

## An association of *Alternaria alternata* and *Scopulariopsis brevicaulis* in cutaneous phaeohyphomycosis

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### ABSTRACT

Rare molds are increasingly emerging as a cause of deep and invasive fungal infections. We report here a rare case of cutaneous phaeohyphomycosis of the lower limbs due to *Alternaria alternata* associated with extra-ungual localization of *Scopulariopsis brevicaulis*. Diagnosis was made based on repeated, direct, microscopic mycological and histological examinations. The study revealed hyphae and fungal cells in a granulomatous dermal infiltrate. Identification of the molds was based on macroscopic appearance on culture of samples from the lesions on Sabouraud's dextrose agar and microscopic appearance on Lactophenol cotton blue following slide culture.

**Key Words:** *Alternaria alternata* (a), Deep fungal infection, Phaeohyphomycosis, *Scopulariopsis brevicaulis*

### INTRODUCTION

Fungal pathogens, some previously unknown or considered saprophytes, are increasingly identified not only in solid organ recipients but also in other immunocompromised patients. The changing patterns of immunosuppressive agents, complex surgical techniques, artificial devices and the advent of acquired immunodeficiency syndrome (AIDS) have all contributed to the intrinsic risk for such fungal infections.<sup>[1,2]</sup>

*Alternaria*, a common fungus found in the environment, is one of the causative agents of phaeohyphomycosis, usually caused by dematiaceous fungi. Although the genus comprises a large number of saprophytic and plant pathogenic species, only a few of these are implicated in human diseases namely, *A. alternata*, *A. infectoria*, *A. tenuissima*, and *A. chartarum*. Their importance as opportunistic pathogens is increasing among immunocompromised patients, especially in transplant recipients.<sup>[3]</sup> Clinically, they are more often encountered as traumatic mycoses. *Scopulariopsis* spp. are common soil saprophytes and have been isolated from a wide variety of

substrates. They are dermatomycotic molds and have been mainly associated with onychomycosis. We present a rare case of cutaneous phaeohyphomycosis caused by *Alternaria alternata* and *Scopulariopsis brevicaulis* in an apparently immunocompetent individual. This case is being reported to heighten the awareness among clinicians of the atypical presentations of fungi of low virulence.

### CASE HISTORY

A 37 year-old female presented to us with complaints of multiple, raised skin lesions over both extremities for the past 20 days associated with fever and difficulty in walking. No definitive history of trauma could be elicited from the patient. She was not a known diabetic, hypertensive or asthmatic and gave no history of long-term therapy with any immunosuppressive drugs such as steroids.

Local examination revealed multiple, erythematous, indurated nodules over both lower limbs with necrosis and areas of hyperemia. A discharging sinus was present over the left leg [Figures 1A, B]. The nails of the right

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Figure 1: (A) A discharging sinus over the left leg of the patient, (B) Leg of the patient showing purpuric nodules

