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Case Report

Fungal endophthalmitis in a case of granulomatosis with polyangitis

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Abstract

A 70-year-old immuno-compromised man, due to multiple comorbidities, particularly granulomatosis with polyangitis (GPA) and its related treatment, presented with generalized weakness, odynophagia and loss of taste sensation. After a complete evaluation, a diagnosis of right frontal lobe brain abscess was made. The patient then developed headache and sudden painful loss of vision in the right eye. Clinical examination revealed anterior chamber cells and flare, vitreous haze and cells, and hemorrhagic chorioretinitis with severe vasculitis in the right eye. Culture from the drained pus of the frontal brain abscess came positive for Aspergillus fumigatus. Incidental echocardiogram showed large vegetation in the mitral valve. Pars plana vitrectomy was done and a specimen was sent for culture that came positive for Aspergillus fumigatus. Although all the necessary medical and surgical interventions were timely carried out in the affected right eye, the patient's vision worsened due to retinal damage.

Keywords: Fungal endophthalmitis, Endogenous endophthalmitis, Aspergillus fumigatus, Granulomatosis with polyangitis, GPA, Wegener's granulomatosis

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Introduction

Granulomatosis with polyangitis (GPA), also known as Wegener's granulomatosis (WG), was first identified as a clinical entity by Friedrich Wegner in 1936.[1] It is an autoimmune disorder of unknown cause characterized by necrotizing granulomatous inflammatory and pauci-immune vasculitis affecting small to medium sized vessels in different systems of the body, most commonly the respiratory system.[1–4] Both ocular and orbital involvements can manifest in GPA patients at the time of diagnosis or later on during the course of the disease.[1–3] Ocular involvement occurs in 50–60% of patients with GPA, and it can affect any structure of the eye, from the eyelid and orbit to the optic nerve.[2,5,6] Retinal and choroidal involvement in GPA is rare.[3] Recognized retinal manifestations of GPA include retinitis, chorioretinitis, macular edema, exudative retinal detachment and retinal necrosis.[6] Endogenous fungal endophthalmitis (EFE) is a serious ocular infection and a medical emergency that requires prompt diagnosis and medical intervention to save vision.[7,8] EFE is preceded by fungemia that occurs with systemic fungal infections.[8] The incidence of EFE in patients with a systemic fungal infection, according to different studies, varies between 2% and 45%.[8] The most common organism implicated in EFE is Candida albicans, followed by Aspergillus species.[9]

We report a case of EFE secondary to fungal endocarditis in a known case of GPA.

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Case report

A 70-year-old man, presented to our emergency medicine with generalized weakness, odynophagia and loss of taste sensation. He was on antihypertensive medications for the last 10 years and underwent angioplasty for ischemic heart disease 2 years back. The patient had prostate carcinoma treated with chemotherapy and radiotherapy 2 years back and was on androgen deprivation therapy on presentation. He underwent cataract extraction with intraocular lens implantation in both eyes more than 5 years ago.

Chart review of the patient showed an ICU admission six months back due to hemoptysis. On investigations he was found to have alveolar hemorrhage, high P-ANCA and C-ANCA levels, therefore, the diagnosis of granulomatosis with polyangitis was made. He was treated with pulse methylprednisolone, plasmapheresis and cyclophosphomide. Following discharge, the patient developed steroid-induced diabetes, and, because of that, oral steroids were slowly tapered with cyclophosphomide dose increased from 25 mg to 50 mg daily. One month ago, the patient was started on rituximab and was due for the second dose.

