ENDOGENOUS ASPERGILLUS ENDOPHTHALMITIS IN AN IMMUNOCOMPETENT PATIENT WITH A REMOTE HISTORY OF PULMONARY TUBERCULOSIS

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Purpose: To report a case of Aspergillus fumigatus endogenous endophthalmitis in an immunocompetent patient initially diagnosed as acute retinal necrosis.

Methods: Case report.

Patient: A 67-year-old woman with a remote history of treated pulmonary tuberculosis and no ocular history presented to an outside retina specialist with a sudden onset of floaters and blurred vision in one eye. Examination and fluorescein angiography at the time revealed findings suspicious for acute retinal necrosis, and the patient was started on oral valganciclovir and an intravitreal injection of ganciclovir. Despite treatment, the patient's vision and pain worsened. After evaluation at the University of Southern California Roski Eye Institute, she was diagnosed with a likely fungal endogenous endophthalmitis based on ultrasound findings and underwent emergent vitrectomy. A chest x-ray demonstrated partial collapse of the right upper lobe with hilar enlargement.

Results: Aspergillus fumigatus was cultured from vitreous, blood, and bronchoalveolar lavage samples, suggesting that the patient's infection had a pulmonary origin, most likely from the right upper lobe that had healed from previous tuberculosis infection.

Discussion: To the best of our knowledge, this is the first reported case of Aspergillus endogenous endophthalmitis in an immunocompetent patient secondary to pulmonary changes that occurred from previously treated tuberculosis.

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Aspergillus species are an uncommon but aggressive cause of endophthalmitis that is usually seen in the setting of immunosuppression and intravenous drug abuse.[1] It has also been reported in exogenous settings from intraocular surgery, trauma, or spread from keratitis.[2] Endogenous aspergillus endophthalmitis has very rarely been reported in immunocompetent patients.

Here, we present the case of a 67-year-old immunocompetent woman from Vietnam who presented with unilateral decreased vision and pain with physical examination findings consistent with endogenous endophthalmitis. Her workup was significant for a remote medical history of treated pulmonary tuberculosis. She underwent urgent vitrectomy, blood cultures, and bronchoalveolar lavage. Fluid from all three samples was positive for Aspergillus fumigatus by polymerase chain reaction (PCR), demonstrating that the patient most likely suffered from chronic pulmonary aspergillosis (CPA) secondary to previously treated tuberculosis. This is the first reported case of Aspergillus fumigatus endogenous endophthalmitis in an immunocompetent patient secondary to pulmonary changes from previously treated tuberculosis.

Case Report

A 67-year-old Vietnamese woman with a past medical history of pulmonary tuberculosis treated over 40 years ago in Vietnam developed a sudden, painless onset of floaters and blurred vision in one eye. She had no previous ocular or surgical history.

On examination, best-corrected visual acuity in the unaffected eye was 20/60 and of the affected eye was 20/400, with intraocular pressure 16 mmHg and 11 mmHg, respectively. The affected eye showed significant panuveitis with white, attenuated retinal arterioles throughout the retinal periphery (Figure 1). Examination of the unaffected eye was unremarkable (Figure 1). She was started on double-strength Bactrim, 900 mg of valganciclovir, Pred Forte 1% every 1 hour, and atropine 1% daily. The initial workup revealed reactive hepatitis A IgG, a positive purified protein derivative (PPD), and a slightly elevated C-reactive protein (CRP) of 7.09. Her chest X-ray was significant for partial collapse of the right upper lobe with associated hilar enlargement but was stable from previous chest X-ray from 2015. Remainder of the uveitis workup including ESR, toxoplasmosis IgG and IgM, angiotensin-converting enzyme, c-ANCA, RPR, FTA-antibody, CBC, urinalysis, hepatitis C IgG, HIV, ANA, and HLA-B27 was negative. Over the course of 2 weeks, the patient's pain worsened and vision deteriorated to hand motion of the affected eye.

The patient was then referred to the University of Southern California uveitis service. Her BCVA was hand motion in the affected eye with intraocular pressure of 10 mmHg. Slit-lamp examination was significant for 3 to 4+ cell and flare, a hypopyon <1 mm in height of the anterior chamber, mild nuclear sclerosis of the lens, and dense vitritis with no view of the posterior segment. A review of systems revealed an unintentional weight loss of 25 lbs over the past year. A B-scan ultrasound demonstrated diffuse vitreous opacities and a superior spherical epiretinal mass within the vitreous articulating on the superior retina (Figure 2). The patient was admitted to the Keck Medical Center for workup for suspected endogenous endophthalmitis and scheduled for diagnostic vitrectomy. Preoperative blood cultures were negative for bacteremia and fungemia; abdominal ultrasound was unremarkable with no evidence of liver abscess.

