# Generalized cutaneous talaromycosis (Penicilliosis) in an immunocompetent individual

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## INTRODUCTION

Talaromyces (previously known as Penicillium) species, namely *T. marneffei*, are fungal organisms commonly causing life-threatening infections in immunocompromised patients, particularly in HIV-infected individuals. This opportunistic pathogen usually presents with progressively disseminating lesions and can include visceral involvement[1,2]; However, infection in immunocompetent individuals can sometimes occur in endemic areas, such as Southeast Asia, and usually manifests as isolated skin involvement.[3]

Here, we describe a case of disseminated cutaneous *T. marneffei* infection without visceral involvement in a previously healthy female.

## CASE PRESENTATION

A 51-year-old woman presented with widespread cutaneous lesions. She had numerous pink and violaceous ulcerative plaques on the right upper extremity, ears (Fig 1, *A* and *B*), forehead, and upper chest. Her skin lesions had begun 15 years prior, with several umbilicated papules on the dorsum of the right hand (Fig 2, *A* and *B*), for which she received various topical and oral antibacterial and antifungal agents without response; her skin lesions continued to gradually spread over the upper extremity. In addition, she reported an acute exacerbation of her skin lesions 2 years prior to her current presentation, occurring 4 weeks after receiving the second dose of the Sinopharm COVID-19 vaccine. A skin biopsy from the lesions of the upper extremity showed a hyperkeratotic epidermis with downward proliferation of the rete ridges, diffuse inflammatory infiltrate composed of histiocytes and giant cells forming a palisading pattern with a small area of necrosis in the superficial and mid-dermis along with capillary proliferation and mild lymphocytic perivascular infiltration with occasional eosinophils. Periodic acid–Schiff staining and Ziehl Neelsen staining were negative for fungal organisms and acid-fast bacilli, respectively. The findings were those of granulomatous inflammation, tuberculoid type. Because of concern for cutaneous tuberculosis, she underwent antituberculosis therapy (including isoniazid, rifampin, pyrazinamide, and ethambutol) with reported partial improvement of cutaneous lesions. Two weeks after the completion of the 6-months of antituberculosis treatment however, her lesions started to progress, and new lesions appeared on the pinnae, forehead, and chest. Hence, she was referred to our dermatologic clinic for further

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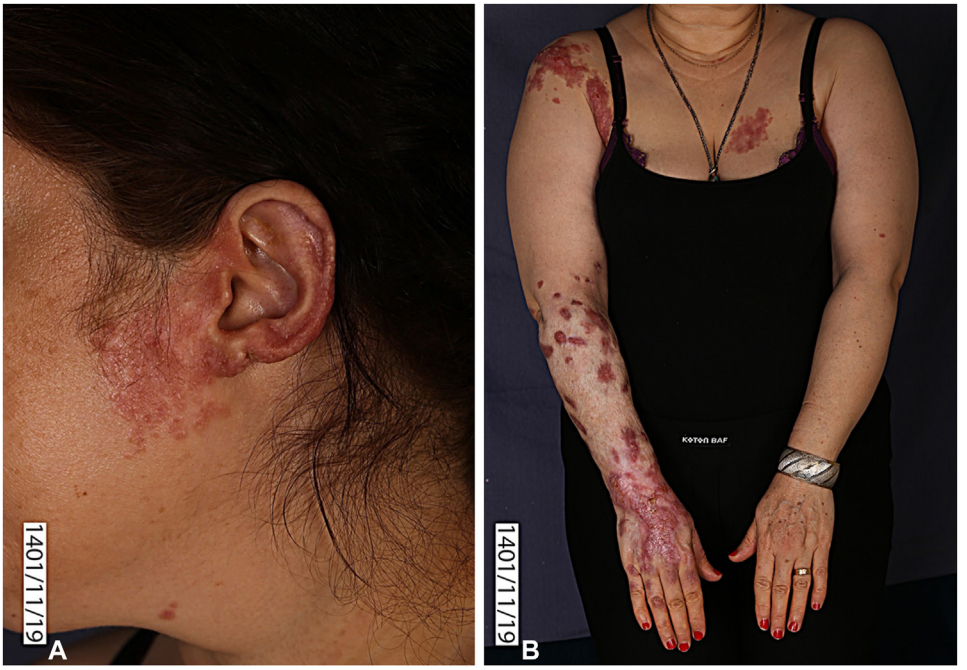


**Fig 1.** Erythematous, ulcerative plaques located in *left* ear (**A**) and *right upper* extremity (**B**) (before initiating treatment).