A thorough neurological evaluation with MRI imaging revealed right frontal subcortical lesion suggestive of brain abscess [Fig. 1], thus, the patient was admitted to the neurosurgery ward. Cyclophosphamide and rituximab were held. While waiting for surgery, the patient developed sudden painful loss of vision in the right eye associated with headache that warranted ophthalmic consultation. On examination, the patient's visual acuity was counting finger at 1 m in the right eye and 20\40 in the left eye. Intraocular pressure was 26 in the right eye and 22 in the left eye. On ocular examination, the right eye showed conjunctival chemosis, clear cornea and grade 4 cells in the anterior chamber with grade 3 flare. The right eye pupil was 3 mm in diameter and not reactive to light. Right eye intraocular lens was seen in place with pigment dusting present on the lens. In addition, there was grade 2 vitreous haze and grade 3 cells in the right eye. Fundus examination revealed right eye hemorrhagic chorioretinitis with severe vasculitis. The patient was started on prednisolone eye drops every hour for anterior chamber reaction and cyclopentolate eye drops every 8 h for mydriasis, and for cycloplegia to relieve pain in the right eye. Lab investigations showed elevated ESR and CRP levels, high WBC count, thrombocytopenia and low hemoglobin. After two days, the patient developed right facial palsy with left hemiparesis, and imaging showed acute small infarcts suggestive of cerebrovascular accident. Two days later, the patient underwent right frontal craniotomy and excision of the brain lesion. Culture from the drained pus was positive for Aspergillus fumigatus, and the patient was put on 250 mg of intravenous voriconazole every 12 h. Blood culture was negative. As a part of the workup, an echocardiogram was done that showed a 1.7 × 1.7 cm large vegetation on the anterior mitral leaflet. After 1 week, the patient's condition of the right eye worsened with the retina showing dense

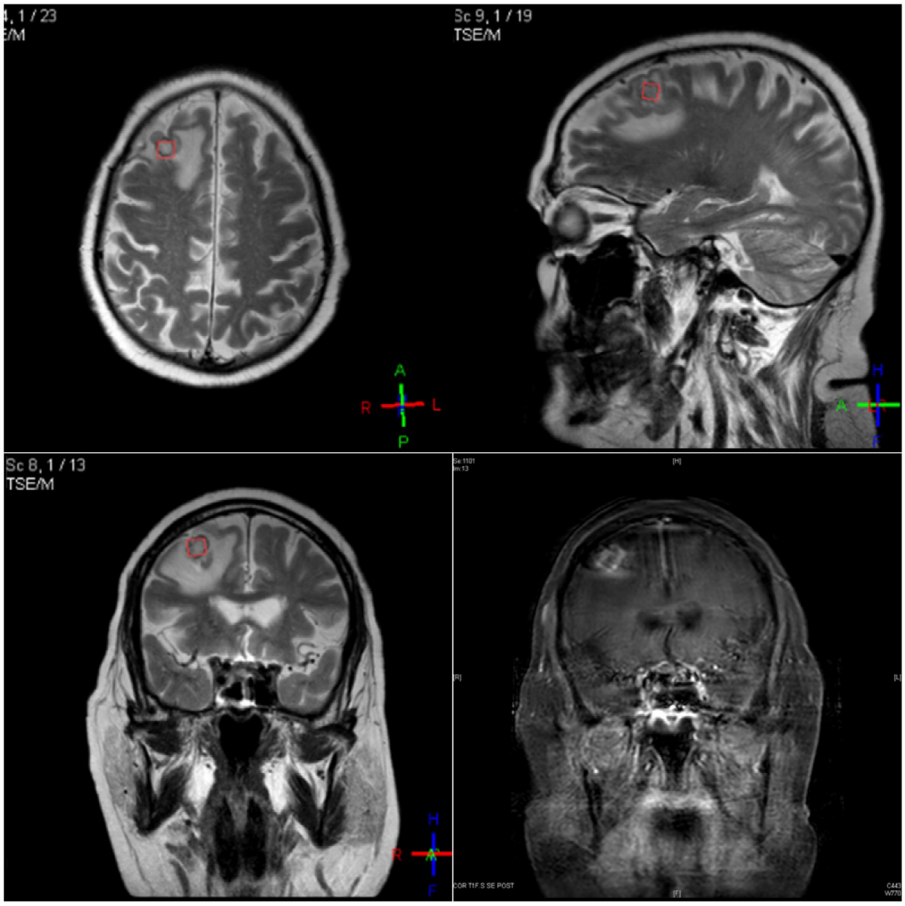

Fig. 1. Brain MRI showing right frontal lobe abscess which showed Aspergillus in aspiration of abscess.

