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Original article

Posterior Segment Optical Coherence Tomography: An Adjunctive Tool in Monitoring Voriconazole Treatment of Fungal Chorioretinitis

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Abstract:

Background: Early management of fungal chorioretinitis is necessary to improve the visual prognosis. **Purpose**: To evaluate the role of posterior segment optical coherence tomography (PS-OCT) in the management of fungal chorioretinitis. **Patients and Methods**: It is a case series of 5 eyes of 3 participants with fungal chorioretinitis. The diagnosis was established clinically and by PS-OCT. All participants were subjected to a complete ophthalmic examination and PS-OCT. Participants received loading 6mg/kg/12 hours intravenous voriconazole for 24 hours then a cycle of an oral voriconazole 200 mg twice daily for 4 weeks. **Results:** At 6 months follow-up, BCVA improved from 1.15 ± 0.28 to 0.30 ± 0.09 LogMAR. The mean duration of the treatment was 4.3±1.5 weeks. Follow-up OCT images demonstrated decreased size of chorioretinal lesions and complete resolution at 6-months follow-up. Neither ocular nor systemic complications were reported during the follow-up period. **Conclusion**: PS-OCT may give an objective tool for systemic antifungal treatments of fungal chorioretinitis assessing the disease progression, monitor therapeutic response, and achieving good functional and anatomical outcomes in our study cohort.

Keywords: Fungal; chorioretinitis; PS-OCT; voriconazole; macula.

Abbreviation: posterior segment optical coherence tomography (PS-OCT), best corrected visual acuity (BCVA), Log of Minimum Angle of Resolution Log MAR, early treatment diabetic retinopathy study (ETDRS, fundus fluorescein angiography (FFA), indocyanine green angiography (ICGA).

Introduction

Fungal chorioretinitis is focal deep chorioretinal lesions without vitreal extension or vitritis, caused by fungal infection mostly candida and aspergillus species. Fungal chorioretinitis is rare, mostly secondary to Fungemia, usually asymptomatic and associated with negative culture. Screening for fungal chorioretinitis should be done in the presence of risk factors as well as ocular surgeries, and trauma, general surgery, extended hospitalization, Diabetes mellitus, IV drug abuse and immunosuppressed

patients to avoid delayed diagnosis and management. Chorioretinitis can eventually extend into the vitreous and progress to endophthalmitis [1-8].

Posterior segment optical coherence tomography (PS-OCT) can provide further insight into the chorioretinal interface. It helps establish the diagnosis and evaluate chorioretinitis progression. The PS-OCT imaging correlates well with early pathological changes in patients with fungal chorioretinitis [9-11].

PS-OCT diagnostic signs of fungal chorioretinitis include two common patterns; chorioretinal infiltration, single or multiple infiltrates appear in the choroid extending into the outer retina and inner hyperreflective retinal infiltration without choroidal involvement. Zhuang H, reported 4 types of fungal retinal lesions; subretinal macular lesions, inner retinal layer lesions, lesions involving the full-thickness retina associated macular edema, and sub-inner limiting membrane lesions [12-14].

The incidence of the ocular fungal infection decreases with the application of new systemic antifungal medications due to better intraocular penetration and less side-effects achieving adequate efficacy of the therapy. Possible complications of fungal chorioretinitis include macular lesions; epiretinal fibrosis; retinal detachment; neovascular choroidal membrane; and visual loss. Fungal chorioretinitis can be treated by azole antifungals agents and intravitreal injection or vitrectomy in severe cases of an antifungal agent. Voriconazole is a triazole potent broad-spectrum antifungal, synthetic derivative of fluconazole, which is characterized by a high ocular bioavailability and permeability [8,15-17].

Few studies have interpreted PS-OCT findings in fungal chorioretinitis. The current study aims to evaluate PS-OCT value in the treatment of patients with Fungal chorioretinitis.

Patients and methods

Patient selection:

It is a prospective observational case series of 5 eyes of 3 participants with Fungal chorioretinitis from January 2020 to July 2023 in Seha Emirates hospital, Abu Dhabi, UAE.

This study enrolled at least 18 years old patients who underwent the treatment for fungal chorioretinitis; white choroidal and/or retinal lesions without vitritis or vitreal involvement.[5] The study excluded vitritis, other causes of chorioretinitis, and macular diseases such as diabetic macular edema and macular degeneration.

Participants subjected to a complete ophthalmic evaluation at baseline and follow-up examination; early treatment diabetic retinopathy study (ETDRS) charts (Light-house, New York, NY) for determine best corrected visual acuity (BCVA), fundoscopy, lit-lamp biomicroscopy, PS-OCT imaging (3D OCT-2000, Topcon, Japan), FFA, ICGA.

Vitreous tap with microscopic examination and culturing was done in all participants.

Transconjunctival sclerotomy was done with 23-gauge trocar cannula system then a vitreous sample (0.5 ml) was aspirated into 3-cc syringes [18].

PS-OCT imaging: macular acquisition was done using the 3D macular 512×128 scan mode over an area of 6×6 mm^2 (Topcon 3D OCT-2000).

