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Permalink
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Journal
Dermatology Online Journal, 26(9)

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Publication Date
2020

DOI
10.5070/D3269050160

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Peer reviewed
Talaromycosis clinically and histopathologically mimicking histoplasmosis in an immunocompromised patient

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Keywords: talaromycosis, histoplasmosis, immunocompromised, human immunodeficiency virus, diagnosis, Talaromyces marneffei, Penicillium marneffei

Abstract

Talaromycosis is caused by the dimorphic fungus Talaromyces marneffei (formerly Penicillium marneffei) endemic in South and Southeast Asia. Its clinical similarity with other dimorphic fungal infections (sometimes) make the diagnosis challenging. We report an immunocompromised patient with talaromycosis mimicking histoplasmosis. A 26-year-old HIV-positive man had suffered from rashes over the face, trunk, and extremities for three months. His physical examination showed centrally necrotic, ulcerated papules and nodules. A biopsied papule revealed granulomas containing numerous oval, yeast-like cells, some displaying central septation. Saboraud agar culture grew mold with diffuse red pigment consistent with T. marneffei. Careful histopathological examination and microbiological culture are important for the accurate diagnosis of fungal infections.

Case Synopsis

A 26-year-old HIV-positive man, without history of antiretroviral treatment came to the dermatology-venereology outpatient clinic with multiple, small, crusted bumps and patches over the face, trunk, and extremities of three-months’ duration. The papules and nodules were asymptomatic and appeared first on the chest and neck before spreading to all body surfaces except the palms and soles in one week. Some papules and nodules enlarged, broke down, and secreted pus. The patient also experienced fever, weight loss, mouth sores, night sweats, dry cough, and loss of appetite. He looked severely weak and...
malnourished. Aside from rhonchi from the upper part of the chest, there were no significant other physical findings. The cutaneous lesions included papules with centrally-necrotic ulceration, nodules, and hypopigmented and erythematous patches (Figure 1). The patient was sent for biopsy with provisional diagnoses of histoplasmosis and cryptococcosis. Specimens were taken for histopathologic examination, and microbial and fungal cultures.

A sample from an umbilicated papule showed granulomas containing numerous oval, yeast-like cells, in the absence of gelatinous capsules, suggesting histoplasmosis (Figure 2A). However, once stained with Grocott-Gomori methenamine silver (GMS), it revealed numerous intra and extracellular, round-to-oval, thin-walled yeast-like organisms, some of which had central septation instead of budding, which is more consistent with talaromycosis (Figure 2B). Fungal culture at 25°C on Sabouraud agar grew into a mold with diffused red pigment within 7 days, consistent with a *T. marneffei* colony. Fungal culture and microscopic examination are shown in Figure 3. The patient was treated with oral itraconazole 200mg twice daily for four weeks.

**Figure 1.** Papules with central-necrotic ulceration on the back.

**Figure 2.** A) Hematoxylin and eosin staining B) Grocott-Gomori methenamine silver (GMS) revealed numerous intra and extracellular, round to oval, thin-walled yeast-like organisms. Central septation was more easily demonstrated with GMS staining.
The cutaneous eruption resolved completely. Medication was continued for 12 months.

**Case Discussion**

Talaromycosis is caused by the dimorphic fungus *T. marneffei* (formerly *P. marneffei*), which is endemic in South and Southeast Asia [1,4]. In this region, talaromycosis is considered to be an Acquired Immunodeficiency Syndrome (AIDS)-defining illness, which usually occurs with CD4 cells <100/μL [1]. Talaromycosis is also reported in HIV-negative patients with different clinical presentations than in HIV-positive ones [1,5,6].

Constitutional symptoms are common such as fever, anemia, weight loss, malaise, respiratory involvement, and skin manifestations [7]. However, these are not specific and can be found in other dimorphic fungal infections such as histoplasmosis caused by *H. capsulatum*. Mucocutaneous lesions are present in nearly 20% of HIV-infected patients with disseminated histoplasmosis [8]. In countries where two pathogens have been reported in immunocompromised patients such as Indonesia, differentiating both pathogens is challenging [6,9-11]. Oral manifestations can occur in talaromycosis; these include erosions or ulcers covered with slough that can extend into the oropharynx [12]. Oral manifestations of histoplasmosis occur less frequently in HIV-positive patients [8]. Umbilicated crusted papules are more common in talaromycosis whereas erythematous plaques are more common in histoplasmosis [3]. Cohen et al. reported that the most commonly observed lesions of disseminated histoplasmosis in HIV-infected patients were papules, nodules, macules and patches, and ulcers, both oral and skin. More than half the patients exhibited more than one morphology and involvement was usually located on the face, arms, trunk, and legs [13]. Nevertheless, skin lesions are not specific and not pathognomonic in either disease [3,9]. The different clinical features of histoplasmosis and talaromycosis are shown in Table 1.

On histopathological examination, the characteristics of *T. marneffei* are sausage-shaped yeast with a central clear septum similar to cells which undergo binary fission [3]. Meanwhile, *Histoplasma* characteristics are oval or round budding yeasts intracellularly and extracellularly. However, since both fungi are organized in clusters and overcrowded in tissues along with phagocytic cells, it is hard to distinguish these forms based on histopathological examination alone [3]. It seems...
that GMS staining visualizes the septae better than the routine hematoxylin and eosin staining [19]. Other staining that can also be used to identify the intracytoplasmic fungal structure is periodic acid-Schiff. This staining should be used on all mucocutaneous biopsies whenever disseminated histoplasmosis is being considered [20]. In this report, microbiological culture was essential to confirm the diagnosis of talaromycosis and to exclude the possibility of histoplasmosis. Source contact avoidance to prevent reinfection is suggested [18,21].

**Conclusion**

This report highlights the importance of microbiological culture together with histological special staining as diagnostic tools in immunocompromised patients. In this case, microbiological culture proved to be essential to confirm the diagnosis of talaromycosis and to exclude the possibility of histoplasmosis.

**Potential conflicts of interest**

The authors declare no conflicts of interests.
References


