

Ocular *Penicillium* Infection Presenting as Combined Rhegmatogenous and Serous Retinal Detachment in an Immunocompetent Patient

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Received date: January 21, 2017; Accepted date: February 16, 2017; Published date: February 28, 2017

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Abstract

Purpose: To report a rare case of ocular *penicillium* infection presenting as combined rhegmatogenous retinal detachment and serous retinal detachment in an immunocompetent patient.

Methods: Case report.

Results: A 44 year old male who had newly diagnosed type 2 diabetes mellitus. He had intermittent blurred vision in his left eye for 2 years, but progressed in recent two and half months. He had cataract surgery in the left eye 2 months before visit. Initial examination showed visual acuity was 6/60, traced cell in anterior chamber and pseudophakia. Fundus examination revealed serous retinal detachment OS first, but Shafter sign developed 11 days later. He underwent pars plana vitrectomy plus scleral buckling immediately. The pathology of vitreous biopsy demonstrated the classical picture of *Penicillium marneffe*. Blood culture showed no fungemia. Under the impression of ocular *Penicillium* infection, he received systemic intravenous infusion of Amphotericin-B 50 mg/day for 14 days and following oral Itraconazole 400 mg/day for 3 months. Besides, 0.15% Amphotericin-B eye drop was administered for next 3 week. The ocular inflammation was silent down after operation. Final visual acuity was 6/15. He didn't have any ocular recurrence or systemic manifestation during 9 months follow up.

Conclusion: *P. marneffe* has not only emerged as an important fungal pathogen that causes disseminated infection in HIV-infected patients residing in or travelling to endemic area, but localized ocular infection of *P. marneffe* could also be possible in immunocompetent patients. Hence, ophthalmologists should be aware of any ocular inflammation with patient who travels to or resides in the Southeast Asia.

Introduction

Penicillium marneffe is a facultative, intracellular pathogen and the only known thermally dimorphic fungus of the genus *Penicillium*. *Penicillium marneffe* is an emerging cause of fatal systemic mycosis in patients infected with the human immunodeficiency virus (HIV) [1-4]. Although both immunocompetent and immunocompromised individuals can become infected, it is extremely rare to diagnose systemic *P. marneffe* infections in patients negative for the human immunodeficiency virus (HIV). Ocular involvement of *P. marneffe* appears limited to case report in a patient with HIV.5 Hence, we present an ocular *Penicillium* infection was diagnosed in an immunocompetent patient that presented with retinal vasculitis and serous retinal detachment (RD).

Case Report

A 44 year old man was referred for a 10 week history of blurred vision oculus sinister (OS) that was unresponsive to both periocular and topical corticosteroids. The presumptive diagnosis by the referring physician was central serous choroidoretinopathy. The patient reported having intermittent blurred vision OS starting 2 years ago that was

only recently exacerbated. Cataract surgery, performed in a local medical clinic 8 weeks previously, improved his vision only shortly. Unfortunately, the blurred vision recurred only 3 days following the cataract surgery. The blurred vision waxed and waned during a course of periocular and topical corticosteroids, but was exacerbated in the two weeks prior to referral. He was ultimately referred for central serous chorioretinitis.

The patient had no specific systemic disease except an impaired fasting glucose that he was controlling through diet alone. He was a professional bus driver, working in Taiwan and offshore Penghu Islands and had travelled to Mainland China several times before and after blurred vision OS developed. He stayed in the Penghu Island for work most, and sometimes driving bus along the west-coast of Taiwan. He denied any dirt or pet contact.

Examination revealed a best-corrected vision of 6/6.7 oculus dexter (OD) and 6/60 OS. No abnormal findings OD were noted except mild cataract. Moderate congestion of the conjunctiva, trace amounts of cells in the anterior chamber, and pseudophakia with a well-centered intraocular lens was noted OS. Fundoscopic examination showed one small, focal area of hemorrhage between the macula and disc, and

serous RD with an obvious shifting sign (Figure 1A). No abnormal findings on the complete blood count and differential, serum biochemistry, and urinalysis were noted; other routine serology tests for various infectious diseases, C-reactive protein, and the erythrocyte sedimentation rate were negative/normal. The patient was positive for

the Varicella zoster virus IgG and Cytomegalovirus (CMV) IgG (but not IgM) and negative for rheumatic factor (RF), treponemal antigen serologic test/Venereal Disease Research Laboratory test (TPHA/VDRL), HIV, and the tuberculin test. Thoracic and lumbosacral radiographs were normal.