On PS-OCT imaging, diagnostic signs of fungal chorioretinitis are a round-shaped homogeneous lesion on the surface of the retina inducing a shadowing effect on the underlying chorioretinal layers structures (rain-cloud sign) [19,20].

Treatment: all patients received loading 6mg/kg/12 hours intravenous voriconazole for 24 hours then a cycle of an oral voriconazole 200 mg twice daily for 4 weeks.

Retreatment was indicated in the case of persistence of fungal chorioretinitis on PS-OCT imaging.

BCVA and PS-OCT changes at 6 months follow-up compared to baseline were the main outcomes variables.

Statistics: outcome measures were represented as percentage or mean with standard deviation. Analyses were done by Student's paired t-test using Windows SPSS software 16.0 (SPSS, Chicago, USA). A P-value less than 0.05 was significant.

Statement of Ethics: The study was approved by the local ethics committee and has followed the tenets of the Declaration of Helsinki. Informed consent was taken from all patients.

Results

Study population:

It is a prospective observational case series of 5 eyes of 3 participants with Fungal chorioretinitis from January 2020 to July 2023. Bilateral Fungal chorioretinitis was recorded in 2 patients. Fungemia was not recorded in any patient. Positive vitreal cultures of Candida albicans were recorded in 2 patients. Postsurgical Fungal chorioretinitis was recorded in 2 patients (66.7%); the 1st patient underwent GI surgery and the second one underwent nasal surgery within 1 month of the presentation.DM was recorded in 2 patients. The follow-up mean time was 8.7± 1.3 months (range: 7 - 11; median: 8.5). The participants' mean age was 44.3± 7.2 years (range: 33 - 52; median: 45.5) with 1 male (33.3%) and 2 females (66.7%).

Clinical results and safety:

At 6-months follow-up, the mean BCVA showed significant improvement from 1.15 ± 0.28 to 0.30 ± 0.09 Log MAR (P-value <0.0001). The mean CFT decreased significantly from 314.8 ± 217.8 to 196.7 ± 9.6 μm (P < 0.0001).

The treatment mean time was 4.3±1.5 weeks. The duration of treatment was 4 and 6 weeks in 2 and 1 patients, respectively.

None of the patients required intravitreal therapy. Neither ocular nor systemic complications were reported during the follow-up time. Chorioretinal reactivation at 6-months follow-up was not recorded.

Imaging: Baseline retinal images of PS-OCT showed chorioretinal hyperreflective lesions with associated shadowing. Subfoveal, foveal and extrafoveal chorioretinal infiltration were recorded in 1 (20%),2 (40%),2 (40%) eyes, respectively. A solitary lesion was recorded in 4 (80%) eyes, while 1 (20%) eye showed multiple lesions. Early hyperfluorescent lesions at the posterior pole were recorded on both FFA and ICGA. Follow-up PS-OCT

images demonstrated the decreased size of chorioretinal lesions and complete resolution at 6-months follow-up (Figure 1, Table 1).

Table 1: Study demography and clinical results

Variable	Result (mean± SD), Range, Median or total (%)
CFT*	
Pre-Treatment	314.8 ± 217.8
6 Months follow up	196.7 ± 9.6
BCVA (Log MAR) *	
Pre treatment	1.15 ± 0.28
6 months follow-up	0.30 ± 0.09
Pattern of OCT lesion (eyes):	
Subfoveal	1 (20%)
Foveal	2 (40%)
Extrafoveal	2 (40%)
Follow-up time(months)	8.7± 1.3

*CFT (central foveal thickness), best corrected visual acuity (BCVA), Log of Minimum Angle of Resolution Log MAR, SD (standard deviation), * (A significant P-value)*

