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Short Communication

Disseminated penicilliosis (non-*Penicillium marneffei*) in an immuno-competent individual in Malaysia

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Abstract

Penicilliosis infection caused by *Penicillium marneffei* is the third most common opportunistic infection in Human Immunodeficiency Virus patients in South-east Asia; however, *Penicillium* infection caused by non-*P. marneffei* is uncommon. We present a case of an immunocompetent male with disseminated penicilliosis (non-*P. marneffei*) presenting with recurrent empyema. The case described illustrates the challenges in managing a complicated systemic infection and the outcomes of a delayed presentation, in a potentially treatable disease.

Keywords

Penicilliosis, *Penicillium marneffei*, HIV, immunocompetent

Introduction

Penicilliosis infection caused by *Penicillium marneffei* is the third most common opportunistic infection in Human Immunodeficiency Virus (HIV) patients in South-east Asia. Both immunocompetent and immunocompromised individuals can be infected; however, it is rare to find systemic infections in individuals without HIV. *Penicillium* infection caused by non-*P. marneffei* is uncommon. Possible routes of transmission are through inhalation, ingestion or skin contact. We describe a case of an immunocompetent male with disseminated penicilliosis presenting with recurrent empyema.

Case report

A 45-year-old gentleman was referred to our centre following chronic episodes of weight loss, intermittent fever, dyspnoea and pleuritic chest pain for a few months. He also had intermittent episodes of absence spells associated with profound hypoxia. His background history included poorly controlled type-2 diabetes mellitus complicated by nephrotic syndrome and chronic kidney disease. He was an ex-smoker. He worked as a janitor at a microbiology laboratory and enjoyed fishing. On examination, there was reduced air entry at both lung bases, with coarse crepitations at the right lung base. There were widespread hyperpigmented ring-like and macular papular lesions on the trunk and lower limbs (Figure 1).

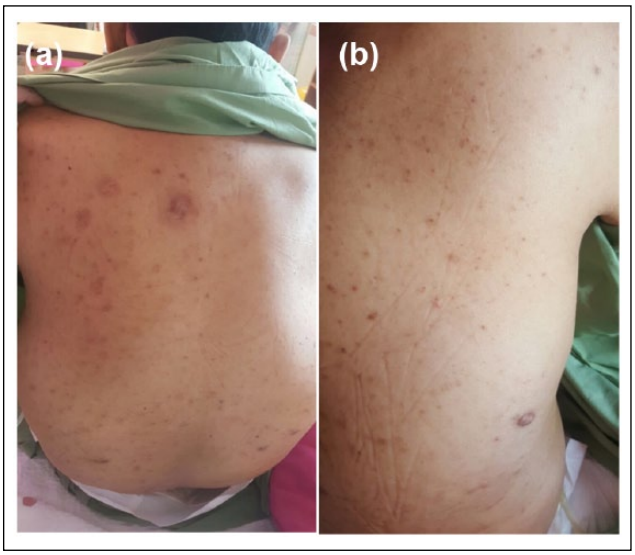

Figure 1. Hyperpigmented macular and papular skin lesions on the torso.

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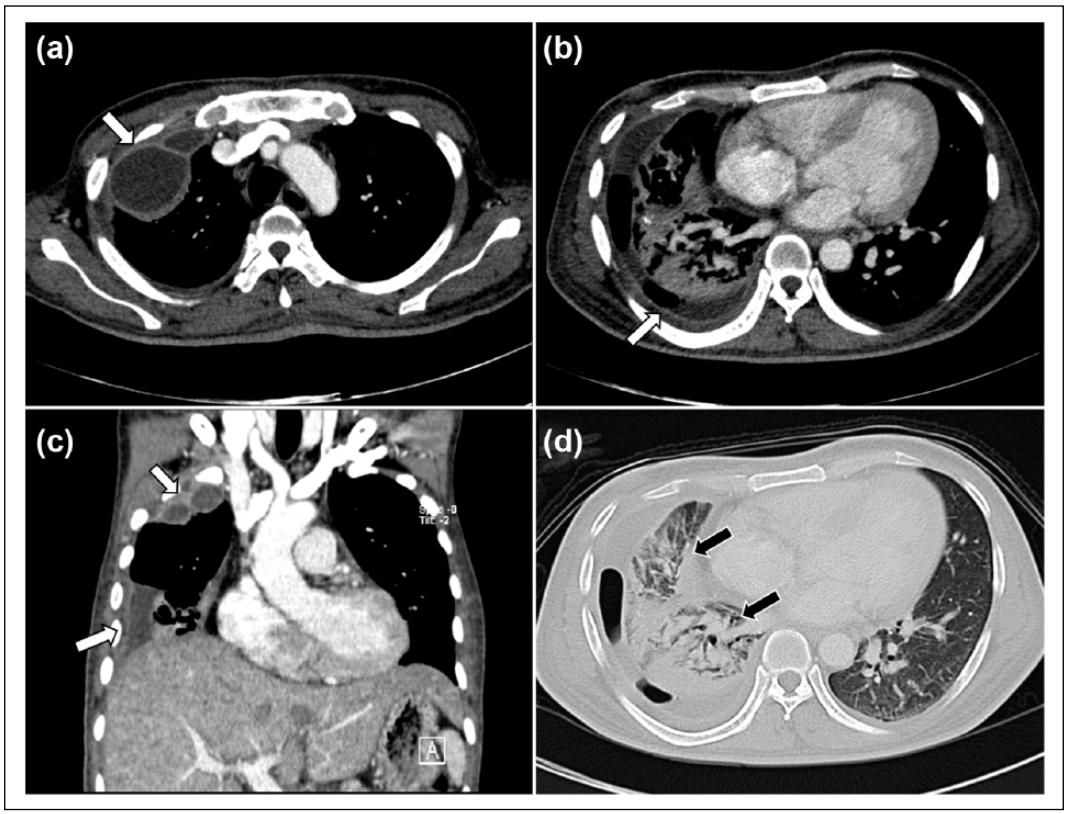

