CASE REPORT

Disseminated fatal *Talaromyces (Penicillium) marneffei* infection in a returning HIV-infected traveller

N P Govender,[1,2] MB BCh, MMed, MSc; **R E Magobo**,[1] MSc; **T G Zulu**,[1] Nat Dip Tech; **M du Plooy**,[3] Nat Dip Tech; **C Corcoran**,[3] MB ChB, MMed

[1] *National Institute for Communicable Diseases (Centre for Opportunistic, Tropical and Hospital Infections), National Health Laboratory Service, Johannesburg, South Africa*

[2] *School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*

[3] *Ampath National Reference Laboratory, Pretoria, South Africa*

Corresponding author: *N P Govender (neleshg@nicd.ac.za)*

We report a case of disseminated fatal *Talaromyces (Penicillium) marneffei* infection in an HIV-infected, antiretroviral treatment-experienced South African woman who had travelled to mainland China. The 37-year-old woman was admitted to a private hospital in fulminant septic shock and died within 12 h of admission. Intracellular yeast-like bodies were observed on the peripheral blood smear. A serum cryptococcal antigen test was negative. Blood cultures flagged positive after 2 days; on direct microscopy, yeast-like bodies were observed and a thermally dimorphic fungus, confirmed as *T. marneffei*, was cultured after 5 days. The clinical features of HIV-associated disseminated penicilliosis overlap with those of tuberculosis and endemic deep fungal infections. In the southern African context, where systemic opportunistic fungal infections such as cryptococcosis are more common among HIV-infected patients with a $CD4^+$ count of <100 cells/μL, this infection is not likely to be considered in the differential diagnosis unless a travel history is obtained.

S Afr J HIV Med 2014;15(4):154-155. DOI:10.7196/SAJHIVMED.1087

We report a case of disseminated fatal *Talaromyces (Penicillium) marneffei* infection in an HIV-infected antiretroviral treatment (ART)-experienced South African (SA) woman who had travelled to mainland China.

Case

A 37-year-old woman was admitted to a private hospital in March 2014 in fulminant septic shock. She was intubated in casualty and immediately transferred to the intensive care unit. On physical examination, she had marked hepatosplenomegaly, and skin lesions resembling those of molluscum contagiosum were noted on her face. The patient was prescribed broad-spectrum antimicrobial therapy on admission, including meropenem, high-dose trimethoprim-sulphamethoxazole and fluconazole. On admission, her HIV-1 viral load was undetectable and her $CD4^+$ T-lymphocyte count was 20 cells/μL. Details of her travel history, date of HIV diagnosis, ART initiation date and ART regimen were unavailable.

Intracellular yeast-like bodies were observed on the peripheral blood smear, which was reported to the treating clinician within a few hours. The patient was also anaemic (haemoglobin of 8.5 g/dL) with marked neutrophilia (17.5×10^9/L), an elevated C-reactive protein level (114 mg/L) and elevated liver enzymes (alkaline phosphatase 227 U/L; aspartate transaminase 107 U/L). The patient died within 12 h of admission. A serum cryptococcal antigen test was negative, but the serum (1,3)-β-D-glucan level was elevated (112 pg/mL), in keeping with a systemic fungal infection. Blood cultures that had been submitted to the laboratory were flagged as positive after 2 days. On direct microscopy, yeast-like bodies were observed, and a fungus was cultured after 5 days. The isolate was referred to the National Institute for Communicable Diseases for phenotypic and molecular identification. At 25°C, the isolate grew as a filamentous mould on Sabouraud agar (Diagnostic Media Products (DMP), National Health Laboratory Service (NHLS), South Africa). The colony was initially grey-green and then turned orange, with a red pigment that readily diffused into the agar (Fig. 1A), and had microscopic characteristics consistent with *T. marneffei*. Phase transition to the yeast form was demonstrated on brain-heart infusion agar after 12 days (DMP, NHLS) at 37°C (Fig. 1B). A portion of the internal transcribed spacer (ITS) region of the fungal ribosomal RNA gene was sequenced, after amplification using ITS1 and ITS4 primers, and the isolate was identified as the recently renamed thermally dimorphic fungus *T. marneffei*.[1]

The potentially fatal systemic infection caused by *T. marneffei* is the third most common AIDS-defining opportunistic infection in parts of South-East Asia, where this thermally dimorphic fungus is endemic.[2] The clinical features of HIV-associated disseminated penicilliosis overlap with those of tuberculosis and deep fungal infections such as cryptococcosis, histoplasmosis and emmonsiosis; fever, weight loss, skin papules with central necrosis, respiratory