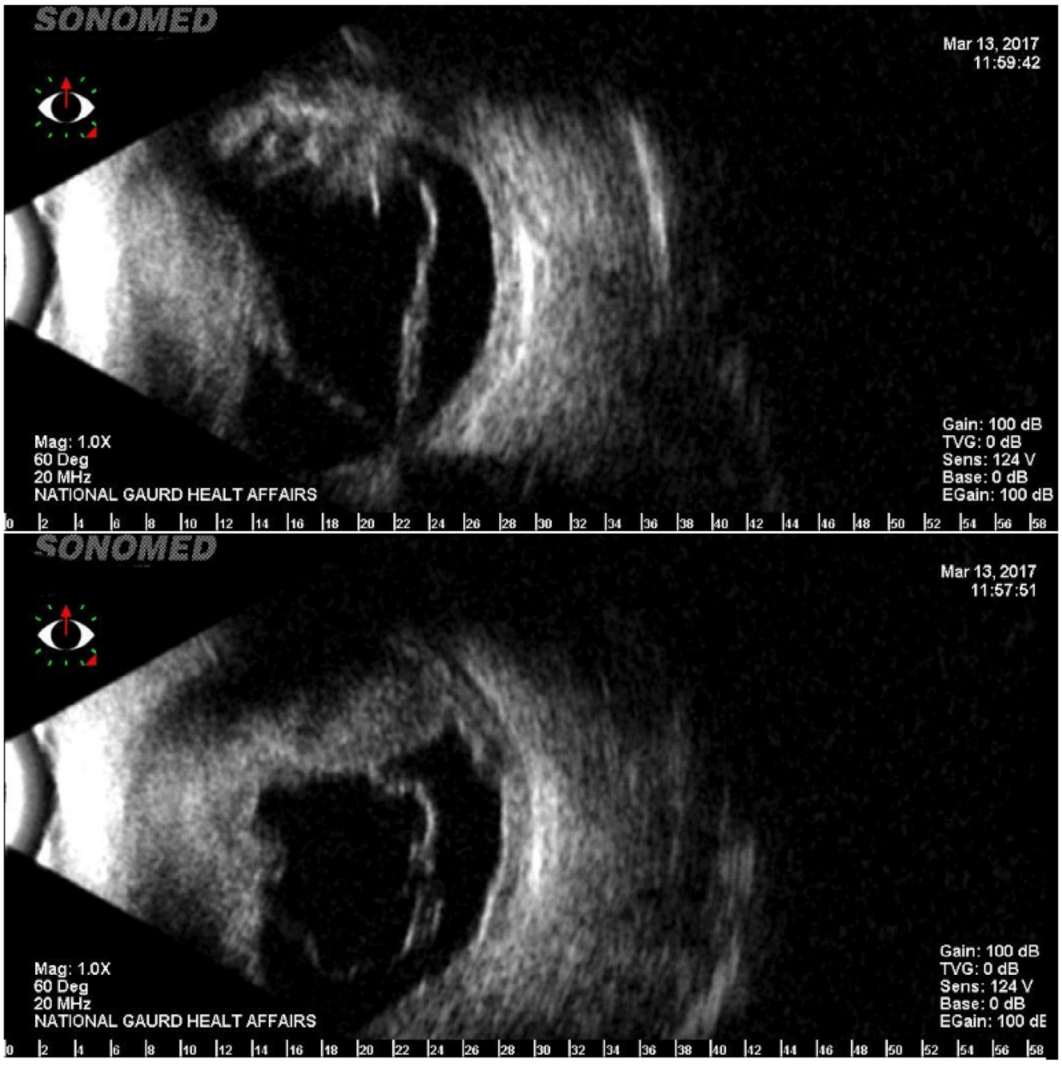

Fig. 2. Ultrasound biomicroscopy/high frequency of the right eye showing vitreous membranes and chorio-retinal involvement along with localized choroidal detachment. The vitreous aspirations results revealed Aspergillus.

vitritis with chorioretinal lesions and retinal hemorrhages in the mid-periphery. The prednisolone eye drops were tapered, and cyclopentolate eye drops were continued every 12 h. A vitreous tap was done and sent for PCR, culture and sensitivity though results came negative. Two days later, the patient was taken as an emergency case for 23 G pars plana vitrectomy, and an undiluted sample of 6 ml dense pus like vitreous aspirate was sent for culture and sensitivity. Voriconazole (100 mcg in 0.1 ml) was injected empirically into the vitreous cavity at the end of the procedure. Slides sent for stains were all negative while the culture report showed a positive result for Aspergillus fumigatus. The patient was given three doses of 10 mcg of intravitreal amphotericin-B, 1 week apart in the right eye. As advised by the infectious diseases division, he also received intravenous 300 mg of amphotericin-B every 24 h as well as 250 mg of voriconazole every 12 h for 8 days after the eye culture was reported positive. The patient remained on regular follow up with ophthalmology. He had persistent right eye pain though his vitritis slowly cleared with organized cyclitic membrane formation in one month. In addition, there was subretinal fluid collection with what clinically appeared as serous retinal