The patient underwent 23-gauge diagnostic pars plana vitrectomy and lensectomy, which demonstrated vitreous hemorrhage and yellow-white dense, purulent vitritis. The vitrectomy cassette was sent for pathology in 10% formalin and microbiology for gram stain, KOH prep, acid-fast bacillus (AFB) stain, cultures, and PCR. Clearance of the vitritis and hemorrhage revealed severe retinal ischemia with peripheral necrosis, a superior and temporal traction–rhegmatogenous retinal detachment, and a temporal hemorrhagic choroidal detachment. Optic nerve pallor and neovascularization of the iris was noted. The retina was reattached with the use of purified perfluoro-n-octane liquid (PFO), 360-degree endolaser placement, and a direct PFO to silicone-oil exchange. Intravitreal injections of vancomycin, ceftazidime, and voriconazole 0.05 mL were injected into the eye at the conclusion of the case.

Later that evening, the patient became unresponsive with hypoxia and hypotension. She was transferred to the intensive care unit (ICU) for presumed sepsis where she underwent intubation and was started on broad-spectrum antibiotics, IV fluids, and pressors. A repeat chest X-ray demonstrated pleural thickening and bronchiectasis. Once the patient was stabilized, she underwent an emergent bronchoscopy and bronchoalveolar lavage. A helical chest computed-tomography (CT) scan demonstrated bilateral thromboembolic disease, a focal wedge-shaped consolidation in the right upper lobe, possibly related to pulmonary infarct, and bilateral groundglass opacities with occasional tree in bud nodules. Right upper lobe cicatricial atelectasis with bronchiectasis and several right upper lobe calcified nodules was also noted. Furthermore, right atrium and right ventricle dilatation were noted, reflecting likely cardiogenic shock. The patient was also started on IV heparin for the bilateral pulmonary emboli.

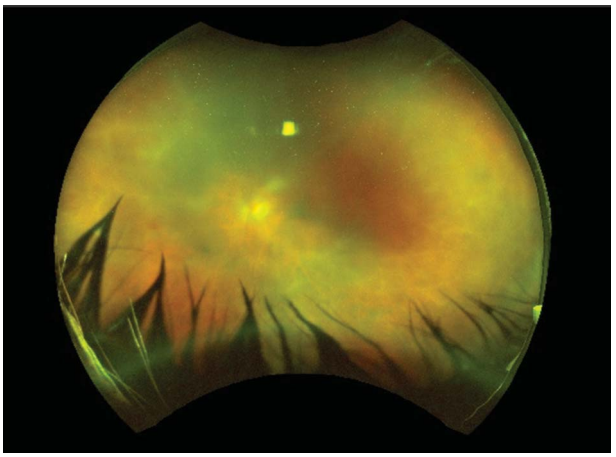

Fig. 1. Fundus photograph of the left eye (OS) on Day 1 of symptoms. Photograph demonstrates vitreous haze, with diffuse edema and possibly early areas of necrosis in the mid-periphery. This could potentially be confused with acute retinal necrosis.

The patient slowly improved systemically over the following 3 days. On ophthalmology examination, the patient was found to have persistent temporal choroidal detachment and some residual vitreous

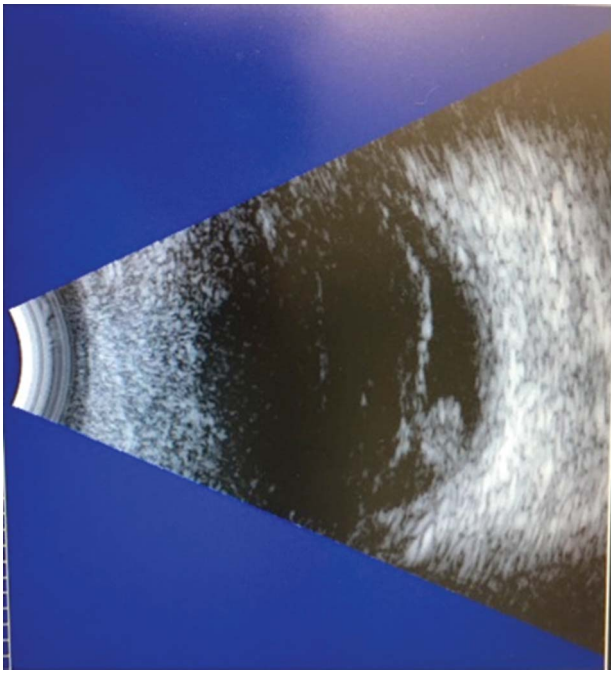

Fig. 2. B-scan ultrasound of the left eye (T12 view). There are numerous vitreous opacities and an epiretinal mass, representing an aspergilloma.