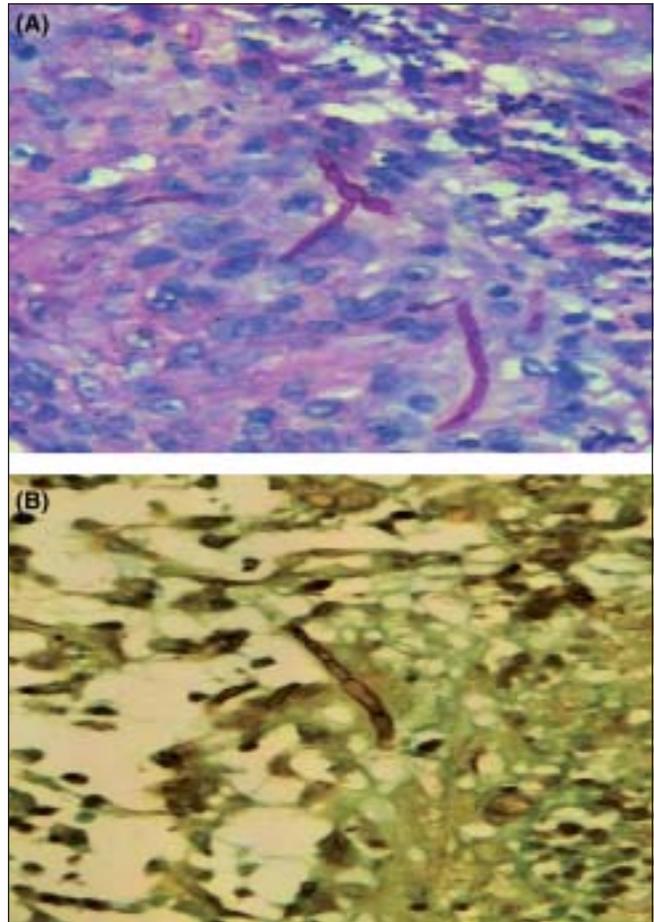


Figure 2: (A) Periodic acid Schiff [PAS] stain showing fungal hyphae in tissue section [x200], (B) Gomori's methenamine silver stain showing fungal hyphae in tissue section [x200]

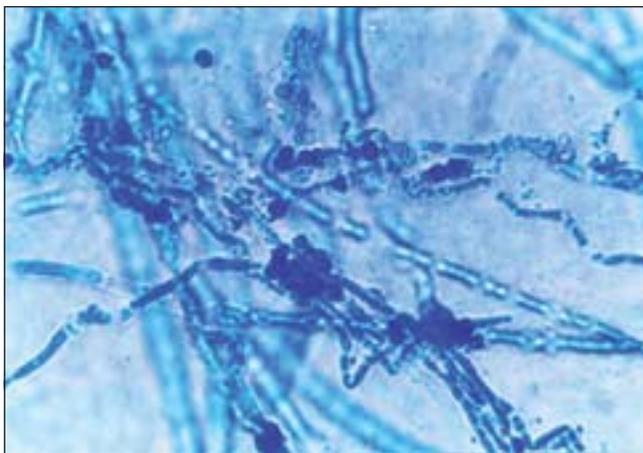


Figure 3: *Alternaria alternata* hyphae showing elliptical conidia in lactophenol cotton blue mount [x200]

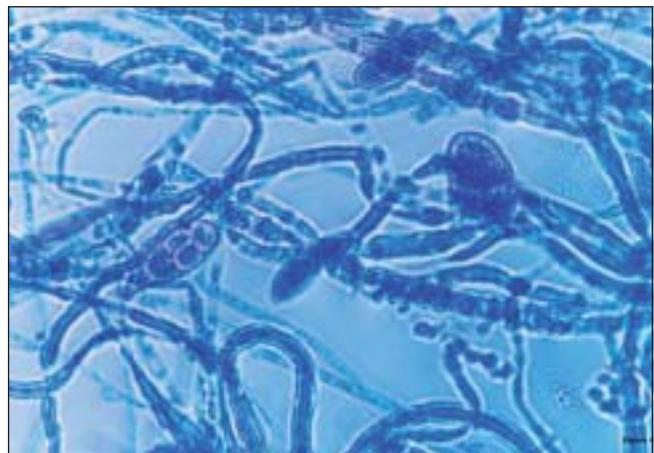


Figure 4: *Scopulariopsis brevicaulis* showing ameroconidia in lactophenol cotton blue mount [x200]

hand and the toenails were dystrophic while the nails of the left hand were normal. Systemic examination did not reveal any abnormality. Liver and renal function tests and blood sugar levels were normal. Investigations revealed a raised total leukocyte count of 16,900 cells/mm<sup>3</sup> with 77%

neutrophils and a hemoglobin level of 10.7g%. Screening tests for human immunodeficiency virus (HIV) infection and hepatitis B infection were negative. A chest X-ray (CXR) and an ultrasonogram (USG) of the abdomen were taken to rule out malignancy. However, neither the USG nor the

CXR showed any abnormality. No further tests could be done to rule out immunosuppression.

Specimens were collected from the affected area, including the discharge from the sinus and sent for microbiological examination. A deep skin biopsy was taken and sent for histopathological examination. Periodic acid Schiff (PAS) and Gomori's methenamine silver stain confirmed the fungus showing broad, septate, branching hyphal forms and large spores - both free and within the cytoplasm of giant cells [Figures 2A, B]. Histopathologic examination indicated the presence of fungi; however, it was not possible to use tissue stains to differentiate the fungi based on their appearance.

