

Penicillium Marneffe infection in an AIDS Patient – A First Case Report from Malaysia

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Summary

We report a 39-year-old male who presented with tuberculous meningitis and was found also to be HIV-infected. In the course of his illness, he developed multiple opportunistic infections such as herpes genitalis, oesophageal candidiasis, CMV retinitis and finally succumbed to *Penicillium marneffe* septicaemia.

Key Words: AIDS, *Penicillium Marneffe*

Introduction

The development of Acquired Immunodeficiency Syndrome (AIDS) may take 7-11 years from the time of seroconversion. The most common AIDS defining illness is *Pneumocystis carinii* pneumonia, however, other opportunistic infections can occur during the course of the illness. When the patient develops severe immunodeficiency as seen by declining CD4+ T lymphocyte counts¹, other infections such as cytomegalovirus (CMV) infection, *Mycobacterium avium* complex infections, and serious fungal infections can occur.

Recently, cases of *Penicillium marneffe* infections in AIDS patients have been documented^{2,3}. *Penicillium marneffe*, a dimorphic fungus, is a rare opportunistic pathogen. It can cause systemic and deep seated infection in immunocompromised patients. The disease is endemic in South East Asian countries. All cases reported in the literature were found in South East Asia and neighbouring countries or in patients who had a history of travelling in South East Asia.

We report a case of *Penicillium marneffe* infection in an AIDS patient in Malaysia.

Case Report

A 39-year-old single male was admitted to the University Hospital, Kuala Lumpur in mid-1992. He complained of fever, headache and vomiting for 2 weeks prior to admission. The headache was severe, bitemporal and biparietal and slightly relieved by taking analgesics. There was no history of convulsions, photophobia, double vision, blurring or loss of vision.

He was previously healthy except for an episode of passing black stools 10 years previously. Since then he had been very well. He worked as a carpenter. He was heterosexual with multiple sex partners.

Physical examination revealed a male of average build who was febrile, with a temperature of 39° Celcius and minimal neck stiffness. There was no neurological deficit. A lumbar puncture showed a predominant lymphocytosis with very low sugar (rbc 12, wbc 80; L 65%, P 35%; sugar 2.0mmol/L, protein 43, stains for organisms, AFB and *Cryptococcus* were negative). These findings were suggestive of *tuberculous meningitis* and he was treated with rifampicin 600mg daily, isoniazid 300mg daily, ethambutol 1.2gm daily, pyrazinamide 1.5gm daily, and pyridoxine 10 mg daily.

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The blood and CSF were negative for cryptococcal antigen. The computerised tomographic (CT) study of the brain was normal. His blood was subsequently tested positive for HIV. The CD4+ T lymphocyte count was 2% (19/uL); (normal range:410/uL-1540/uL)¹. Serological titres for toxoplasma, cytomegalovirus and herpes were negative. He was diagnosed as having Acquired Immunodeficiency Syndrome (AIDS). Prophylaxis against *Pneumocystis carinii* was instituted.

Other tests done included a full blood count which showed a hemoglobin of 13.8gm/ml, platelet count 251×10^3 /uL, wbc 8500/uL and an erythrocyte sedimentation rate (ESR) of 50mm/Hr. His liver function test showed slightly raised transaminases.

Despite treatment, the patient's condition deteriorated, with increasing headache, drowsiness and restlessness. He became comatose and was responding only to deep pain. A repeat lumbar puncture showed similar findings as previously. He developed *oral candidiasis* which was treated with ketoconazole.

Six weeks after the first admission, *Mycobacterium tuberculosis* was isolated from the CSF.

After 6 weeks of anti-TB therapy, he became more alert, was able to obey simple commands and move all 4 limbs. Eventually he managed to ambulate with help. He was discharged from the hospital 9 weeks after admission. He was advised to continue with the anti-TB therapy for at least 2 years and prophylaxis against *Pneumocystis carinii*.

On followup 2 weeks later, he complained of headache and photophobia. He had not been taking his medications regularly. A repeat CT scan of the brain showed cerebral infarction or cerebral toxoplasmosis. However the toxoplasma titres were negative. Anti-tuberculous treatment was continued.

Two weeks later he developed a fungating lesion on the scrotum. A biopsy confirmed that the mass was herpes genitalis. He was successfully treated with acyclovir and local washings with a 1:10,000 aqueous solution of potassium permanganate.

He was relatively well for 2 months when he

developed diplopia. Fundoscopy showed changes in the right fundus consistent with inactive cytomegalovirus (CMV) retinitis. The CMV titres were raised. Anti-CMV therapy was withheld because his vision was stable.

Six months later he was re-admitted with fever, weight loss and dysphagia. Physical examination showed severe wasting and oral thrush. A chest radiograph showed a hilar mass on the right side. Aspergillus antigen was detected in his blood and blood cultures grew *Penicillium marneffeii*. He was treated with oral ketoconazole, Amphotericin-B infusion and oral 5-flucytosine. He improved temporarily but died 3 weeks later.

