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Disseminated talaromycosis with presentations of painful oral ulcers and generalized papules in a 44-year-old man with advanced HIV infection

KEYWORDS
Penicillium marneffei;
Talaromyces marneffei;
Liposomal amphotericin B;
Acquired immunodeficiency syndrome (AIDS);
Galactomannan

Dear Editor,

Talaromyces marneffei infection is one of the most common opportunistic infections in people living with HIV (PLWH).[1] However, the diagnosis of talaromycosis could be challenging because of the diverse clinical features.[2] Here, we present the clinical course of an individual presenting with HIV-related talaromycosis with manifestations including pharyngitis and generalized umbilicated papules.

A 44-year-old man had been in his usual state of health until two months prior to this admission, when sore throat, productive cough and exertional dyspnea developed. Two weeks later, fever up to 39 °C occurred with generalized rashes. He was a man who has sex with men and was diagnosed with HIV infection 16 years prior to this admission. He had regular antiretroviral therapy until three years earlier before this evaluation, when drug refill was interrupted due to the pandemic of COVID-19 during his stay in Zhejiang, China. He reported no ingestion of raw food, insect bite, or unprotected sex during the last one year. Due to persistent fever, he returned to Taiwan and was admitted to our hospital for isolation according to national policy of quarantine.

Upon admission, physical examination was remarkable for painful oral ulcers, lumps with regular margin at the level III of bilateral neck and papules with central umbilication on his face, trunk, back and four extremities (Fig. 1A and B). The plasma HIV RNA was 468,862 copies/mL, and the CD4 cell count was 11 cells/μL. A test for serum galactomannan (GM) was positive with an index of 4.91 (reference, <0.5). A chest radiograph disclosed a widening mediastinum. Computed tomography of the chest, abdomen, and pelvis showed lymphadenopathy involving bilateral neck, the mediastinum and para-aortic region (Fig. 1C). There was no focal lesion at liver, spleen or kidneys.

Coformulated bictegravir, emtricitabine, and tenofovir alafenamide were initiated and liposomal amphotericin B (LAmB) (5 mg/kg/day) was started when a tentative diagnosis of talaromycosis was made. Co-trimoxazole was also prescribed for prophylaxis. On the fourth day of admission, all of the blood cultures and swab cultures of the oral ulcer and facial papules obtained on admission yielded *T. marneffei*. Endobronchial ultrasound-guided transbronchial needle aspiration of peri-hilum lymphadenopathy was performed and the results of tissue culture and pathology were consistent with talaromycosis. After a 14-day treatment with LAmB, he was discharged with oral itraconazole (200 mg twice daily) with resolution of fever and regression

Abbreviations: (HIV), Human immunodeficiency virus; (PLWH), people living with human immunodeficiency virus; (ART), antiretroviral therapy; (MSM), men who have sex with men; (GM), galactomannan; (COVID-19), Coronavirus disease 2019; (IRIS), immune reconstitution inflammatory syndrome; (OI), opportunistic infection.

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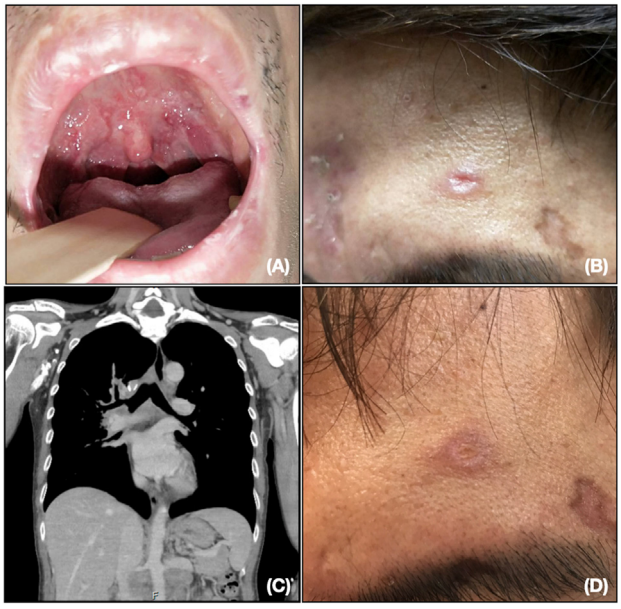

Figure 1. Physical examination findings in our patient with disseminated talaromycosis included painful oral ulcers (1A) and papules with central umbilication over his face (1B). The selected cut of CT scan showed mediastinal and paraaortic lymphadenopathies (1C). After one-week of liposomal amphotericin B treatment, the facial lesions resolved (1D).

of oral ulcer and cutaneous lesions (Fig. 1D). There was no severe infusion reaction or acute kidney injury during the treatment of LAmB.

Serum GM test was determined once per week until his discharge, which GM index remained high (5.42) after 2-week LAmB treatment despite significant clinical improvement. Itraconazole was kept for 10 weeks as consolidation treatment. Neither immune reconstitution inflammatory syndrome (IRIS) nor new episode of opportunistic infection (OI) developed during out-patient follow-up.

Talaromycosis is a common invasive fungal infection in PLWH with CD4 count $<$200 cells/μL in endemic regions, including Southeast Asia (Thailand, Vietnam, and Myanmar), East Asia (Taiwan, Hong Kong and southern China), and northeastern India.[3,4] Previous studies have demonstrated that skin biopsy or scrapings showed higher sensitivity than blood culture and lymph node biopsy for accurate diagnosis.[3] However, recognition of the physical findings of talaromycosis may be challenging when oral-pharyngeal involvement is the presenting symptom.[5] As shown in our case, previous study by Huang et al. suggested that a positive test by GM immunoassay may facilitate earlier diagnosis because of the cross-reactivity with *T. marneffei*.[6] The cross-reactivity was also observed in other fungal infection including *Fusarium* species, *Histoplasma capsulatum*, Trichosporon species, and medication including intravenous immunoglobulin.[7] Moreover, real-world experience with LAmB, a recommended treatment of disseminated talaromycosis, is rare.[8] In our case, LAmB was administered with a good clinical response and tolerance.

Our case highlights timely diagnosis of talaromycosis among PLWH relies on physicians' awareness and comprehensive approaches, including blood culture, swab culture of cutaneous lesions and serum GM immunoassay. LAmB is a well-tolerated treatment option for disseminated talaromycosis in PLWH.

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Te-Yao Hsueh
Kai-Hsiang Chen
Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan
E-mail addresses: s95017@gmail.com, ted8019@gmail.com

Wang-Da Liu*
Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan
Department of Medicine, National Taiwan University Cancer Center, Taipei, Taiwan

Chien-Ching Hung
Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan
Department of Internal Medicine, National Taiwan University Hospital Yunlin Branch, Yunlin, Taiwan
Department of Tropical Medicine and Parasitology, National Taiwan University College of Medicine, Taipei, Taiwan
E-mail address: hcc0401@ntu.edu.tw

*Corresponding author. Department of Internal Medicine, National Taiwan University Hospital, 7 Chung-Shan South Rd., Taipei City 10002, Taiwan.
E-mail address: b95401043@ntu.edu.tw (W.-D. Liu)

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