

Case Report

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Fever, Rash and Fungemia in a Traveler from South China

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Abstract

Introduction: *Penicillium (Talaromyces) marneffei* is a dimorphic fungus that is endemic in Southeast Asia and South China, but rarely seen the United States except in immunosuppressed patients who have had travel-related exposure.

Case Presentation: A 28 year-old man with advanced HIV/AIDS presented with dyspnea, cough and fever two weeks after returning from Shenzhen, South China. He was treated for presumptive *Pneumocystis jiroveci* pneumonia with improvement in his symptoms and was then started on antiretroviral therapy. Three weeks later he developed rash and fever, and blood culture grew *Penicillium (Talaromyces) marneffei*.

Conclusion: This case highlights the importance of obtaining a detailed travel history in order to incorporate travel-related diseases in a differential diagnosis.

Keywords: HIV/AIDS; Anti-retroviral therapy; *Pneumocystis jiroveci* pneumonia

Abbreviations: ART: Antiretroviral Therapy; PJP: *Pneumocystis jiroveci* pneumonia; MALDI- TOF: Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry

Introduction

Talaromyces marneffei (formerly *Penicillium marneffei*) is a dimorphic fungus endemic in Southeast Asia and South China, and is a natural part of the flora inhabiting vegetation and soil. The route of human infection is still unresolved, but exposure to soil, especially during the rainy season, may be the critical factor [1]. Transmission is likely through an airborne route by inhalation of conidia from an environmental reservoir, a mode similar to other endemic fungi [1].

In the early years of the HIV epidemic, systemic infection with *T. marneffei* was relatively common in specific geographic regions, but similar to trends observed with other opportunistic infections, rates have decreased due to the availability and wide use of Anti-Retroviral Therapy (ART) [2]. However, *T. marneffei* remains an important cause of severe infection and death in immunocompromised patients and in HIV infected patients who are not on ART. In the United States, *T. marneffei* infection is occasionally seen in immunosuppressed patients who have had travel-related exposure.

T. marneffei was first isolated in 1956 from a bamboo rat (*Rhizomys sinensis*) found in Vietnam [3]. The bamboo rat is the only animal that is known to be naturally infected by *T. marneffei* [2]. In 1989, Sathapatayavongs and colleagues reported the first case of *P. marneffei* infection in a HIV-infected patient from Bangkok [4], and since then cases have been reported in HIV/AIDS patients who had traveled in Southeast Asia and were later diagnosed in Europe, the United States and Australia [5].

The current case illustrates the importance of obtaining a travel history when evaluating a febrile patient, and of recognizing diseases which can present after the traveler has returned home.

Case Report

A 28-year male with untreated HIV/AIDS (CD4=10 cells/mm³) presented with shortness of breath and fever for two weeks. Of note, the patient had moved to Shenzhen, South China six months earlier, and had returned to the United States two weeks prior to his presentation.

A chest x-ray demonstrated bilateral pulmonary infiltrates compatible with *Pneumocystis jiroveci* pneumonia (PJP). Sputum stained for acid-fast bacilli was negative three times, and the patient refused bronchoscopy. He was treated for presumptive PJP with trimethoprim/sulfamethoxazole, with improvement in his dyspnea.

Approximately one week after discharge the patient was prescribed an ART regimen of tenofovir, emtricitabine and rilpivirine. Three weeks later he was re-admitted with fever, rash and headache. Vital signs were a temperature 103°F, blood pressure 112/72 mmHg, heart rate 103/minute, and oxygen saturation of 100% on room air. Physical examination was unremarkable, except for several slightly hyperpigmented papules over the upper and lower extremities (Figure 1). A serum cryptococcal antigen



Figure 1: Clinical images of the patient showing skin lesion on right arm, similar lesions when also on the forehead, trunk and lower extremities.