Wet mounts of samples sent for mycological examination revealed numerous, brownish, septate hyphae and ovoid structures. Culture on Sabouraud's Dextrose agar [SDA] with chloramphenicol showed gray-white colonies of *Alternaria* spp. with a dark brown pigment on the undersurface. Slide culture and microscopic observation using lactophenol cotton blue [LPCB] stain for identification of the fungus, revealed hyphae with typical conidia which were ellipsoidal with a short cylindrical beak, rugose with muriform septation showing transverse and longitudinal septa and a single scar at the tip. The conidia were arranged in long chains [Figure 3].

Repeatedly collected and cultured samples from the affected site grew both fungi. Identification of the second fungus, *Scopulariopsis brevicaulis*, was done by macroscopic appearance as whitish, felt-like colonies on culture, which later became pinkish-brown with the reverse color of creamish to brown. Both the slide culture technique and lactophenol cotton blue mount showed chains of single-celled annelloconidia (ameroconidia) produced in basipetal succession following a series of short, percurrent proliferations (annellations) by a specialized conidiogenous cell called an annellide. The conidia were rough-walled with a truncated base [Figure 4]. A diagnosis of *Alternaria alternata* associated with *Scopulariopsis brevicaulis* infection was made based on histopathological and mycological examination.

The patient was initially treated with systemic steroids followed by antifungal agents - itraconazole and terbinafine. The patient appeared to improve after beginning antifungal therapy. However, she developed electrolyte imbalance and her vitals began to fluctuate. She was transferred to the intensive care unit. As her oxygen saturation also decreased, she was placed on a ventilator. Her condition however deteriorated over a period of time and she was discharged

against medical advice, on the request of her relatives. She subsequently died at home.

## DISCUSSION

Phaeohyphomycosis caused by *Alternaria alternata* may be difficult to recognize because lesions are variable in size and aspect, ranging from crusted lesions to erythematous macules or subcutaneous nodules. Cutaneous and subcutaneous deep tissue infections due to *Alternaria* species tend to occur most often in immunosuppressed patients, especially in organ transplant recipients.<sup>[2-6]</sup> Most of the clinical presentations were localized skin infections resulting from direct, traumatic inoculation, even if systemic spread is possible in a compromised host.<sup>[1,2]</sup> The clinical presentation of multiple, erythematous, indurated purpuric nodules over both lower limbs in our case was atypical.

Onychomycosis is most often caused by dermatophytes. Other agents such as yeasts and nondermatophytic molds (NDMs) may cause onychomycosis as well. Historically, NDMs have largely been discounted as mere contaminants, especially when a dermatophyte was present concurrently. The dual etiology of the lesion may account for its atypical manifestation. As scopulariopsis may be associated with deep fungal infection, the invasive property of the fungus may account for the rapid deterioration of this patient.<sup>[7]</sup>

*Scopulariopsis brevicaulis* has rarely been reported as a cause of deep fungal infections. We believe that the implantation of this fungus in the extra-ungual site probably occurred due to scratching. Tosti *et al.* reported patients with a typical, distal, subungual onychomycosis characterized by subungual hyperkeratosis and onycholysis of the distal nail plate.<sup>[8]</sup> In addition, some isolates of *S. brevicaulis* have been demonstrated to be pathogenic in murine models of disseminated infection.<sup>[9]</sup> It should be noted that cutaneous mycoses caused by such fungi, are characterized by brownish hyphal elements in tissue, whereas subcutaneous mycoses often consist of large, hyaline, yeast-like cells. The production of melanin-like pigment is one of the major characteristics of this mould.

This case is being reported to heighten the awareness among clinicians of the atypical presentations of fungi of low virulence. The association of these two fungi is rare, especially in a case of cutaneous phaeohyphomycosis. The emergence of less common but medically important fungal pathogens contributes to diagnostic dilemmas, especially when accompanied by atypical manifestations. Early recognition of the lesion and treatment with appropriate

antifungal therapy is essential to reduce morbidity and mortality.

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