Cryptococcus gattii endogenous chorioretinitis

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A B S T R A C T

Purpose: To present a case of subretinal abscess associated with pneumonia and meningitis caused by Cryptococcus gattii in an immunocompetent host.

Observations: A 37-year-old man presented with sub-acute painless unilateral vision loss and a white submacular elevation. Systemic evaluation revealed a lung lesion and cerebrospinal fluid evidence of Cryptococcus gattii infection.

Conclusions and importance: While Cryptococcus neoformans has been well described as a cause of chorioretinitis in immunocompetent and immunocompromised hosts, this report demonstrates that Cryptococcus gattii is a related uncommon pathogen to be considered in similar presentations. Submacular surgical debridement may be challenging and OCT imaging may be helpful to detect full-thickness retinal necrosis.

1. Case report

A 37-year-old Caucasian male reported painless, progressive unilateral vision loss over two days. Visual acuity was 20/20 and 20/200 in the right and left eyes, respectively, with normal intraocular pressure and no anterior segment inflammation. Right eye examination was unremarkable. The left had an approximately 3 × 3 mm, subretinal, white-yellow, elevated macular lesion with indistinct borders, a fine, superficial vascular frond, and subretinal fluid (Fig. 1A). The patient was obese and eight months prior to presentation, he had a 2–3 week flu-like illness manifested with fever and cough with no history of immunosuppression. Review of systems was otherwise negative with no symptoms of pneumonia or meningismus. He worked as a truck driver, enjoyed hunting, traveled domestically, smoked cigarettes, yet denied international travel, other drug use or high-risk sexual behaviors.

Spectral domain optical coherence tomography (OCT) demonstrated ill-defined subretinal hyper-reflective material with subretinal and intraretinal fluid and punctuate, hyper-reflective vitreous opacities (Fig. 1B). Fluorescein angiography (FA) revealed late leakage, indocyanine green angiography showed blocked fluorescence, and an OCT angiogram highlighted lacy superficial vessels (Fig. 1C and D,E). Fundus autofluorescence (FAF) showed central hypoauflorescence with surrounding hyperautofluorescence. Lesion thickness measured 2.5 mm on B-scan ultrasonography with homogeneous, medium internal reflectivity on standardized A-Scan.

A subretinal abscess was suspected, prompting infectious workup. Chest CT showed an approximately 6 × 5 cm, hyperintense, solid mass-lesion in the left upper lung lobe with irregular borders (Fig. 1F & G). Fungal culture of bronchoalveolar lavage identified Cryptococcus gattii with Cryptococcus spp. yeasts on histopathology (Fig. 1H & I). Cerebrospinal fluid (CSF) studies showed 272 nucleated cells/ml, 13% neutrophils, protein 124 mg/dL, glucose 45 mg/dL and were positive for Cryptococcal antigen at 1:20 (which is sensitive to both C. neoformans and C. gattii) and fungal CSF cultures identified C. gattii by matrix assisted laser desorption time-of-flight mass spectrometry (MALDI-TOF MS). Serum cryptococcal antigen titer was >1:2560 and serum studies for were negative or normal for CD4 count, immunoglobulins, CBC, BMP, HIV, Q fever antibody (Ab), Coccidiomycosis Ab, and Blastomycesis Ab, Histoplasma Ab, Enterovirus PCR, Toxoplasma gondii PCR, Coccidoides Ab, Bartonella Ab panel, quantiferon TB gold, and RPR.

Systemic therapy for C. gattii infection with lung and meningeal involvement was initiated and included fluconosine and amphotericin B induction. Cryptococcal antigen in the CSF became undetectable after the third lumbar puncture at ten weeks after presentation and then therapy was transitioned to fluconazole for another 12 months. Weekly intravitreal amphotericin B alternating with voriconazole was also
within the genus of solidifies the diagnosis of cryptococcal chorioretinitis, differentiating present case, the tissue identification of methenamine silver stain (H) shows variably-sized yeasts (5 μm). Intraretinal fluid. (C) Fluorescein angiography shows leakage overlying the lesion with predominantly blockage on indocyanine green angiography (D). OCT (Fig. 2C & D). A diagnostic and therapeutic pars plana vitrectomy confirmed necrotic neurosensory retina and dense, adherent subretinal material that could not be aspirated without risking severe macular injury.