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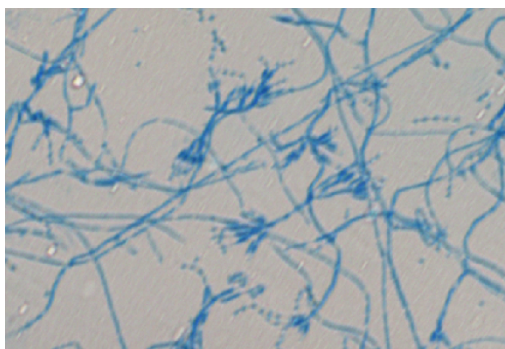


Figure 2: Microscopy of the mold form of *P. marneffei* showing septate hyphae with lateral and terminal conidiophores. Fruiting structure composed of branching metulae and phialides with spherical conidia in chains (lactophenol cotton blue $\times 400$).

assay was negative, and a chest x-ray demonstrated resolution of the prior infiltrates. Blood cultures drawn at admission were positive for growth of a fungus after four days of incubation.

Investigation

A fungal element was identified from blood culture and was negative for *Candida albicans/parapsilosis* by PNA-FISH. This fungus produced red pigment on Sabouraud agar at 25°C, which is a characteristic feature of *T. marneffei*. Microscopy showed mycelia, hyphae and terminal conidiophores as depicted on Figure 2. A qualitative serum galactomannan assay was positive, a white blood count was 9.7mm^3 and liver function tests were normal.

The culture was sent to a reference laboratory where it was identified using MALDI TOF as *T. marneffei*.

Treatment

Based on published guidelines [6], our patient received induction therapy with intravenous liposomal amphotericin B 5 mg/kg/day for 2 weeks followed by oral itraconazole 200 mg orally twice daily for 10 weeks, with a plan to continue itraconazole 200 mg daily until the CD4 count is greater than 100 cells/mm³ for 6 months.

Outcome and Follow up

The patient experienced resolution of his fever and rash, and continues to do well.

Discussion

T. marneffei is endemic in most countries in Southeast Asia [7]. In the United States it is occasionally seen in immunosuppressed patients who have had travel-related exposure. The use of ART has led to a decreased incidence of infection, but *T. marneffei* continues to cause morbidity and mortality in HIV/AIDS patients with low CD4 cell counts.

The clinical syndrome caused by *T. marneffei* varies from subclinical infection to lethal disease. Affected patients are usually immunocompromised, especially those with advanced HIV who have a CD4 cell count of $<100\text{ cells/mm}^3$ or have other acquired cellular immune deficits [8,9]. Disseminated *T. marneffei* infection usually presents with fever, weight loss and generalized skin papules with central umbilication resembling molluscum contagiosum. Other organ involvement, such as bone marrow, central nervous system, lung, liver and intestine has been reported [10,11]. Prevention of infection in patients with HIV/AIDS hinges on immune reconstitution through the use of ART. For patients

with a CD4 count of less than 100 cell/mm³, primary prophylaxis with itraconazole 200 mg daily is recommended [6].

Definitive diagnosis of *T. marneffei* infection is made by growth of the fungus from blood, bone marrow, or skin. Histopathological examination can demonstrate characteristic yeast cells with a clear, central septum. *T. marneffei* is a dimorphic fungus, and it grows as a mold at 25°C on Sabouraud dextrose agar. Aged colonies produce a soluble red pigment that diffuses into the agar. When transferred to brain-heart infusion agar and incubated at 37°C, white colonies of round to oval yeast cells with central septum develop [7]. As shown in this case, galactomannan testing, which is primarily used for the detection of aspergillosis, can show cross-reactivity with *T. marneffei* [12], but titers appear to be lower with penicilliosis [13].

In the case presented, *T. marneffei* infection only became evident after initiation of ART, raising the possibility of “unmasking Immune Reconstitution Inflammatory Syndrome (IRIS)”. The term “IRIS” is used to describe an exaggerated immune response directed against pathogens causing latent or subclinical infection following the initiation ART. This usually happens in the context of increasing CD4⁺ cell count and/or decreasing plasma HIV RNA level [14]. There are generally two forms of IRIS: “paradoxical IRIS,” which requires worsening of a recognized infection, and “unmasking IRIS,” which is when an unrecognized, pre-existing infection worsens in the setting of improving immunologic function [15]. Although IRIS was classically described in association with *Mycobacterium tuberculosis*, it has also been reported to be associated with other bacterial, viral and fungal pathogens, including *T. marneffei* [16].