Mycological Examination

The blood sample was inoculated into a biphasic fungal blood culture medium (brain heart infusion agar plus brain heart infusion broth with 10% glucose) and incubated at 37°C. The blood culture was checked daily for growth. White opaque colonies of 3 to 4 mm in diameter, round and elevated were seen after 48 hours of incubation. The Gram's stain of the colony showed a yeast-like gram-positive organism. The isolate was then subcultured onto Sabouraud's Dextrose Agar (SDA) and blood agar. The SDA was incubated at 30°C (or room temperature) and the blood agar was incubated at 37°C. The plates were examined daily for growth. At 48 hours, yeast-like colonies appeared on the blood agar incubated at 37°C. The colonies were soft, white to tan in appearance. They were gram-positive, unicellular, ellipsoidal to rectangular; there was no budding and the new cells appeared to be produced by fission rather than by budding. Carbohydrates assimilation and fermentation tests were carried out and the results showed that the isolated organism did not belong to any of the yeast-like organisms.

At room temperature, mould-like colonies appeared. The colonies were downy and grayish pink in appearance (Fig. 1A). A soluble and diffusible red pigment around the colonies was seen. A wet smear stained with lactophenol cotton blue revealed a typical penicillium-like morphology (Fig. 1B), it consisted of conidiophores with basal stipes bearing terminal verticils of 3 to 4 metulae, the subterminal metulae

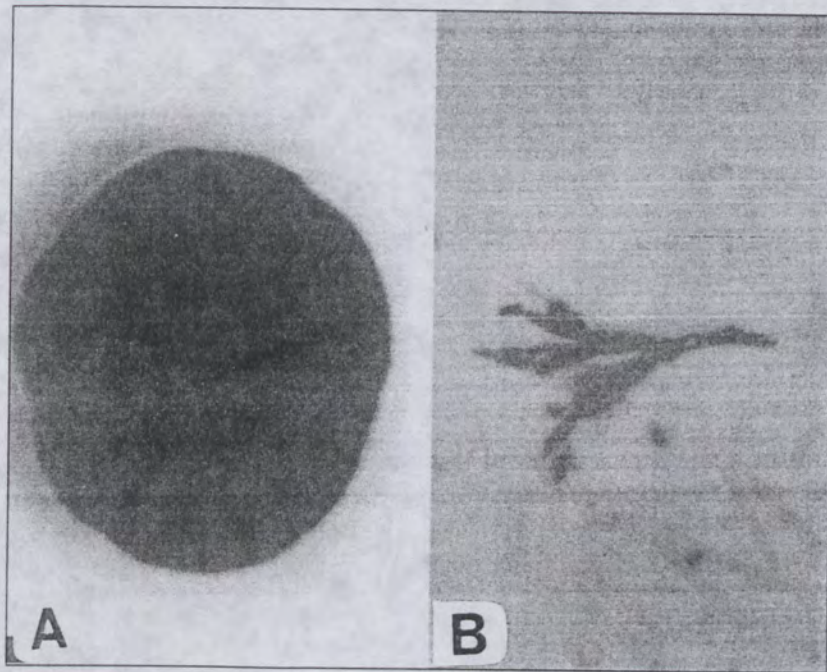


Fig. 1: Morphology of *Penicillium marneffeii* grown on SDA incubated at room temperature (A) and conidophores in Lactophenol cotton blue mount, x1000 (B)

in verticils bore 4 to 7 phialides which arranged in a verticillate manner, and these phialides produced chains of ellipsoidal, smooth-walled conidia.

The isolate was identified as *Penicillium marneffeii* by its dimorphic character, penicillium-like colonial morphology and the production of pink pigment which diffused into the medium around the colony. Microscopically, the isolate showed a typical penicillium-like structure.

Discussion

P. marneffeii is the only known dimorphic fungus in the genus *Penicillium* which causes both localized and systemic infection in humans. The fungus is an opportunistic pathogen endemic in South East Asia and its neighbouring countries. The common clinical manifestations are fever, hepatomegaly, generalized lymphadenopathy, soft tissue abscesses and chronic skin ulcers. The fungus is most often isolated from the skin, bone marrow, lymph nodes and blood. The fungus may have gained entry into the host by the fungating herpetic lesion in the groin.

The differentiation of *P. marneffeii* from *Histoplasma*

capsulatum in tissue sections may be difficult because both fungi show similar microscopic morphology and both are intracellular organisms. However, *P. marneffeii* multiply by schizogony but in contrast, *H. capsulatum* multiply by budding and this feature is helpful for differentiating the organisms. *Candida glabrata* may also complicate the diagnosis because of similar morphology. The most reliable method of diagnosis of *P. marneffeii* is by culture on SDA at 30°C. *P. marneffeii* can be identified by its dimorphic nature and a mould-like colony with red pigment diffusing into the medium surrounding the colony. On blood agar at 37°C, it appears as a yeast-like colony.

Infection with *P. marneffeii* can manifest with papular skin-coloured lesions with umbilicated centre that may resemble molluscum contagiosum. However, chronic skin ulcers have been described². Often fever, weight loss and generalised lymphadenopathy may be the presenting symptoms. A high index of suspicion and early diagnosis and treatment will improve outcome of the infection.

Amphotericin-B is the most effective treatment for *P. marneffeii* infection². However, mortality rate remains high and the survival rate is about 20%. Favourable

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outcome of treatment depends on the early institution of therapy. Triazoles such as itraconazole has been shown to be effective in the treatment of *P. marneffeii* infection².

Conclusion

Symptomatic HIV disease (AIDS) presents with the

onset of various opportunistic infections. In South East Asia, because of the endemicity of *P. marneffeii*, infections caused by this organism may need to be considered as an AIDS defining illness in patients with laboratory evidence of HIV infection and low CD4+ T-lymphocyte counts.

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