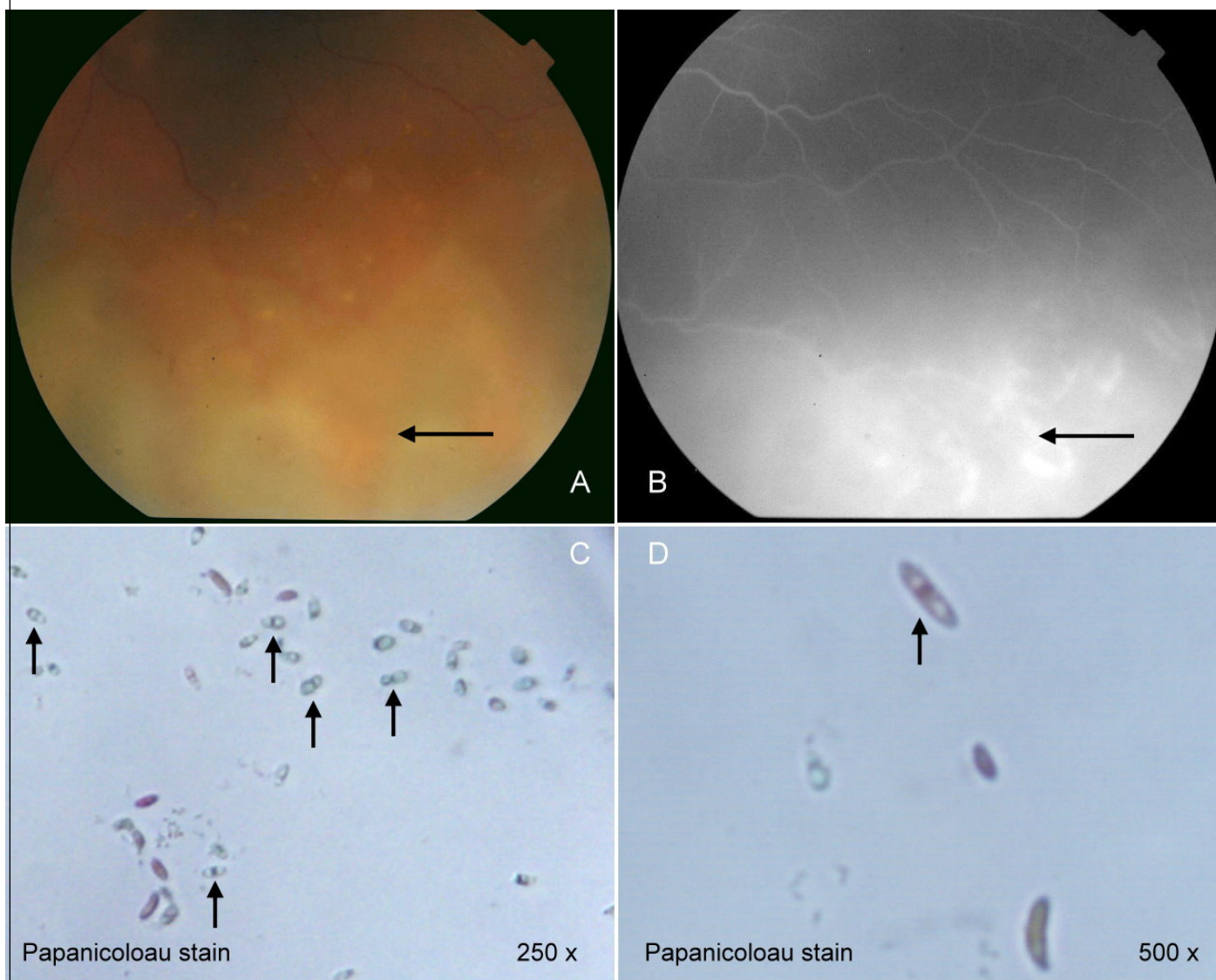


Figure 1: A: Prominent inferior serous retinal detachment (arrow) with shifting sign. B: Peripheral vascular leakage and pooling (arrow) in the late phase. C: The characteristic transverse septum (arrows) within the yeast cell can be seen in Papanicolaou stain in 250x. D: Papanicolaou stain in 500x.