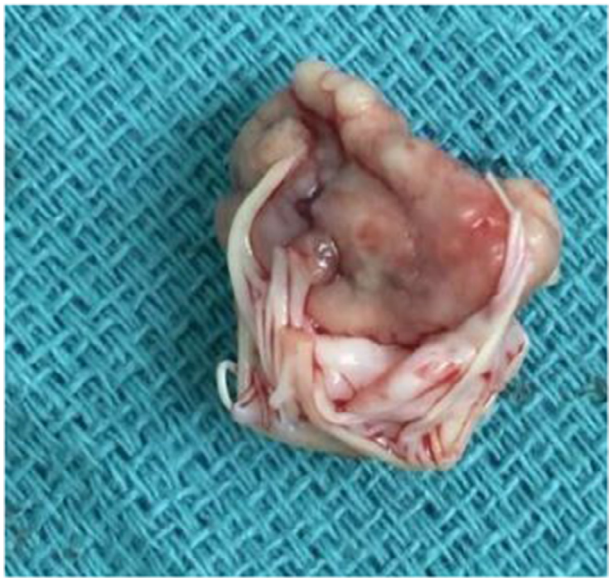

Fig. 3. Valve tissue and fungal ball that were sent for bacterial and fungal cultures which showed the evidence of Aspergillus in the vegetation.

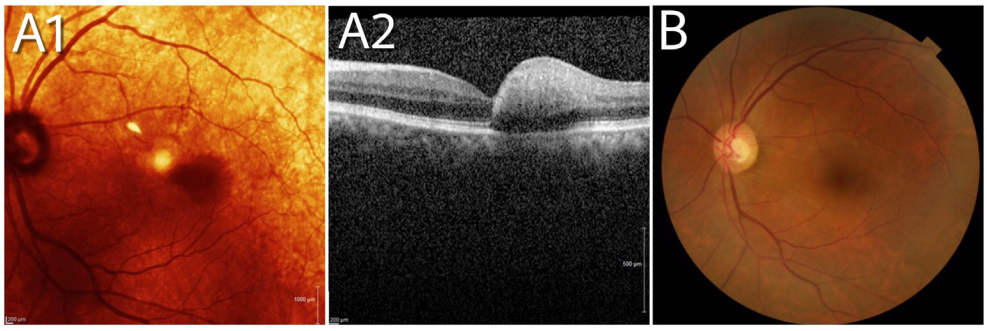

Fig. 4. Fundus photography and Enhanced Depth Imaging-Optical Coherence Tomography (EDI-OCT) of the left eye showing preretinal hemorrhage covering temporal fovea (A1 and A2). This hemorrhage completely cleared on followed without any intervention with the patient regaining his vision from 20/60 to 20/20 in his pseudophakic left eye (B).

and choroidal detachment inferiorly, for which no intervention was made because of the infectious nature [Fig. 2]. Three months later, the patient was taken for cardiac surgery to resect the native mitral valve with the large fungal ball [Fig. 3]. Mitral valve replacement was done with Carpentier-Edwards (CE) tissue valve No: 29. Three weeks post cardiac surgery, the patient came to the ophthalmology clinic with blurred vision in the left eye. On examination, right eye vision was doubtful perception of light, and left eye vision was 20/60. Complete ocular examination revealed right eye retinal detachment with extensive preretinal fibrosis along with fibrotic bands covering the ciliary body region and left eye with preretinal hemorrhage covering temporal fovea [Fig. 4 (A1 and A2)]. The patient denied any Valsalva maneuver, and this new finding could unlikely be related to diabetes or hypertension. The patient was followed up closely and, in the last visit, his visual acuity in the right eye was no perception of light and in the left eye was 20/20. The Right eye was painless, hypotonous and had the evidence of cyclitic vascular membrane with retinal detachment for which no intervention was advised [Fig. 5]. The left eye hemorrhage cleared completely over a period of two months without leaving any visual disturbances [Fig. 4(B)]. Intravenous amphotericin-B was stopped on discharge, and 200 mg of oral voriconazole twice daily was started to complete a four-month prophylactic course following which internists decided to start methotrexate.

