

The Disease Course of Bilateral Endogenous Fungal Endophthalmitis

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Abstract

Purpose: To report the dynamic disease course of a case of bilateral endogenous fungal endophthalmitis, which was successfully treated.

Case Report: A 54 year old Chinese man with a history of extracorporeal shock wave lithotripsy (ESWL) and ureteroscopy was referred to our center. After 1 week, his best corrected Snellen visual acuity (BCVA) values were 20/100 and 20/25; the interface between the posterior vitreous face and the retinal surface appeared to be rough in the right eye, and a similar, larger, low-rounded circumscribed apophysis could be observed in the left eye. During the 2nd week, his BCVA values decreased to 20/400 and 20/32. He was diagnosed with bilateral endogenous *Candida albicans* endophthalmitis after a vitreous biopsy and then underwent binocular pars plana vitrectomy (PPV) with silicone oil injection in both eyes. Postoperatively, his BCVA values were 20/63 and 20/32, and funduscopy and optical coherence tomography (OCT) showed a regular and smooth interface and retina surface after the removal of the silicone oil at 3 months.

Conclusions: We concluded that the rough interface between the posterior vitreous face and the retinal surface is one of the early typical sign of endogenous fungal endophthalmitis, which was treated with PPV with silicone oil injection and antifungal reagents.

Keywords: Endogenous fungal endophthalmitis; Disease course

Introduction

Endogenous endophthalmitis (EE) is an uncommon but very serious disease; it occurs in only 2-15% of all cases of endophthalmitis, and the average annual incidence is approximately 5 per 10,000 hospitalized patients. However, fungal infections account for the majority of such cases, and *Candida albicans* is usually the responsible pathogen [1]. Symptoms of endogenous fungal endophthalmitis (EFE) include visual loss, red eye, photophobia and pain, but some patients remain asymptomatic during the initial stage or have a lesion that is in the peripheral retina [2]. Thus, misdiagnoses or missed diagnoses can delay prompt treatment and result in a worse prognosis. A presumptive diagnosis of fungal endophthalmitis can be made if typical clinical features can be noted in the earlier period, as clinical suspicion plays an important role in identifying patients and formulating effective therapies. Here, we report a case of EFE, describe the dynamic disease progression from the early to the late stages as recorded by optical coherence tomography (OCT) and fundus photography, and show distinctive features of the retina, interface and vitreous body, which could provide a clinical reference and clues for the early and accurate diagnosis of EFE.

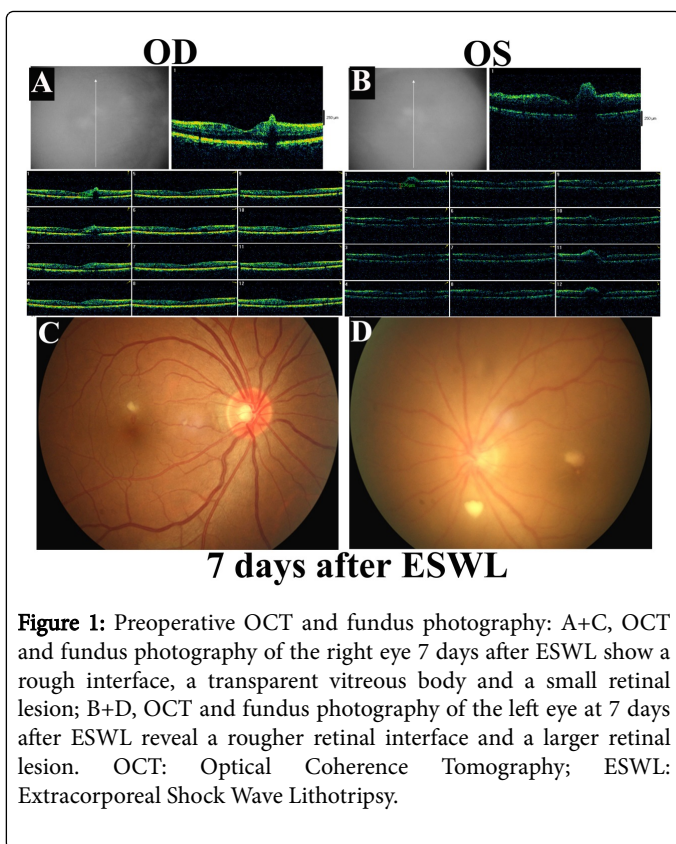
Case Description

In March 2016, a 54 year old Chinese man with a 30 year history of alcoholic liver disease had received systematic broad-spectrum

antibiotics for a persistent fever of 38°C for 7 days. The radiological evaluation revealed right kidney calculi with 3 stones of 3 mm in size. The patient received extracorporeal shock wave lithotripsy (ESWL) and ureteroscopy, and a double-J stent was placed in the right pelvis for drainage.

