

Case Report

Cutaneous phaeohyphomycosis in an immunocompromised host

一名免疫力不全者的皮膚暗色絲孢黴病

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Phaeohyphomycosis is an infection caused by dematiaceous fungi in which fungi are present as yeast-like cells or hyphal elements. We report a case of phaeohyphomycosis of the right forearm in a 72 year-old patient with low grade B cell lymphoma and background endogenous eczema. An unusual feature of this case is that tissue fungal cultures isolated two fungal species, namely *Exophiala jeanselmei* and *Cladophialophora* species. We seek to highlight phaeohyphomycosis as an emerging mycosis in immunocompromised patients. Physicians should also maintain a high clinical suspicion for unusual skin signs in immunocompromised individuals as they are more prone to developing opportunistic skin infections.

暗色絲孢黴病是暗色黴菌造成的皮膚病之一。在這種暗色絲孢黴病裡，暗色黴菌可存在為酵母細胞和菌絲。我們報告一位七十二歲患有低度惡性 B 細胞淋巴瘤和內源性濕疹病人的右前臂中，發現有暗色絲孢黴病的情況。此病例不尋常之處為皮膚抽樣培養出不僅一類，而是兩類暗色黴菌——甄氏外瓶黴及 *Cladophialophora* 種。在免疫系統功能受影響的病人，暗色絲孢黴病越來越常見。醫生在診斷這些病人時，應該考慮異常微生物的伺機皮膚感染。

Keywords: *Cladophialophora*, dematiaceous fungi, *Exophiala jeanselmei*, immunocompromised, Phaeohyphomycosis

關鍵詞：*Cladophialophora*、暗色孢屬真菌、甄氏外瓶黴、免疫功能低下、暗色絲孢黴病

Introduction

In recent years, there has been an increased incidence of phaeohyphomycosis, especially

among a group of immunosuppressed hosts. Coined by Ajello in 1979,¹ phaeohyphomycosis refers to an infection caused by dematiaceous fungi, in which isolated pigmented fungal elements are characterised by the presence of septate hyphae, yeasts or yeast-like forms. Phaeohyphomycosis can be further classified into four categories: i) superficial, ii) cutaneous and corneal, iii) subcutaneous and iv) systemic.² We highlight a case of cutaneous phaeohyphomycosis in an immunocompromised host, in which two fungal species were isolated.

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Case report

In June 2010, a 72 year-old Chinese woman presented with a pruritic plaque over her right forearm for two months. She did not experience any fever, chills, rigors or weight loss. There was no antecedent trauma. Her other medical problems included low grade lymphoplasmacytic lymphoma for which she had declined treatment. In the three months prior to presentation, she was also receiving up to 40 mg of prednisolone per day for auto-immune haemolytic anaemia. In addition, she was on follow-up in our institution for mild endogenous eczema.

Examination revealed an erythematous, vesiculated plaque on her right forearm with no regional lymphadenopathy (Figure 1A). She was initially treated as eczema herpeticum with oral acyclovir with poor response. A course of cephalexin was then initiated for empirical treatment of infected eczema but the plaque in her forearm increased in size. A biopsy of the skin lesion was then performed.

Histological analysis revealed that there was an ulcer to the level of the lower reticular dermis (Figure 1B). There were abundant fungal hyphal elements within the ulcer cavity (Figure 1C).