Figure 2. Selected axial ((a), (b) and (d)) and coronal (c) computed tomography images showing multi-loculated pleural collections with enhancing thickened pleura consistent with empyema in the right hemithorax (white arrows). In addition, there are consolidations in the right lower and middle lobe (black arrows).

The chest radiographs revealed a right lower lobe consolidation associated with ipsilateral pleural effusion. He had a few thoracic computed tomography (CT) scans, all revealing similar findings. There were loculated right pleural collections with enhancing thickened pleura suggestive of empyema. In addition, there were consolidations with air bronchograms in the right lower and middle lobes. There was also presence of right hilar lymphadenopathy but no nodules or cavitations in the lung parenchyma (Figure 2). He was initially commenced on a prolonged course of intravenous (IV) followed by oral antibiotics.

In view of worsening clinical condition and radiological findings, he was finally referred to our respiratory unit. Extensive investigations were completed. Malignancy, tuberculous and fungal infections were the main differentials. He received IV diuretics in view of fluid overload state and anti-epileptic medications. Investigations for *Mycobacterium tuberculosis* (mTB) complex from the sputum and pleurocentesis were negative. Fungal culture from the pleural fluid grew *Penicillium* sp. Bronchoscopy with broncho-alveolar lavage also revealed *Penicillium* sp. HIV test was negative (Figure 3).

Both cerebral CT and magnetic resonance imaging scans (non-contrasted) revealed generalized cerebral atrophy and multifocal infarcts. A lumbar puncture was performed and the cerebrospinal fluid (CSF) revealed slightly raised protein levels with normal CSF to serum glucose levels. The CSF was negative for gram-stain, culture and mTB complex. A skin biopsy revealed budding spherical to oval yeast-like organism within hair follicles consistent with fungal bodies, with mild peri-follicular chronic infiltrates.

The patient was treated as having disseminated penicilliosis with lung, skin and possible central nervous system involvement. He was given different forms of antifungals. The patient was initially treated with oral voriconazole 200 mg twice daily for one week, followed by syrup and capsule forms of itraconazole 200 mg twice daily alternately for about three weeks before being started on IV liposomal amphotericin B 250 mg o.d. (5 mg/kg) for one week when he showed poor clinical improvement. The treatment had to be switched back to syrup form itraconazole in view of stock availability. IV liposomal amphotericin B was restarted when he deteriorated. He showed partial response to IV amphotericin B, of which a three-week course was given. Unfortunately, he had a prolonged hospital stay due to a complicated disease course. He required mechanical ventilation and dialysis support and died after being in the hospital for eight weeks.

Mycological examination

Bronchoalveolar lavage was inoculated onto Sabouraud's dextrose agar and incubated at 30°C. Green and dense mould-like colonies appeared on the culture plates. No red pigmentation was seen. Microscopically, the colonies consisted of septated branched hyphae with conidiophores. These features were consistent with *Penicillium* species. Polymerase chain reaction subsequently revealed the final species as *Penicillium chrysogenum*.

