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Brief Report

Cryptococcal choroiditis in advanced AIDS with clinicopathologic correlation

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ABSTRACT

Purpose: To describe a case of disseminated cryptococcal meningitis with multifocal choroiditis and provide optical coherence tomography (OCT) findings correlated with described histopathology in a patient with advanced acquired immunodeficiency syndrome (AIDS).

Observations: The patient was a 54-year-old man with AIDS who presented with dyspnea and headache followed by acute vision loss. OCT demonstrated a lesion with a small area of fluid that was limited by a more prominent and irregular external limiting membrane with underlying nodular choroidal thickening, mild RPE disorganization, and hyperreflectivity of the overlying photoreceptor layer. Patient was found to have disseminated cryptococcal infection and passed away despite aggressive therapy. Autopsy was performed including bilateral enucleation and a *Cryptococcus* lesion was confirmed on histopathology.

Conclusion and importance: This case highlights the clinical, imaging, and histopathologic findings of cryptococcal choroiditis and provides a review of the updated treatment recommendations for disseminated infection in a patient with advanced AIDS. Although currently fundoscopy has proven most useful in directing the diagnostic algorithm in choroiditis in the setting of advanced immunosuppression, OCT may provide insight into the spread of *Cryptococcus* within the eye.

1. Introduction

Cryptococcus neoformans is an encapsulated yeast found in dried pigeon excrement that is transmitted via aerosolization. Primary infection in immunocompromised hosts originates in the lungs with hematogenous dissemination to other organs including the skin, heart, joints, bones, eyes, brain, and meninges. Meningoencephalitis and meningitis are the most common manifestations of cryptococcosis, which portend a grim prognosis.[1] Cryptococcal meningitis has a 90-day mortality rate of 9% in developed countries such as the US, East Asia, and Western Europe, but that rate jumps to 55% in Asia and South America and to 70% in Sub-Saharan Africa due to poor access to care and delayed treatment.[2]

Approximately 40% of patients with cryptococcal meningitis will develop ocular involvement. Kestelyn et al. described papilledema (32.5%), visual loss (9%), abducens nerve palsy (9%), and optic atrophy (2.5%) in 80 HIV patients with *Cryptococcus neoformans* infection.[3] Although choroidal involvement is rare, *Cryptococcus neoformans* was reported as the most common cause of infectious choroiditis in patients with HIV, found in approximately 3% of patients at autopsy.[4]

We report a case of bilateral cryptococcal choroiditis in a patient with advanced acquired immunodeficiency syndrome (AIDS) and provide optical coherence tomography (OCT) findings with histopathologic correlation.

2. Case report

A 54-year-old man with HIV diagnosed 21 years ago and a history of noncompliance with antiretroviral therapy was admitted to the hospital for dyspnea, weakness, and headache. His past medical history was also notable for multi-drug resistant tuberculosis requiring a six-drug treatment regimen, chronic hepatitis C, disseminated *Mycobacterium avium* complex (MAC), previously treated syphilis, oral thrush, anal

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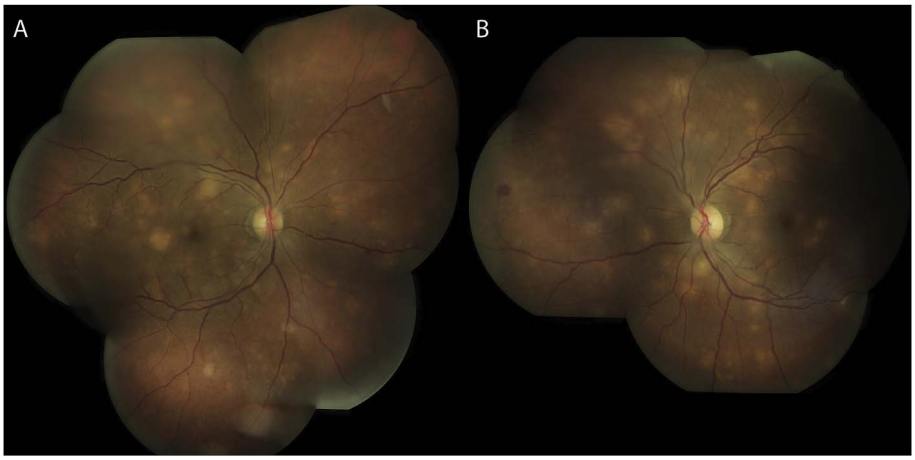

Fig. 1. Color fundus photographs of multifocal choroiditis. Color fundus photographs of the right eye (A) and the left eye (B) revealed bilateral multifocal creamy yellow choroidal lesions, mild optic disc edema, and vascular tortuosity. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

condylomata, and peripheral neuropathy. On admission, his CD4 count was 7 cells/microliter, consistent with advanced AIDS. He was started on empiric treatment for community-acquired pneumonia and *Pneumocystis* pneumonia with ceftriaxone, trimethoprim-sulfamethoxazole, and prednisone. In addition, he was started on MAC and fungal prophylaxis with azithromycin and fluconazole.