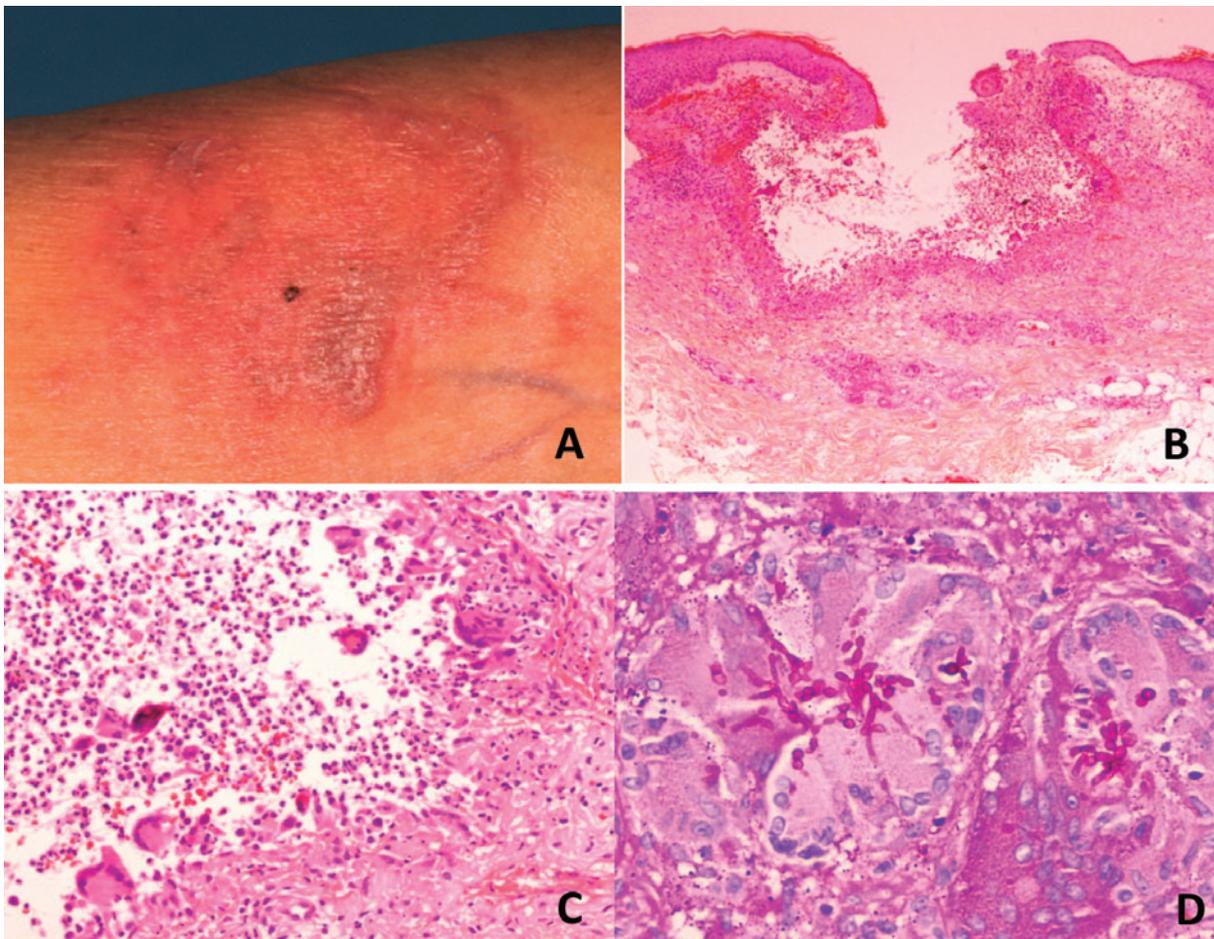


Figure 1. (A) An erythematous, vesiculated plaque on the flexor surface of the right forearm. (B) Ulcer with granulomatous inflammation (Haematoxylin-eosin stain; x40). (C) Granulomatous infiltrate with neutrophils and multinucleated giant cells at the base of ulcer (Haematoxylin-eosin stain; x200). (D) Yeast-like forms in clusters and chains as well as septated hyphae within the giant cells (Periodic Acid-Schiff stain; x400).

Surrounding the ulcer were neutrophils, epithelioid histiocytes and multinucleated giant cells (Figure 1D). No sclerotic bodies were visualised and Ziehl-Neelsen stain did not reveal any acid-fast bacilli. Fungal cultures eventually isolated *Cladophialophora* species.

She was started on terbinafine but the lesion persisted and evolved. Crusted vesicles and superficial pustules on an erythematous base were visualised (Figure 2A). A repeat skin

biopsy, obtained two months after the previous biopsy, revealed compact hyperkeratosis, pseudoepitheliomatous hyperplasia, and a dermal infiltrate consisting tuberculoid granulomas, lymphocytes and neutrophils (Figure 2B). Light brown fungal elements exhibiting yeast-like forms in chains and clusters, as well as septate hyphae were seen within multinucleated giant cells (Figures 2C & 2D). Fungal cultures grew *Exophiala jeanselmei*.