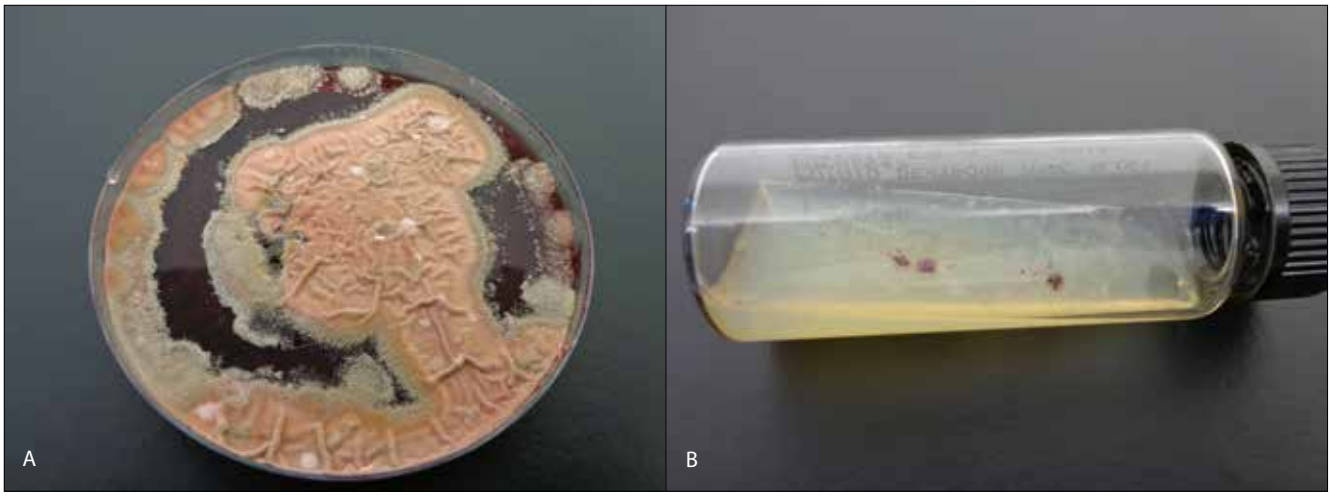

Fig. 1. Mould phase of Talaromyces (Penicillium) marneffei *on Sabouraud agar (A), and yeast phase of* Talaromyces (Penicillium) marneffei *on brain-heart infusion agar (pale-cream mucoid colonies) (B).*

involvement, lymphadenopathy and hepatosplenomegaly are most commonly reported.[3] It is possible that this patient developed an immune reconstitution inflammatory syndrome related to penicilliosis following ART initiation, though this cannot be confirmed.[4] In the southern African context, where systemic opportunistic fungal infections such as cryptococcosis are far more common among HIV-infected patients with a $CD4^+$ count <100 cells/μL, this infection is not likely to be considered in the differential diagnosis unless a travel history is obtained.[5] This is particularly important in cases where fluconazole is selected as an empiric antifungal agent instead of broader-spectrum agents such as amphotericin B or itraconazole.[6] We are aware of only one previously diagnosed case of penicilliosis in SA (personal communication with M du Plooy). Hazard Group 3 fungal pathogens such as *T. marneffei* should also be handled with great care in diagnostic laboratories.

References

1. Samson RA, Yilmaz N, Houbraken J, et al. Phylogeny and nomenclature of the genus Talaromyces and taxa accommodated in Penicillium subgenus Biverticillium. Stud Mycol 2011;70(1):159-183. [http://dx.doi.org/ 10.3114/sim.2011.70.04]
2. Vanittanakom N, Cooper CR Jr, Fisher MC, Sirisanthana T. Penicillium marneffei infection and recent advances in the epidemiology and molecular biology aspects. Clin Microbiol Rev 2006;19(1):95-110. [http://dx.doi.org/10.1128/CMR.19.1.95-110.2006]
3. Larsson M, Nguyen LH, Wertheim HF, et al. Clinical characteristics and outcome of Penicillium marneffei infection among HIV-infected patients in northern Vietnam. AIDS Res Ther 2012;9(1):24-29. [http://dx.doi.org/ 10.1186/1742-6405-9-24]
4. Hall C, Hajjawi R, Barlow G, Thaker H, Adams K, Moss P. Penicillium marneffei presenting as an immune reconstitution inflammatory syndrome (IRIS) in a patient with advanced HIV. BMJ Case Rep 2013. [http://dx.doi.org/ 10.1136/bcr-2012-007555]
5. Meiring ST, Quan VC, Cohen C, et al. A comparison of cases of paediatric-onset and adult-onset cryptococcosis detected through population-based surveillance, 2005-2007. AIDS 2012;26(18):2307-2314. [http://dx.doi.org/ 10.1097/QAD.0b013e3283570567]
6. Le T, Hong Chau TT, Kim Cuc NT, et al. AIDS-associated Cryptococcus neoformans and Penicillium marneffei coinfection: A therapeutic dilemma in resource-limited settings. Clin Infect Dis 2010;51(9):e65-e68. [http://dx.doi.org/10.1086/656685]