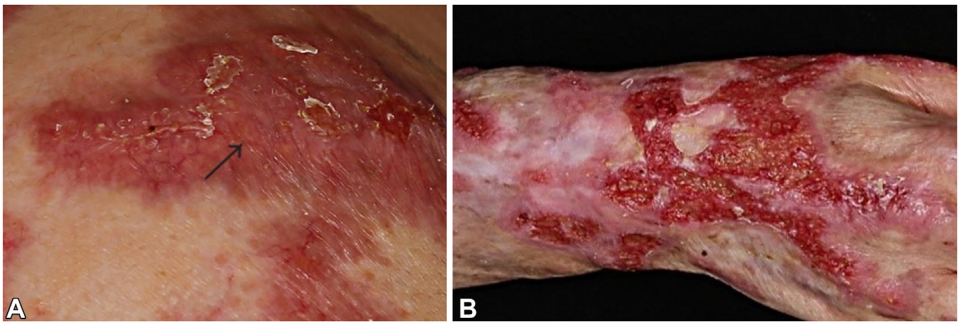


**Fig 2.** Some umbilicated lesions located on shoulder (**A**) and hand (**B**). The *black arrow* shows one of the umbilcated lesions located on patient's hand and shoulder.

evaluation. On physical exam, there were pink and violaceous plaques, some of which were ulcerated on the right extremity, including the dorsum of the hand, forearm, and shoulder, along with right axillary lymph node enlargement. Thus, we performed an ultrasound of the neck, axillae, and inguinal regions, which revealed right axillary, submental, and bilateral parotid lymphadenopathy. Owing to the granulomatous inflammation reported in the previous histopathologic report, we suspected sarcoidosis as a potential differential diagnosis; therefore, a chest x-ray was performed, which showed bilateral hilar enlargement with no parenchymal involvement. Due to this finding, confirmation with chest computed tomography scan was performed, and was normal. Her laboratory tests were only significant for an elevated plasma C-reactive protein level of 100 mg/L, while other tests including HIV serology, interferon gamma release assays, rheumatologic tests, and angiotensin I-converting enzyme level were in normal ranges. She underwent repeat skin biopsy, which showed multiple granulomas with foci of fibrinoid changes with focal pseudohyphae and hyphae on periodic acid–Schiff staining (Fig 3), compatible with deep mycosis. Polymerase chain reaction for mycobacterium tuberculosis DNA, Ziehl Neelsen staining for acid-fast bacilli, and Leishman's stain and culture were all negative. She was treated with itraconazole, which led to significant clinical improvement of the cutaneous lesions (Fig 4, *A* and *B*). One month later, mycological culture of skin biopsy specimen on

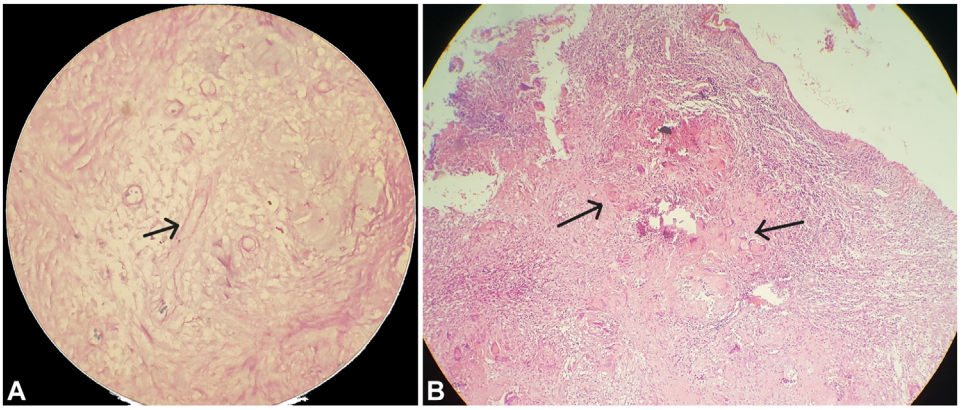


**Fig 3.** Strings of hyphae on periodic acid–Schiff (PAS) staining ×40 (**A**), multinucleated giant cells and Langerhans types forming multiple granulomas with foci of fibrinoid change, hematoxylin & eosin stain (H&E) ×10 (**B**). The *black arrow* shows one of the umbilcated lesions located on patient's hand and shoulder.