Several days after admission, he reported vision loss prompting an ophthalmology consult. Visual acuity was 20/50 with pinhole improvement in each eye. Pupils, extraocular motility, and intraocular pressure were unremarkable. Anterior slit lamp exam was also normal without anterior chamber or vitreous inflammation. Dilated fundus exam was notable for bilateral multifocal creamy yellow choroidal lesions of varying sizes distributed diffusely throughout the posterior pole, mild optic disc edema, and vascular tortuosity (Fig. 1). Fluorescein angiography revealed blocked choroidal filling of these lesions in early phases of the study (Fig. 2A) and showed either mild or no staining in late frames (Fig. 2B). The differential diagnosis remained broad at that time, but his presentation was highly suspicious for an infectious etiology.

Serologies for *Histoplasma* antigen, *Toxoplasma* IgG, and *Coccidiodes* Ab were negative and serum RPR titer of 1:2 was consistent with his previously treated Syphilis (prior titer 1:8). Serum *Cryptococcus* antigen was strongly positive (1:8192). Lumbar puncture revealed encapsulated yeast with positive *Cryptococcus* antigen (1:1024). Chest x-ray was notable for diffuse hazy opacities with bibasilar predominance. Bronchoalveolar lavage and bronchial biopsy were positive for moderate round budding yeast, consistent with disseminated *Cryptococcus neoformans* infection.

The patient was started on liposomal amphotericin B (220 mg IV daily) and flucytosine (1500 mg orally four times daily) according to the guidelines for induction therapy for cryptococcal meningitis in HIV infected patients.[2] Intravitreal amphotericin was also injected into both eyes (5 mcg/0.1 mL). Unfortunately, the patient continued to deteriorate despite broad antibiotic and anti-fungal therapy and succumbed to sepsis one week after presentation.

2.1. OCT and clinicopathologic correlation

OCT over one of the lesions (Fig. 3), that was later confirmed to be cryptococcal choroiditis on histopathology, demonstrated a small area of fluid that was limited by a more prominent and irregular external limiting membrane with underlying nodular choroidal thickening, mild RPE disorganization and hyperreflectivity of the overlying photoreceptor layer. All the retinal layers above the lesions appeared mildly disrupted with an irregular contour although this may reflect the underlying disrupted contour of the outer retina.

An autopsy was performed post-mortem included a bilateral enucleation. Grossly, both globes were notable for diffuse nodular choroidal infiltrates (Fig. 4A and B) that corresponded to the lesions noted on fundoscopy (Fig. 1). On hematoxalin and eosin stained sections, multiple lobular infiltrates were visible in the choroid which were devoid of normal choroidal vasculature (Fig. 4C). The retinal pigment epithelium overlying the lesions had was focally atrophic (Fig. 4C, arrows). At higher power, viable foamy histiocytes were seen infiltrating the choroid. Notably, there was no significant lymphoplasmacytic response in the choroid, retina, or vitreous, which is consistent with the patient's severe immunosuppression. Grocott's methanamine silver stain is positive for small round organisms within the histiocytic infiltrate (Fig. 4D). Periodic acid-Schiff stained sections revealed widespread small round organisms within the histiocytes. Of note, the blood vessels of the choriocapillaris are infiltrated with organisms (Fig. 4E), favoring hematogenous rather than leptomeningeal spread of the infection.

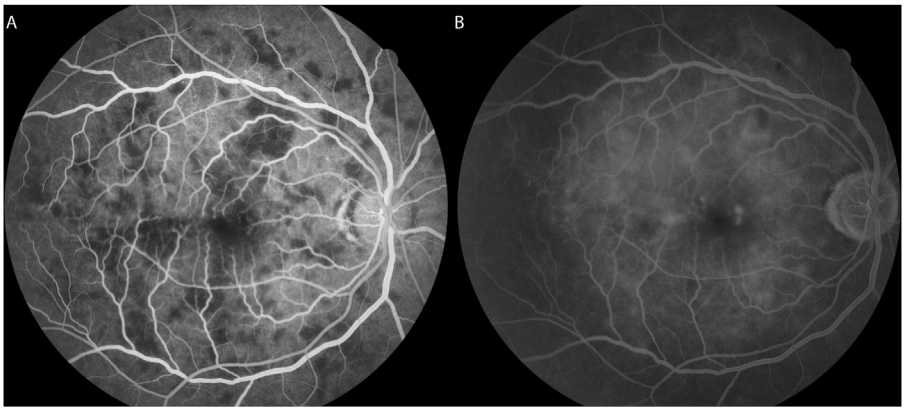

Fig. 2. Fluorescein angiogram of multifocal choroiditis. Fluorescein angiogram of the right eye showing early blockage of choroidal filling (A) mild late staining corresponding to these lesions (B).