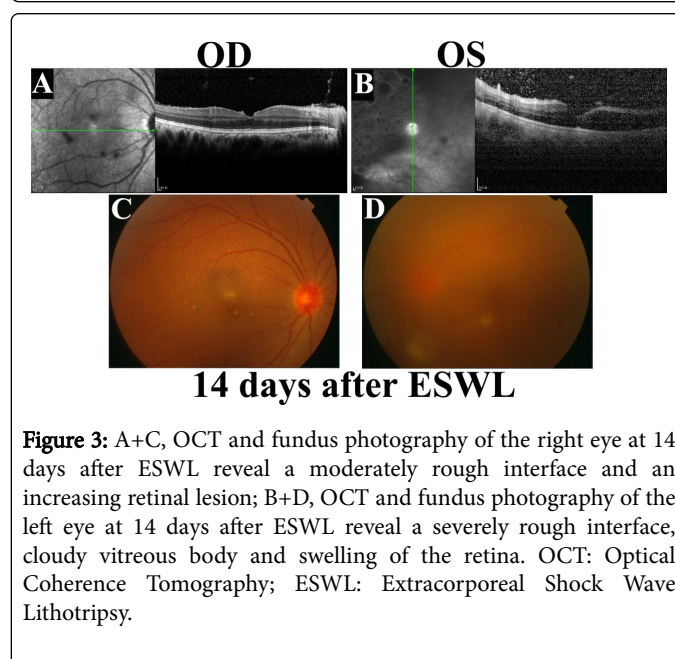
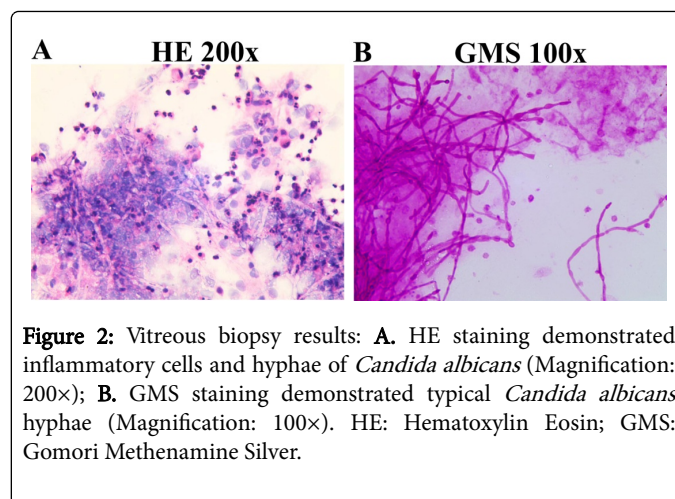
On day 7 after ureteroscopy, he complained of progressive blurring and gradual vision loss and was referred to the Zhongshan Ophthalmic Center. His best corrected Snellen visual acuity (BCVA) values were 20/100 and 20/25, and his intraocular pressure (IOP) values were 13 and 14 mmHg in his left and right eye, respectively. The vitreous body was transparent without any floaters, while the interface between the posterior vitreous face and the retinal surface appeared to be rough.

A small “chimney” protuberance lesion near the macula, vertically oriented from the retina to the vitreous body, could be observed in the right eye (Figures 1A and 1C). In the left eye, a similar, larger, low-rounded circumscribed apophysis could be observed, along with a rougher retinal interface and a transparent vitreous body (Figures 1B and 1D). OCT showed a transparent vitreous body and a small protuberance in the right eye and slight vitreous haze and a massive, low-rounded, circumscribed apophysis in the left eye. Both lesions were located close to the macula and oriented vertically from the retina to the vitreous body.



The patient was suspected to have bilateral EFE with clinical features and provided urine and blood cultures that were positive for *Candida albicans*. Then he underwent a vitreous biopsy and was administered topical natamycin, fluconazole eye drops four times daily, and fluconazole ointment once per night, combined with 200 mg oral voriconazole twice daily for 1 week. However, the patient responded poorly to topical therapy.