**Fig 4.** Lesions at mentioned locations about 3 months after treatment ((**A**): *left* ear, (**B**): *right upper* extremity).

Sabouraud's agar medium showed *T. marneffei* growth. The treatment continued for 7 months, and currently the lesions have improved.

## DISCUSSION

*T. marneffei* (penicillium) is an emerging dimorphic pathogenic fungus, which can cause severe and disseminated infections especially in immune deficient patients. Localized and mild forms of the disease can occur in immunocompetent individuals. This opportunistic infection is geographically endemic in southern China and Southeast Asia. The systemic infection usually is acquired through inhalation of the fungal spores; however, isolated cutaneous involvement may occur after trauma, as cases have been reported following gardening or in farmers.[4,5]

Papules with central necrotic umbilication, which resemble molluscum contagiosum lesions, comprise the classic cutaneous manifestation of talaromycosis.[6] Skin can be involved as an isolated presentation or be a feature of disseminated infection. The latter

can be manifested as cutaneous lesions most commonly on the face, upper trunk, pinnae, and arms along with involvement of the lungs, liver, spleen, liver, bone marrow, and lymph node.[7] Localized infection is defined as involvement of a single organ, which is a rare occurrence.[8] In our case, lymphadenopathy was observed along with widespread skin involvement, consistent with disseminated infection.

Clinical manifestations of talaromycosis are primarily consistent among all HIV-positive patients.[9,10] The skin lesions of HIV-positive patients mainly consist of ulcerated papules[9] and umbilicated lesions.[3] However, the presentation can vary in non-HIV patients with different morphologies.[11] According to a study by He et al, nodules and subcutaneous abscesses comprise a higher proportion of skin lesions in non-HIV patients.[9] Another study by Chan et al reported that umbilicated lesions rarely occur in non-HIV patients.[3]

Diagnosis of talaromycosis is challenging since it is often misdiagnosed as tuberculosis, cryptococcosis, or histoplasmosis in endemic areas.[12] Our patient had also been misdiagnosed as having cutaneous tuberculosis for which she received antituberculosis treatment. Although she reported a partial response after the treatment, she was referred due to progression of the lesions. According to a study by Pan et al, prolonged treatment with antituberculosis agents can lead to widespread talaromyces infection.[13] Other differential diagnoses of cutaneous talaromycosis include discoid lupus erythematosus, sarcoidosis, leishmaniasis, leprosy, mycosis fungoides, and mucinosis.[14] Almost all of these differential diagnoses were excluded with paraclinical workup.

Biopsy and fungal direct smear and cultures of skin lesions are the diagnostic method of choice for fungal infections including talaromycosis. Demonstration of oval or elongated yeast-like organisms with central septum under Grocott methenamine silver stain is characteristic for *T. marneffei*. In addition, mycelial colonies of *T. marneffei* have typical flat green surfaces with red pigment in culture growth.[15,16] Direct identification of fungal DNA in skin biopsy specimen by molecular methods such as polymerase chain reaction can be useful.

Early detection and treatment is the key element in improving the outcome of fungal infections including talaromycosis. Systemic amphotericin B is the most effective therapeutic choice for severe and disseminated talaromycosis; however, oral agents like itraconazole and fluconazole can be considered for less severe cases and isolated cutaneous involvement.[17]

The occurrence of skin fungal infection has been previously reported following SARS-CoV-2 vaccination. The underlying mechanism could be COVID vaccine-induced increased proinflammatory cytokines, which leads to elevated serum ferritin levels, and provides a suitable environment for fungal growth.[18]

In summary, we report a rare case of cutaneous talaromyces infection in an immunocompetent individual, where cutaneous findings also worsened following antituberculoid therapy and SARS-CoV-2 vaccination.

## Conflicts of interest

None declared.

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