2. Discussion

Fungal chorioretinitis is a well characterized sequelae of systemic infection, with Candida albicans constituting the most common causative organism, traditionally in the setting of intravenous catheter use. Other fungi implicated in ocular infections include Blastomyces spp., Coccidioides spp., Histoplasma capsulatum, and Cryptococcus neoformans. In the present case, the tissue identification of C. gattii from the lung specimen solidifies the diagnosis of cryptococcal chorioretinitis, differentiating the etiology from other considerations such as metastasis, non-infectious granuloma or sub retinal abscess due to a bacterial or another pathogen. Within the genus of Cryptococcus, C. neoformans is a commonly reported ocular pathogen classically associated with immunosuppression with peak prevalence during the AIDS epidemic, although immunocompetent cases also occur. Both the neoformsans and gattii cryptococcal species systemically affect the central nervous system (CNS) and lungs and can rarely affect additional organ systems such as the skin, heart, joints, and bones, although C. gattii is more associated with pneumonia and immunocompetence. Vision complications from C. neoformans result from CNS infection such as papilledema, cranial nerve palsy and optic atrophy with vision loss occurring in >50% of meningitis cases.

The natural reservoir of C. gattii has been described as two species of Eucalyptus trees in association with past outbreaks in Papua New Guinea and Australia. In North America, an outbreak of C. gattii was noted in the pacific northwest region in the 1990s and C. gattii has been found in local species of pine tree as well as the soil. The route of infection in our patient is unclear but hypothesized to be environmental inhalation given his domestic travel as a truck driver and recreational hunting. Of interest, Cryptococcus spp. have also been associated with contaminated tobacco and cannabis, although our patient denies use of the latter. The tobacco used by our patient was described as “cheap, off-brand cigarettes”, which were not available for testing to rule out contamination as possible risk for infection.

To the authors’ knowledge, human C. gattii chorioretinitis has been reported in detail in only one prior publication in the ophthalmology literature (MEDLINE search June 2021, key words: C. gattii, C. neoformans var. gattii, retina, choroid, chorioretinitis, endophthalmitis). The previous case from Lin et al. reports a 60-year-old Taiwanese woman with a similar sub retinal mass on exam with no obvious environmental risk factors and or history of immunosuppression. In that case, lung pathology was also found but appeared inactive and a diagnostic specimen was obtained via full thickness retinal biopsy. In the veterinary literature, one case has been reported in a ferret and other reports mention possible endophthalmitis due to C. gattii without further characterization.

In our case, pars plana vitrectomy as a therapeutic modality was challenging, given the thick, adherent nature of the infiltrate and the presence of full-thickness neurosensory retinal necrosis. Systemic

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**Fig. 1.** Chorioretinitis and lung lesion due to Cryptococcus gattii. (A) Color fundus photograph of the left eye shows a macular lesion and focal, anomalous retinal vasculature. (B) Spectral domain OCT (cross section of green arrow in panel (A) shows a large hyper-reflective subretinal lesion with associated subretinal and intraretinal fluid. (C) Fluorescein angiography shows leakage overlying the lesion with predominantly blockage on indocyanine green angiography (D). OCT angiography demonstrates anomalous retinal vessels (E). (F & G) Chest CT scan shows an approximatively 6 × 5 cm necrotic lesion in the left upper lobe, and Gomori’s methenamine silver stain (H) shows variably-sized yeasts (5-15 μm) with narrow-based budding (arrow) consistent with Cryptococcus spp. (400x magnification). The presence of a capsule surrounding each yeast was demonstrated on mucicarmine stain (I) and confirms the diagnosis of Cryptococcus sp. (400x magnification) Culture grew C. gattii. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)
antifungal therapy did not rapidly control the sub retinal lesion even with the addition of intra vitreal antifungal injections. The penetration of antibiotics may have been limited from both the systemic and intraocular routes given the size and thick consistency of the infectious material. Other reports have shown a possible benefit from vitrectomy in the setting of sub retinal abscess or chorioretinitis, particularly in the setting of disease progression despite systemic therapy. In particular, prompt vitrectomy and sub retinal abscess drainage for endogenous Klebsiella infection was posited to be beneficial. In the other prior report of *C. gattii* endophthalmitis with choroidal mass, full thickness retinal biopsy was required to obtain a specimen, highlighting the difficulty of debulking the infection by retinotomy and aspiration as was attempted in our case. Perhaps earlier intervention would have been beneficial; however, we have no evidence from this case to support the role of vitrectomy surgery.

3. Conclusions

*Cryptococcus gattii* represents a rarely reported organism capable of causing chorioretinitis from an endogenous source and management with surgical debridement may be challenging.

Patient consent

This report does not contain any personal identifying information.

Acknowledgements and disclosures

None.

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Fig. 2. Expansion of subretinal lesion despite systemic and intravitreal antifungal treatment at two weeks (A) and three weeks (B) after presentation. Three weeks after presentation, OCT (C & D) showed full thickness retinal necrosis, increasing subretinal fluid, and worsening overlying vitreous debris (arrowhead).