In conclusion, *T. marneffei* is an endemic fungus found in Southeast Asia which can cause systemic infections among immunocompromised patients, including those with HIV/AIDS. Clinicians practicing in the United States should be aware of the endemic regions for *T. marneffei*, and the clinical manifestations of disease. This case highlights the importance of soliciting a travel history when evaluating patients, especially those with suppressed immune systems who may acquire unusual pathogens.

Ethical Statement

This case has been anonymized in order to protect patient's identity. The authors declare no conflicts of interest.

References

1. Chariyalertsak S, Sirisanthana T, Supparatpinyo K, Praparatanapan J, Nelson KE (1997) Case-control study of risk factors for *Penicillium marneffei* infection in Human Immunodeficiency Virus-infected patients in northern Thailand. Clin Infect Dis 24: 1080-1086.
2. Le T, Wolbers M, Chi NH, Quang VM, Chinh NT, et al. (2011) Epidemiology, seasonality, and predictors of outcome of AIDS-associated *Penicillium marneffei* infection in Ho Chi Minh City, Viet Nam. Clin Infect Dis 52: 945.
3. Capponi M, Segretain G, Sureau P (1956) [Penicilliosis from *Rhizomys sinensis*]. Bull Soc Pathol Exot Filiales 49: 418-421.
4. Sathapatayavongs B, Damrongkitchaiporn S, Saengditha P, Kiatboonsri S, Jayanetra P (1989) Disseminated penicilliosis associated with HIV infection. J Infect 19: 84-85.
5. Drouhet E (1993) Penicilliosis due to *Penicillium marneffei*: a new emerging systemic mycosis in AIDS patients travelling or living in Southeast Asia Review of 44 cases reported in HIV infected patients during the last 5 years compared to 44 cases of non AIDS patients reported over 20 years. J Mycol Méd 4: 195-224.
6. Kaplan JE, Benson C, Holmes KK, Brooks JT, Pau A, et al. (2009) Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm Rep 58(RR04): 1-207.

7. Supparatpinyo K, Khamwan C, Baosoung V, Nelson KE, Sirisanthana T (1994) Disseminated *Penicillium marneffei* infection in southeast Asia. *Lancet* 344: 110-113.
8. Chan YH, Wong KM, Lee KC, Kwok PC, Chak WL et al. (2004) Pneumonia and mesenteric lymphadenopathy caused by disseminated *Penicillium marneffei* infection in a cadaveric renal transplant recipient. *Transpl Infect Dis* 6: 28-32.
9. Wong SS, Wong KH, Hui WT, Lee SS, Lo JY, et al. (2001) Differences in clinical and laboratory diagnostic characteristics of penicilliosis marneffei in human immunodeficiency virus (HIV)- and non-HIV-infected patients. *J Clin Microbiol* 39: 4535-4540.
10. Ustianowski AP, Sieu TP, Day JN (2008) *Penicillium marneffei* infection in HIV. *Curr Opin Infect Dis* 21: 31-36.
11. Louthrenoo W, Thamprasert K, Sirisanthana T (1994) Osteoarticular penicilliosis marneffei. A report of eight cases and review of the literature. *Br J Rheumatol* 33: 1145-1150.
12. Huang YT, Hung CC, Liao CH, Sun HY, Chang SC et al. (2007) A Detection of circulating galactomannan in serum samples for diagnosis of *Penicillium marneffei* infection and cryptococcosis among patients infected with human immunodeficiency virus. *J Clin Microbiol* 45: 2858-2862.
13. Huang YT, Hung CC, Hsueh PR (2007) *Aspergillus* galactomannan antigenemia in penicilliosis marneffei. *AIDS* 21: 1990-1991.
14. French MA, Lenzo N, John M, Mallal SA, McKinnon EJ, et al. (2000) Immune restoration disease after the treatment of immunodeficient HIV-infected patients with highly active antiretroviral therapy. *HIV Med* 1: 107-115.
15. Haddow LJ, Easterbrook PJ, Mosam A, Khanyile NG, Parboosing R, et al. (2009) Defining immune reconstitution inflammatory syndrome: evaluation of expert opinion versus 2 case definitions in a South African cohort. *Clin Infect Dis* 49: 1424-1432.
16. Ho A, Shankland GS, Seaton RA (2010) *Penicillium marneffei* infection presenting as an immune reconstitution inflammatory syndrome in an HIV patient. *Int J STD AIDS* 21: 780-782.