Fundus fluorescein angiography showed vascular leakage and dye pooling indicative of vasculitis at the inferior retina (Figure 1B). Eleven days after the initial visit, pigment appeared in the vitreous cavity with decreased shifting sign. Rhegmatogenous RD was diagnosed, and a pars plana vitrectomy with scleral buckling was performed. A small break was identified at the 8 o'clock position intraoperatively. Owing to the suspicion of infectious uveitis-related retinal detachment, a dry core biopsy of the vitreous was obtained for culture and cytological analysis. The culture was negative for bacteria, but round to oval shaped fungal microorganisms measuring 3-7 microns in diameter

were identified that reproduced by central fission rather than budding (Figures 1C and 1D). *Penicillium marneffei* was diagnosed by the pathologist, and supported by our infection specialist.

The infection specialist speculated that the ocular infection was metastatic from fungemia, although the blood fungus culture was negative due to the low culture rate in our laboratory. The patient was prescribed intravenous amphotericin B (50 mg/day for 14 days) then oral itraconazole (400 mg/day for 3 months) and topical 0.15% amphotericin B every one hour for 7 days, which was subsequently tapered over the next 3 week. Tobradex ointment was also prescribed

for the first 3 weeks of treatment. The retina attached well, and the eye remained silent postoperatively. At the 9 month follow-up examination, the best corrected visual acuity was 6/20.

Discussion

Penicillium marneffei was first described in 1959 after isolation from a bamboo rat [2]. It is now endemic in tropical Asia (following the HIV pandemic in Asia) [1,3-5]. With the increase in global travel and migration, cases are now diagnosed worldwide. *P. marneffei* infections usually occur in HIV-infected/immunodeficient patients. The clinical manifestations are nonspecific and share similarities with other systemic infectious diseases. The most common clinical signs and symptoms of disseminated disease include fever, weight loss, non-productive cough, skin lesions, hepatosplenomegaly, and generalized lymphadenopathy [1-3]. Diagnosis of *P. marneffei* is commonly achieved by identifying the fungus in clinical specimens via microscopy and culture. The organism appear as either fission arthroconidia or unicellular round to oval cells, which may divide by cross-wall formation in macrophages or histiocytes. The characteristic intracellular transverse septum differentiates *P. marneffei* from *Histoplasma capsulatum*, which also appear as intracellular yeasts [2]. If not treated early and adequately, the mortality of *P. marneffei* is typically high [2,3]. For patients with severe disseminated disease or who cannot tolerate oral medication, IV amphotericin B (0.6 mg/kg daily for 2 weeks) followed by oral itraconazole (200 mg q 12 h for 10 weeks) is the preferred regimen for *P. marneffei* [2].

The patient described herein was generally healthy, which is unusual in *P. marneffei* infections. The initial clinical manifestation included retinal vasculitis with serous RD. Rhegmatogenous RD could have been a result of acute posterior vitreous change caused by inflammation. Vitreous cytology confirmed the diagnosis of ocular *P. marneffei* infection. Theoretically, an intravitreal injection of

amphotericin B is the treatment of choice for ocular fungal infections, but because the eye was gas-filled and silent postoperatively and although he had no symptoms/signs of a systemic infection, he was prescribed IV amphotericin B followed by itraconazole because ocular infections should be treated as central nervous system infections. The patient's eye remained silent with retinal reattachment. No ocular recurrence or systemic manifestations occurred during the 9 month follow-up period.

This report highlights that not only has *P. marneffei* emerged as an important fungal pathogen that causes disseminated infection in HIV-infected patients residing in or travelling to Southeast Asia where the disease is endemic, but also localized ocular infections in even immunocompetent patients. Ophthalmologists should be aware that ocular inflammation in patients who travel to or reside in Southeast Asia could be affected by this new, emerging ocular fungal infection.

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