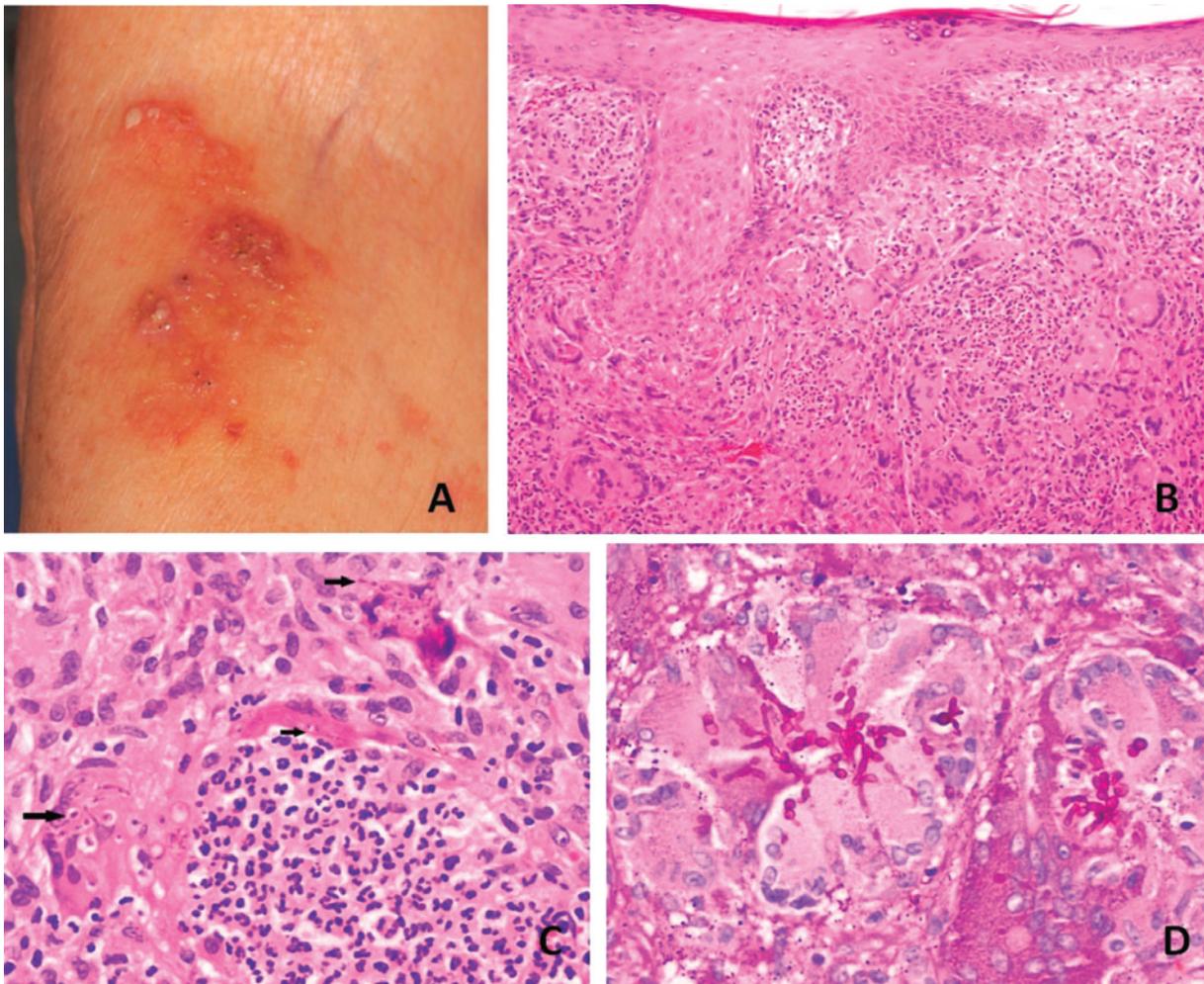


Figure 2. (A) Two months later, there was a crusted erythematous plaque with overlying vesicles and pustules. (B) Compact hyperkeratosis and pseudoepitheliomatous hyperplasia with a dermal infiltrate of lymphocytes, histiocytes and tuberculoid granulomas were visualised (Haematoxylin-eosin stain; x100). (C) Neutrophils and pigmented yeast-like forms in chains and clusters (bold arrows) within multinucleated giant cells were seen (Haematoxylin-eosin stain; x400). (D) Yeast-like forms in clusters and chains as well as septated hyphae within the giant cells (Periodic Acid-Schiff stain; x400).

Surgical opinion was obtained with regard to the possibility of excision but poor wound healing was a concern. A six-month course of itraconazole at 200 milligrammes per day was then completed with complete clinical resolution. Fourteen months after the cessation of itraconazole, the patient remains well with no evidence of recurrence.