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hemorrhage, but an otherwise flat retina. The patient's vitreous, blood, and bronchoalveolar lavage (BAL) cultures returned positive for Aspergillus fumigatus for which she was treated with IV voriconazole. Her condition improved rapidly after initiation of voriconazole, and she was ultimately extubated and discharged 1 week later.

At 5 weeks after the initial vitrectomy, the patient underwent a second surgery for persistent anterior chamber hyphema and vitreous hemorrhage. Intraoperatively, the patient was noted to have recurrent macula-off rhegmatogenous retinal detachment, choroidal rupture, and proliferative vitreoretinopathy for which she underwent anterior chamber washout, silicone-oil exchange, 360-degree retinectomy, and membrane peel. One month postoperatively, the patient's visual acuity was measured to be 20/200. Hematology and malignancy workup were negative for focal disease.

Discussion

Aspergillus endophthalmitis is a rare but aggressive form of intraocular infection, which generally results in poor visual outcomes. Exogenous presentations have been reported after various forms of intraocular surgery (most often cataract surgery), trauma, and extension of fungal keratitis.[2] Endogenous forms are most commonly seen in IV drug abusers or in immunocompromised patients, particularly those who have undergone organ transplantation or aortic valve replacement surgery.[3,4]

There seem to be only a few reported cases of endogenous Aspergillus endophthalmitis in immunocompetent patients. Of these, three cases were not found to have any identifiable cause for the infection.[5–7] Another case in India was hypothesized to be due to an infusion of contaminated dextrose solution, which the patient had received 2 weeks before presentation.[8] In a recent case, however, the patient was found to have evidence of focal bronchiectasis of unknown etiology, which presumably created a nidus for superinfection within an air-filled cavity of the lung.[9]

Similarly, in the case presented here, the patient was found to be immunocompetent but with underlying structural pulmonary changes. In this case, it was due to a remote history of previously treated pulmonary tuberculosis. The development of pulmonary aspergillosis in immunocompetent patients secondary to structural lung changes is a well-described phenomenon known as CPA. Pulmonary diseases such as chronic obstructive pulmonary disease (COPD), sarcoidosis, cystic fibrosis, prior or concurrent tuberculosis (TB), or non–tuberculous mycobacterial disease allow for the development of CPA due to the formation of an air-filled cavity or bulla, which permits aspergillus colonization and superinfection.[10]

To the best of our knowledge, this is the first reported case of endogenous Aspergillus endophthalmitis in an immunocompetent, nondiabetic patient with previously treated tuberculosis. This comes as a surprise given that the most common predisposing factor for CPA is previously treated tuberculosis.[9] Indeed, the proportion of patients with CPA with previous TB varies from 15.3% in Manchester, UK, to 93% in Korea.[10,11] The persistence of lung cavities on chest X-ray 6 months after successful TB treatment has been found to range up to 23% in a North American study. Aspergillomas have been detected in 14% of patients treated for tuberculosis 1 year after sputum tested negative for acid-fast bacteria and 22% at 4 years according to a UK study.[10–13]

Patients with CPA often present with constitutional symptoms similar to those of tuberculosis (weight loss, malaise, night sweats, and anorexia), as well as pulmonary symptoms such as a productive cough or hemoptysis. In addition, they may have radiologic findings on chest X-ray and/or chest CT scan, which may include lung cavities with or without an aspergilloma, infiltrates, nodules, and various degrees of lung or pleural fibrosis.[10] The most reliable test is Aspergillus IgG supported by evidence of Aspergillus in sputum culture, PCR, or biopsy/aspiration.[10]

The patient in this report initially presented only with ocular symptoms, namely floaters and decreased vision. Physical examination demonstrated vitritis and retinal edema suspicious for possible acute retinal necrosis, but with nonspecific fluorescein angiography findings. She had a known history of previously treated pulmonary tuberculosis as well as a 1-year history of decreased appetite and unintentional weight loss, but without pulmonary symptoms. She also had significant radiologic findings of upper lobe collapse with surrounding fibrosis and hilar enlargement. These findings were suspicious for possible reactivation of tuberculosis; however, the aggressive and rapid inflammation with subsequent development of hypopyon was more consistent with an endogenous endophthalmitis, which was confirmed by blood cultures, bronchoalveolar lavage, and vitreous sampling. The patient's postoperative course was complicated by bilateral thromboembolic and cardiogenic shock, likely due to the patient's underlying CPA.

In conclusion, Aspergillus endogenous endophthalmitis secondary to CPA is an important clinical entity to consider when treating patients with underlying pulmonary disease who present with inflammation of the posterior segment. The patient may be immunocompetent and without pulmonary symptoms. A thorough review of systems and a chest X-ray should be performed to properly evaluate for the possibility of this disease.

Key words: Aspergillus endophthalmitis, chronic pulmonary aspergillosis, endogenous endophthalmitis, fungal endophthalmitis.

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