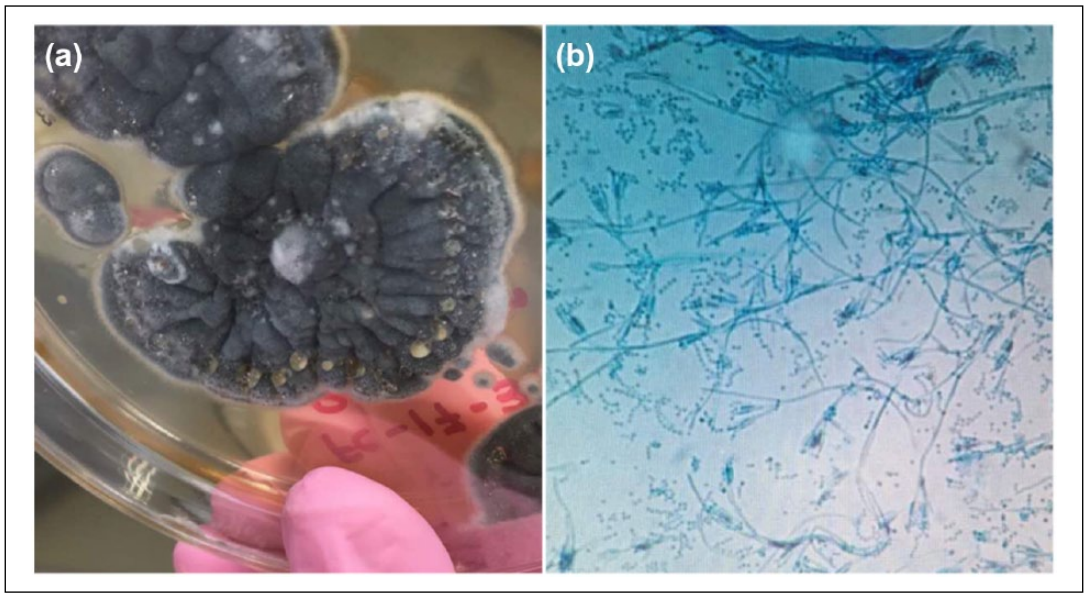

Figure 3. (a) Macroscopic picture showing green and dense, mould-like colonies with no red pigmentation seen. (b) Microscopically, the colonies consist of septated branched hyphae with conidiophores. The conidiophores consist of two to three branches of metulae, which bear four to seven phialides. Each phialides produces long chains of conidia, which are round in shape. These features are consistent with *Penicillium* species.

Discussion

Disseminated penicilliosis is the third most common infection in HIV individuals after tuberculosis and cryptococcosis in northern Thailand.[1] This infection is rare in immunocompetent individuals. Infections caused by non-*P. marneffei* are uncommon. Possible routes of transmission are through inhalation, ingestion or skin contact. *Penicillium* sp. is a genus of ascomycatous fungi. A common and virulent species is *P. marneffei*, an intracellular pathogen primarily hosted by bamboo rats. It was initially thought to be limited to immune-suppressed individuals. Its incidence in both immunosuppressed and immunocompetent individuals has been rising over the years, especially in endemic areas such as South-east Asia.

The first case of penicilliosis was reported in 1995.[2] There is lack of literature reporting the exact incidence and prevalence of the disease in Malaysia.[3] Cases of invasive penicilliosis from non-*P. marneffei* species are rare, as reviewed by Chen et al. and Lyratzouplous et al.[4,5] There have been various cases of disseminated penicilliosis being described in patients with connective tissue diseases (e.g. systemic lupus erythematosus, rheumatoid arthritis and Henoch–Schönlein syndrome), autoimmune diseases (e.g. myasthenia gravis), those on immunosuppressive therapy (e.g. renal transplant patients) and haematological and also non-haematological malignancies (with or without chemotherapy treatment).[6–10]

We hypothesize in our patient: the combination of diabetes with possible occupational hazards (working with air-conditioning and heating units) might be a possible route of transmission through aerosolization. The break in the skin with fungal infection might have also been a possible route of skin contact through soil contamination from fishing. Nonetheless there has been no previous literature report of disseminated penicilliosis (either from *P. marneffei* or from other species) that have been linked to occupational hazards or other environmental exposures. The patient resided in Paya Jaras, a suburban area just north of Kuala Lumpur, and had no travel history to areas where penicilliosis was endemic. He was not taking any immunosuppressants, including steroid therapy, for his nephrotic syndrome and, unfortunately, we note that he was never tested for immunodeficiency syndromes, including acquired conditions. He denied being unwell or having any hospital admissions prior to this episode.

The case discussed above is unique and was very challenging to manage. It highlights the importance of considering fungal infections, especially in those suffering from chronic illnesses with minimal response to prolonged course of antibiotics or anti-tuberculosis therapy. Although cure is possible and fluconazole and amphotericin B have been shown effective, a delayed diagnosis, however, has been associated with fatal outcomes. Supparatpinyo and colleagues' reported survival rates of 59%.[11] To the best of our knowledge, this is first reported case of disseminated penicilliosis from a non-*P. marneffei* species (from both pleural effusion and bronchoalveolar lavage sampling), within Malaysia and South-east Asia in an individual who tested negative for HIV.

Acknowledgements

Informed consent was obtained from the patient.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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