Discussion

More than 100 species and 60 genera of dematiaceous fungi have been associated with cutaneous phaeohyphomycosis.³ Common fungal isolates in subcutaneous phaeohyphomycosis include *Exophiala jeanselmei*, *Wangiella dermatitidis* and *Bipolaris* species.⁴ More unusual fungi such as *Colletrichium* species are being isolated in immunocompromised hosts.⁵ Cutaneous phaeohyphomycosis is a growing entity among immunocompromised populations, with increasing prevalence among solid-organ transplant recipients who are iatrogenically immunosuppressed.⁶

The usual presentation is that of an indolent, cystic and solitary nodule that is localised to the extremities. A history of inoculation after trauma may be elicited, or plant fragments identified on biopsy. In contrast, clinical presentation is more pleomorphic in immunosuppression, with an increased propensity for multiple nodules with draining sinuses, pustular plaques, ulcers and even eschars in disseminated disease.⁷ Our patient, who had a haematological malignancy and was on steroid therapy, also presented atypically.

Other differential diagnoses to be considered in an immunocompromised host include deep fungal infections such as eumycetoma or chromoblastomycosis and atypical mycobacterial infections. Given the patient's background of endogenous eczema, we also considered the differential diagnoses of eczema herpeticum and secondary bacterial infection of an eczematous plaque.

Histological analysis may reveal a localised abscess surrounded by dense collagenous deposition that gives the appearance of a pseudo-cyst. The centre of the abscess is filled with necrotic debris and fungal elements, with surrounding palisading macrophages and multinucleated giant cells. Less commonly, histology may reveal epidermal hyperplasia and a granulomatous infiltrate in the dermis,⁸ as in the case of our patient. This pattern is similar to chromoblastomycosis, which is often mistaken for phaeohyphomycosis. Hence, in phaeohyphomycosis, it is important to note the lack of pathognomonic muriform sclerotic bodies of chromoblastomycosis on biopsy.²

Despite the identification of dematiaceous fungi on histology, definitive cultures should be obtained to guide treatment and aid prognostication. Some fungi may have an increased propensity for dissemination or have a tropism for certain organs. For example, *Cladosporium bantianum* has a tendency for central nervous system spread.⁵

A unique feature in this case is the isolation of two fungal species on biopsies spaced two months apart. To the best of our knowledge, this has only been reported twice in the literature. One was a case of re-infection, in which *Alternaria alternata* was first identified from a cyst which recurred 12 months later and cultures isolated *Colletotrichum gloeosporioides*.⁶ The second was the presentation of seborrhoeic-keratoses like lesions on the scrotum of an immunocompromised host, which was diagnosed as co-infection with *Bipolaris* species and *Curvularia* species.⁹ The isolation of *Exophiala jeanselmei* and *Cladophialophora* spp in our case could indicate that there was a re-infection in a susceptible host. There could also have been contamination by either fungi as both are ubiquitous in the environment. Less possibly, there could have been co-infection with the two species in the first place but only one species was identified at each time. Colonies of dematiaceous fungi can occasionally produce colonies with barely perceptible differences. On Sabouraud

dextrose agar, *Cladophialophora* species produces powdery, dark gray to black colonies and *Exophiala jeanselmei* produces olive-brown to black velvety colonies.

Surgical excision is generally recommended, but is not always possible, as in the case of our patient.⁵ Itraconazole, which demonstrates a consistent *in vitro* antifungal activity against many species of dematiaceous fungi and has a good safety profile, has been recommended as the first line antifungal agent of choice.¹⁰ Combination therapy with surgical excision and a six-month course of itraconazole has proven to be an effective regimen in renal transplant patients.⁶ Owing to the heterogenous presentation of subcutaneous phaeohyphomycosis and the variable level of immunosuppression in patients with the disease, management should always be individually tailored.

Conclusion

We seek to highlight phaeohyphomycoses as an emerging mycosis in immunocompromised hosts. The physician should always look out for any unusual skin signs in the immunocompromised, as they are more prone to developing opportunistic infections. Phaeohyphomycosis in the immunocompromised individual presents more variably and, as a result, it may be more difficult to make the diagnosis. The possibility of a co-infection or re-infection with different species of

dematiaceous fungi is also raised in this case report, and physicians should be aware of this possibility in a recurrent skin lesion or a lesion unresponsive to appropriate antifungal treatment.

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