mNGS and confirmed through vitreous humor culture. It has been reported that over 30% of cases of endogenous fungal endophthalmitis are primarily caused by infections of *Candida albicans*, which can easily affect both eyes<sup>[3]</sup>. However, according to the negative vitreous humor culture of *Propionibacterium acnes*, its detection through mNGS could potentially be a false positive result due to specimen contamination. Although *Propionibacterium acnes* is a common symbiotic organism found in the conjunctival fornix of humans, irrigation with povidone-iodine for 20-30s achieves a bacterial kill rate of over 96.2%<sup>[4]</sup>. Therefore, considering the thorough preoperative disinfection, the higher relative abundance of *Propionibacterium acnes*, the poor sensitivity of vitreous humor culture for *Propionibacterium acnes*, the increase in serum procalcitonin and urine white blood cells, and the positive result of the midstream urine culture for bacteria, we were unable to rule out the possibility of *Propionibacterium acnes* infection.

Patients with chronic renal failure often need hemodialysis to maintain a normal life. Due to their compromised immune system, which affects both innate and adaptive immunity, makes them more susceptible to infectious diseases, primarily those caused by gram-positive bacteria<sup>[5-6]</sup>. Due to the increased occurrence of bloodstream infections, bacteria often spread to various organs, potentially including the eye as a reservoir for infectious agents. However, only a few case reports in the literature have described endogenous endophthalmitis in hemodialysis patients. These reports emphasize that vascular access should be considered as a possible and unique source of infection in this population<sup>[7]</sup>. All patients with endophthalmitis had arteriovenous grafts or tunneled cuffed catheters, indicating a higher risk of bloodstream infection when using vascular access other than native AVF. Another retrospective study showed a low incidence (2.5%) of endogenous endophthalmitis in hemodialysis patients with catheter-related candidemia<sup>[8]</sup>. Consequently, it is rare for hemodialysis patients using native AVF to develop endogenous fungal endophthalmitis.

In conclusion, this case study presents crucial information for ophthalmologists and nephrologists. First, it is recommended that hemodialysis patients, who have a higher incidence of endogenous endophthalmitis, be vigilant about any eye symptoms and promptly referred to ophthalmologists to preserve their visual function. Second, while bacteria are commonly responsible for endogenous endophthalmitis, it is important to be aware of fungal infections, particularly those caused by *Candida albicans*, in hemodialysis patients. Third, the use of highly specific methods, such as mNGS, may provide an accurate and rapid diagnosis of endogenous endophthalmitis, which contribute to improved anatomical and visual outcomes through early and appropriate treatment.

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