On the 14th day after ESWL, the vitreous biopsy revealed to be many infiltrated inflammatory cells and *Candida albicans* via Hematoxylin Eosin (HE) (Figure 2A) and Gomori methenamine silver (GMS) staining (Figure 2B), and the patient was diagnosed with bilateral EFE. At that time, his BCVA values decreased to 20/400 and 20/32, and his IOP was normal in both eyes. A significant change in the rough retina interface further supported the diagnosis of endophthalmitis. Apart from the rough surface and the increasing retinal lesion, a consecutive, vertical and punctiform shadow of the retina interface was visible temporal to the fovea, with “firework”-like vitreous floaters located closely above the interface. These findings suggested that the exudation had broken through the layers of the retina and interface, floated into the posterior vitreous body and proliferated in the whole vitreous body of the right eye (Figures 3A and 3C). The condition of the left eye was more serious and exhibited cloudy vitreous exudation, a rough interface and multiple retinal lesions (Figures 3B and 3D). Several retinal mini-protuberances, except for one near the macula, could be observed in the right eye, while the left eye could not be clearly scanned using OCT at 2 weeks, and showed serious swelling of the retina only through the cloudy vitreous body.



After the diagnosis, the patient underwent binocular pars plana vitrectomy (PPV) with silicone oil injection with vitreous biopsy and intraocular antifungal reagent (fluconazole) irrigation on 14 day of the left eye first, and then the right eye was subjected to the same surgery 5 days later. During surgery, the lens was still transparent, and no retinal tear was observed; the vitreous body was divided into several pieces for pathological biopsy, HE and GMS staining, and cultures of bacterial and fungal, which turned to be *Candida albicans* again. The topical and systemic antifungal reagents that had been used preoperatively were prescribed for 1 month. At the 3rd postoperative month, after removing the silicone oil, the BCVA values were 20/63 and 20/32, with a refractive status of +2 DS, -0.5 DC and +1 DS, -0.5 DC in the left and right eye, respectively, and the IOP was normal in both eyes. Fundoscopy and OCT showed a regular and smooth interface and retina surface without vitreous opacities or retinal surface abnormalities (Figures 4A-4D).

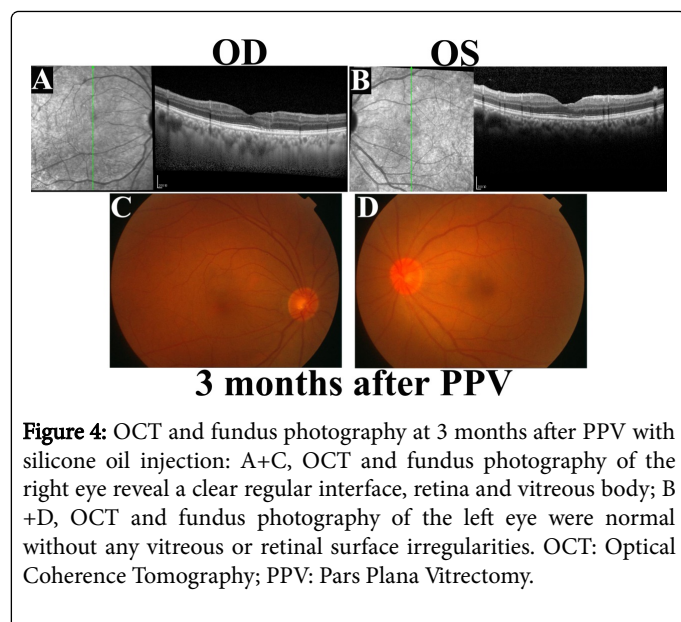


Figure 4: OCT and fundus photography at 3 months after PPV with silicone oil injection: A+C, OCT and fundus photography of the right eye reveal a clear regular interface, retina and vitreous body; B +D, OCT and fundus photography of the left eye were normal without any vitreous or retinal surface irregularities. OCT: Optical Coherence Tomography; PPV: Pars Plana Vitrectomy.

Discussion

EE is a potentially devastating intraocular infection in which pathogens reach the eye via the blood stream. It is rare, occurring in only 2-15% of all cases of endophthalmitis. A fungal infection is more common than a bacterial infection, with a ratio of 62:38, and the incidence of fungal infections has been increasing in recent decades [1,3]. Among the different fungal species, *Candida* is the most common cause of infection because it is a commensal organism that resides in the human body and is normally found in the female genital tract, gastrointestinal tract, and respiratory tract [4]. When a breakdown in the host immune system occurs, fungi may spread throughout various organs, including the eye, which can be affected by the spread of fungi through the bloodstream after genitourinary surgeries or dental procedures [4]. Possible risk factors include chronic diseases, in-dwelling catheters, organ transplantation or pregnancy [5,6]. The patient in our study had a 30 year history of alcoholic liver disease and received 7 days of broad-spectrum antibiotics and ESWL. There is no direct evidence that ESWL caused EFE, but the patient complained of symptoms of EFE shortly after ESWL, suggesting a possible relationship between ESWL and EFE. More cases of *Candida albicans* endophthalmitis after ESWL have gradually been reported [7].