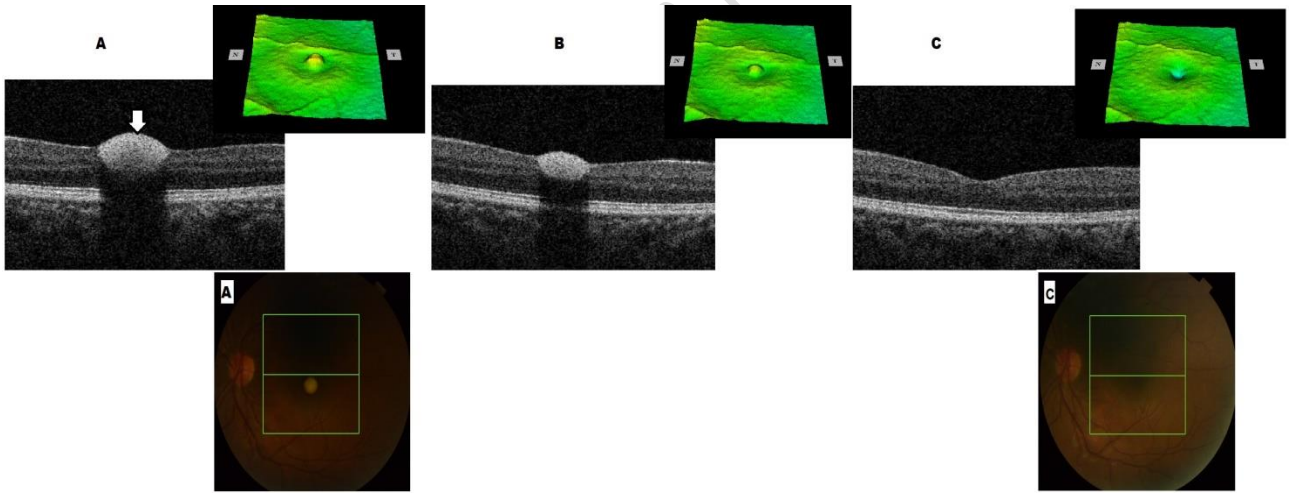

Figure 1: PS-OCT left eye Subfoveal chorioretinitis; [A] Baseline: Subfoveal chorioretinal infiltration with shadowing (arrow) [B] 2 weeks follow up: decreased size [C] 6 months follow up: complete resolution.
Fundus of the left eye [A]baseline subfoveal chorioretinal lesion and [B] 6 months follow up complete resolution

Discussion:

Few reports have evaluated the role of OCT retinal imaging in the management of fungal vitreoretinal diseases. Early diagnosis of fungal chorioretinitis and initiation of antifungal treatment is necessary to improve

the visual prognosis and minimize vision-threatening conditions.

Culture negativity may occur in cases of fungal chorioretinitis and endophthalmitis. Clinical findings and patient history are important guidelines for starting treatment in order to prevent vision loss ([21].

Fluconazole and voriconazole show excellent intraocular penetration and achieve adequate concentrations in the vitreous, explaining their high efficacy in the treatment of fungal chorioretinitis without vitreal extension. Amphotericin B application is not preferable due to serious adverse effects. Intravitreal injection of an antifungal agent, voriconazole and vitrectomy are treatment of choice in case of sight-threatening macular conditions and vitritis [22-24].

There is a debate over the appropriate duration of fungal chorioretinitis treatment. The guidelines of infectious diseases society of America (IDSA) recommended treating fungal chorioretinitis for at least 4–6 weeks and continuing the regimen until the complete resolution of vitreoretinal lesions [25].

Our cohort showed good visual recovery and an improvement of BCVA in all cases after the treatment with systemic voriconazole. Good visual recovery could be explained by the rapid initiation of the treatment, the absence of vitritis, and the appropriate duration of the treatment under OCT-guided monitoring.

The treatment mean time was 4.3±1.5 weeks which is objectively monitored by OCT. The duration of the treatment is closer to IDSA recommendation. The endpoint of the treatment was the disappearance of the chorioretinal lesions which were confirmed by OCT imaging. OCT imaging ascertains the resolution of the lesions quantitatively and objectively more than the clinical examination guiding the safe cessation of the treatment in our study.

Systemic surgeries and Diabetes mellitus were the main risk factors for chorioretinitis in this case series.

Our case series uses systemic voriconazole as sole therapy for the treatment of chorioretinitis. Whereas previous reports applied systemic antifungals therapy as fluconazole with or without intravitreal injections as intravitreal voriconazole (100 lg/0.1 ml) [1,7,9,26].

Voriconazole is a preferred therapy due to its excellent vitreous concentration and safety. Its activity against Aspergillus species and fluconazole resistant Candida species gives it an advantage over fluconazole, However, few studies showed a failure of fluconazole in the management of Fungal chorioretinitis [22].

Clinical efficacies of systemic voriconazole have been reported in a few numbers of reports evaluating fungal chorioretinitis [21,22].

Subfoveal chorioretinal infiltration was associated with the worst visual prognosis due to significant loss of central outer retinal anatomy. Surprisingly, we recorded subfoveal chorioretinal infiltration in 1 eye (20%) which showed a good visual outcome, this could be attributed to apparent rearrangement of retinal structure at perifoveal zone [9].

PS-OCT allows quantitative and objective evaluation of the chorioretinal interface helping to assess the fungal chorioretinitis stage, monitoring therapeutic response, and

visual prognosis, and to decide safe cessation of antifungal treatment [9-13].

Stephens et al. reported two OCT patterns of fungal chorioretinitis; retinal infiltration associated with choroidal involvement and superficial only retinal infiltration [9].

Chorioretinal hyperreflective infiltration and lesions with associated shadowing was the predominant OCT pattern in our study. Follow-up OCT images demonstrated the decreased size of chorioretinal lesions and complete resolution at 6-months follow-up.

Some reports compared OCTA and PS-OCT B scan role and suggested that OCTA could give important data on the pathogenesis of candida chorioretinitis than OCT B scan [11].

This cohort highlight that rapid systemic anti-fungal voriconazole associated with PS-OCT monitoring showed favorable response in the management of fungal chorioretinitis

Low number of participants is the main study limitation. A prospective design gives our cohort strength.

Further evaluation of new antifungal medication and application of new imaging modalities as OCTA would improve the prognosis in the management of fungal chorioretinitis.

Conclusion:

PS-OCT may give an objective tool for systemic antifungal treatments of Fungal chorioretinitis assessing the disease progression, monitor therapeutic response, and achieving good functional and anatomical outcomes in our study cohort.

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