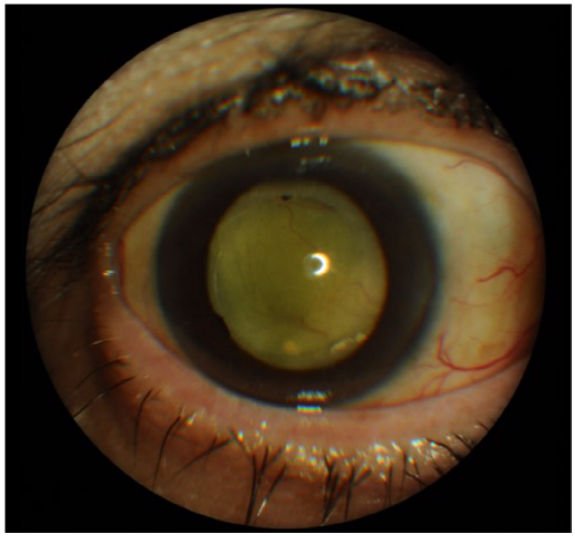

Fig. 5. Anterior segment photograph showing detached retinal behind the intraocular lens of the right eye.

Discussion

Aspergillus is the second commonest cause of EFE and is usually trauma related.[10–13] EFE is usually associated with intravenous drug abuse or long-term immunosuppression as seen in this case.[11–13] This report presents a case of endogenous Aspergillus endophthalmitis with the source being infective endocarditis in a known patient of GPA. Our case emphasizes the importance of looking for an internal source in a patient with endophthalmitis in presence of a known risk factor, i.e. immunosuppression. In this case, hematogenous spread of the fungus from the mitral valve vegetation took place although the blood cultures were negative. In a similar case reported by Gattringer et al., a known patient of GPA was diagnosed with EFE; however, in contrast to our case, the initial source of infection was preexisting thyroid nodules (abscesses) caused by the fungus Aspergillus flavus.[14]

Intravitreal and systemic antifungals along with vitrectomy are advised for the treatment of mold endophthalmitis.[7,15] Despite the intensive treatment with intravitreal and systemic antifungals combined with timely diagnostic and therapeutic surgical intervention by pars plana vitrectomy, the right eye vision in our patient could not be salvaged. Visual acuity in the affected right eye worsened from counting fingers at 1 m to no perception of light. Only 8% of eyes affected with Aspergillus endophthalmitis reportedly recover useful vision.[16] In addition, the right eye chronic retinal detachment that developed during the course of EFE lead to worsening of visual acuity. Gattringer et al., in their case report, could not describe visual outcome because of death of their patient in the course of disease.[14]

Our patient developed isolated evanescent preretinal hemorrhage in the left eye in the course of follow up without any residual changes. Recognized common causes for this clinical presentation include retinal vascular disorders, proliferative diabetic retinopathy, hypertension or senility.[17–20] Physical exertion or Valsalva maneuver may also cause rupture of normal retinal vasculature.[18] There was no history of Valsalva maneuver although our patient aged 70 years and had been hypertensive for 10 years. Both of these factors could be causative factors in our patient for observed

preretinal hemorrhage, as we do not believe this isolated finding has any relation to EFE in the absence of any haze or cellular activity in the vitreous cavity of his left eye. Moreover, apart from aspirin received by our patient post mitral valve replacement, he was not on any blood thinners that could be related to the left eye preretinal hemorrhage.

Multidisciplinary management has an important role in treating EFE, and is even more important in patients who are on immunosuppressive treatment for systemic diseases like GPA. The coordination of neurosurgeons, ophthalmologists, internists, infective disease experts, cardiologists and cardiac surgeons made the identification of source as infective Aspergillus endocarditis of mitral valve and its replacement by prosthetic valve. It is the coordinated teamwork that saved the life of this extremely moribund patient albeit not vision in the involved eye.

Conclusions

EFE may present as an ophthalmic emergency along with other systemic illnesses in a patient with GPA who is undergoing treatment for granulomatosis from a source of vegetation like the mitral valve, as is the case in this report. Although the vision could not be salvaged in the involved eye of our patient as a consequence of EFE, the evidence based management, multidisciplinary teamwork and timely intervention by each specialty saved the patient's life.

Conflict of interest

The authors declared that there is no conflict of interest.

Acknowledgments and Disclosures

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