Several studies have shown that patients may be asymptomatic if the lesion is in the peripheral retina or if the patient is moribund, and symptoms are not useful factors for assessing the presence of EFE in patients who are at risk [8,9]. Therefore, the patient in our study did not realize that he had an infection in his right eye until a thorough fundus examination showed susceptible clinical features. Clinically, a lack of obvious symptoms or typical signs contributes to the high rate of EFE misdiagnosis and missed diagnoses. The diagnosis of EFE is based on the results of polymerase chain reaction and Giemsa, GMS, and periodic-acid Schiff staining [9], and these invasive methods are unlikely to be accepted by patients and could enhance the risks of further endogenous infection. Other diagnostic methods such as fluorescein angiography, OCT and ophthalmofunduscopy could facilitate a diagnosis when typical features are noted in severe cases or in the late stage; however, during the early stage, some signs that are also typical can easily be ignored. Misdiagnosis at an initial

presentation has been reported in 16 to 63% of cases, thus delaying the diagnosis and proper management of the disease [10].

In our study, we recorded a typical and dynamic disease progression of a case of EFE using OCT and ophthalmofunduscopy and concluded that some typical signs could be noted during the early stage. Seven days after ESWL, the rough retinal surface and a small raised retinal lesion oriented vertically from the retina to the vitreous body in the right eye were considered to constitute the first phase of EFE. After 14 days, the interface was rougher, the exudation broke through the retina to the interface and subsequently to the vitreous body, and the number of retinal lesions increased in the patient's right eye. These characteristics represented the second phase. After 14 days, the left eye exhibited an extremely irregular interface, a cloudy vitreous body and an indistinct retina, which constituted the third phase. A rough retina interface and a retinal lesion, especially an increasingly rough and large lesion, suggest the possibility of endophthalmitis.

The presence of an intact interface or posterior hyaloid provides a scaffold for vascular growth and anteroposterior traction; moreover, anomalous adhesions between the posterior vitreous face and the retinal surface can cause numerous vitreoretinal complications such as proliferative diabetic retinopathy and macular edema [11]. Although no reports have been published examining the relationship between the interface and EFE, we suspect that the probable mechanism, which is based on experimental studies of endogenous *Candida* endophthalmitis in rabbits, is as follows [12]. First, the *Candida* spp enter the eye by seeding the highly vascular choroid; second, the yeasts proliferate and invoke focal inflammation; third, the infection worsens and breaks through the interface; therefore, the interface gradually become rough; finally, the yeast perforates the retina and involves the vitreous body, which exhibits marked vitritis. Because the interface of the vitreous base, optic disk, fovea, and the major retinal blood vessels is composed of vitreous cortical fibrils and it is very firm, EFE often presents with choroiditis or chorioretinitis, which presents as a rough or irregular interface during the early stage. When the infection further enters the vitreous body, it becomes clouded, and numerous retinal lesions are formed, which is considered to be the late stage of the disease. Therefore, a rough retina interface is considered a representative sign of early-stage EFE, which may facilitate early diagnosis. More cases should be evaluated to further verify this hypothesis and grade the different stages of EFE in future studies.

Treatment for endogenous fungal endophthalmitis depends on the extent of ocular involvement. For patients who have *Candida* chorioretinitis with no vitreal involvement, systemic therapy antifungal agents are appropriate as long as repeated examinations show no extension into the vitreous or the macula [13]. No studies have defined the appropriate duration of therapy, and a reasonable approach, consistent with the IDSA guidelines, is to treat for at least 4-6 weeks. For sight-threatening macular involvement, besides systemic antifungal agents, vitrectomy and intravitreal injection should be considered to decrease the burden of organisms and to allow the removal of fungal abscesses that are inaccessible to systemic antifungal agents; moreover, silicone oil tamponade was antimicrobial and helpful for better anatomical and functional results in endophthalmitis [14]. The patient in our study had a good prognosis with a satisfactory BCVA and a regular and smooth interface and retina surface after PPV.

Conclusion

Conclusively, this case showed the dynamic process of progression from the early to the late stage of EFE using OCT and fundus photography and provides good clinical references.

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Potential Conflicts of Interest

All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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