Penicilliosis marneffei Complicated with Interstitial Pneumonia

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Abstract

A 71-year-old man with interstitial pneumonia was hospitalized due to a pulmonary infection. He had been living in Thailand and had returned to Japan three months earlier. Antibiotic therapy initially cleared the infection; however, the patient’s condition relapsed. Pseudomonas aeruginosa and Penicillium sp. were both detected in sputum and bronchial lavage fluid cultures and Penicillium sp. was identified to be *P. marneffei*. The infiltration observed on chest radiographs improved following treatment with itraconazole and tazobactam/piperacillin, and no relapse occurred. We herein report the first case of a non-HIV patient with *P. marneffei* infection in Japan.

Key words: Penicillium marneffei, interstitial pneumonia, itraconazole, *Pseudomonas aeruginosa*


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Introduction

*Penicillium marneffei* (*P. marneffei*) is an emerging pathogenic fungus that can cause fatal systemic mycosis in immunocompromised hosts. *P. marneffei* infection has become an important opportunistic pathogen in HIV-positive individuals and appears with a high prevalence in tropical Asia, especially Thailand, India, China, Vietnam and Taiwan (1). There have also been rare reports of *P. marneffei* infection in the absence of HIV infection in immunosuppressive individuals with systemic lupus erythematosus (2), hyper IgE syndrome (3) or a history of renal transplantation (4). Only a few cases of *P. marneffei* infection have been reported in Japan, and all of the affected individuals had traveled to a *P. marneffei* endemic area and were compromised with HIV infection (5, 6). Penicilliosis usually develops rapidly and can be fatal without the timely administration of antifungal therapy. We herein report the case of a non-HIV patient with interstitial pneumonia and *P. marneffei* infection with a chronic clinical course.

Case Report

A 71-year-old man was diagnosed with interstitial pneumonia on a medical checkup conducted in 2006 and was observed without therapy for several years. Soon after moving to Chiang Mai, Thailand in 2009, he presented to a local hospital with symptoms of coughing and dyspnea. The interstitial pneumonia had clearly worsened; therefore, he was started on prednisolone (10 mg daily) and azathioprine. One year later, he contracted bacterial pneumonia and had to discontinue these medications. In the same year, 2011, he moved to Tokyo, Japan and was admitted to our hospital for the treatment of interstitial pneumonia and bacterial pneumonia. He had no past medical history other than interstitial pneumonia and bacterial pneumonia, although he had been a smoker for 50 pack-years. Fine crackles were audible near the precordial lesion on chest auscultation; however, no skin lesions were noted. A blood examination revealed leukocytosis (white blood cell count: 1.14×10⁹/L) and an elevated C-reactive protein level (CRP: 43.3 mg/L). The Krebs von den Lungen-6 (KL-6) and surfactant protein-D (SP-D) levels were elevated to 743 U/mL and 266 ng/mL, respectively.

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The serum titers of β-D glucan, HIV antibodies and Candida, Aspergillus and Cryptococcus antigens were negative or within the normal limits. A chest radiograph revealed consolidative changes and cysts in the right upper field. Computed tomography revealed bilateral ground-glass abnormalities superimposed on bibasilar subpleural reticular abnormalities, traction bronchiectasis, honeycombing and centrilobular emphysema. Fluid was observed in the right upper lobe (Fig. 1A). The patient was diagnosed with idiopathic pulmonary fibrosis according to the criteria of the American Thoracic Society/European Respiratory Society (ATS/ERS) international consensus statement (7). Sputum cultures showed no pathogenic bacteria apart from *Penicillium* species. Initially suspecting the *Penicillium* sp. to not be pathogenic or contaminative, we started the patient on ampicillin/sulbactam. The response to therapy was favorable; the CRP level fell to 13.6 mg/L, the infiltration on chest radiography partially resolved and we were able to discharge the patient. However, the pneumonia soon relapsed after hospital discharge, and the patient was readmitted three times within the ensuing six months.

P. marneffei, a thermally dimorphic fungus with a high prevalence in Southeast Asia, is the third most opportunistic cause of infection in HIV patients in areas where it prevails. The most common symptoms are fever, anemia, coughing, weight loss and skin lesions (8). Abnormal chest radiographs are reported to be present in approximately one-third of patients (30 of 96 cases). Deesomchok et al. investigated 12 cases of *P. marneffei* pneumonia and found that six patients exhibited diffuse infiltration, four patients demonstrated localized infiltration and two patients presented with cavitory lesions. Six of the 12 patients were coinfected with other pathogens, namely, *Mycobacterium tuberculosis*, *Cryptococcus neoformans*, *Pneumocystis jirovecii* or other bacteria (9). The mortality of patients infected with *P. marneffei* is quite high, unless the infection is diagnosed accurately and appropriate therapy is promptly administered (10). The mortality of penicilliosis does not differ significantly between HIV and non-HIV patients, although the time to diagnosis is conspicuously longer in the latter (5.5 weeks) than...
the former (1 week) (11). Saadiah et al. reported a non-HIV patient who was diagnosed with \textit{P. marneffei} infection seven months after the patient’s first visit that responded well to amphotericin B followed by oral itraconazole (12). The time of \textit{P. marneffei} infection was unclear in this case; however, the patient’s doctors delayed making a definitive diagnosis for at least nine months. The penicilliosis remained localized in the lungs when the diagnosis was finally reached, and the desired treatment effect was attained with itraconazole alone.

The use of induction therapy with amphotericin B was therefore omissible, according to the CDC guidelines (13). Previous reports have described two clinical disease courses therefore omissible, according to the CDC guidelines (13). Previous reports have described two clinical disease courses in patients infected with \textit{P. marneffei}: focal infection and fatal, progressive, disseminated infection (14). Disseminated infection is much more common in patients infected with HIV, while localized infection is more prevalent in non-HIV or immunocompetent cases (15). This case is the first report of a patient complicated with \textit{P. marneffei} infection and interstitial pneumonia. Fungal infections are often observed in patients with pulmonary diseases with structural changes, including healed tuberculosis, interstitial pneumonia and pneumocociosis. Since the onset is insidious and asymptomatic, a delay in diagnosis frequently occurs. Therefore, undiagnosed \textit{P. marneffei} infection may exist in patients with prior pulmonary diseases. Clinicians should be aware of this disease in the differential diagnosis of fungal infections complicated by prior pulmonary diseases, especially in patients who have travelled or lived in tropical Asia.

The authors state that they have no Conflict of Interest (COI).

References


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