

Cutaneous Granulomatous Infection Caused by *Scopulariopsis brevicaulis*

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Sir,

Scopulariopsis is a genus of non-dermatophytic filamentous fungi. These common saprophytic fungi are found in soil, on vegetables and other organic waste, and have a wide geographic distribution. *Scopulariopsis brevicaulis* is not generally considered to be a skin pathogen, although it is the cause of nearly 2% of reported cases of onychomycoses. Several case reports have described *S. brevicaulis* infections of deep tissue or skin in immunocompromised hosts and there have been sporadic cases of ocular infection. We describe here an otherwise healthy person presenting a slowly progressive granulomatous skin infection caused by *S. brevicaulis*.

CASE REPORT

A 19-year-old man presented with an intensely itchy irregular granulomatous induration on the right submental area of his face (Fig. 1A), which had been present for 2 months. Initially he developed eczema-like lesions at the infra-orbital area, which he scratched often, and subsequent lesions had developed on the right side of his chin (Fig. 1B). He had been treated previously by doctors at local clinics with topical corticosteroids and oral antihistamine without benefit. He was otherwise in good health. He had not had a previous significant illness and was not receiving any drug therapy when the skin lesions appeared. The patient's medical history included atopic diathesis and asthma with allergic rhinitis. A thorough dermatological examination revealed no dermatological signs of atopic dermatitis.

The patient was suspected clinically of having acne excoriée complicated with impetigo. A specimen taken from the right submental area showed focal ulceration of epidermis with splitting at the dermal-epidermal junction and mixed inflammatory infiltrates

in the necrotizing dermis (Figs 2A, B). Small intra-epidermal neutrophilic pustules were also seen. Several fungal hyphae in necrotic dermis and stratum corneum were stained with Periodic acid-Schiff (PAS) (Fig. 2C) and Grocott's Methenamine Silver (GMS) (Fig. 2D). No micro-organisms were found in the bacterial cultures of the skin specimens. Fungal cultures grew *S. brevicaulis*. The colonies were powdery white, slightly buff in colour. Under the microscope, the fungi appear as hyalined and septated hyphae with conidiophores terminating in groups of 2–4 annellophores in a broom-like structure. The annelloconidia were globose to ovoid and had a distinctly truncated base (Fig. 2E). The fungal samples were sent to Taiwan's National Medical Mycology Laboratory for direct DNA sequencing and were confirmed to be *S. brevicaulis* by Basic Local Alignment and Search Tool (BLAST).

In our laboratory studies, complete blood count was normal except for high eosinophil count ($16.2\% \times 9860$). Eosinophil cationic protein (ECP) was $32.2 \mu\text{g/l}$ ($< 18 \mu\text{g/l}$) and immunoglobulin E (IgE) was 3302 IU/ml ($66.4\text{--}109.0 \text{ IU/ml}$). Total T-cell and B-cell counts were within normal limits, whereas active T-cell counts were low (5.89 %; normal range 9.69–22.03%). HIV test was negative. HLA-DR positive lymphocytes were low (26.70%; normal range 28.36–46.10%).

Initially, the patient was prescribed doxycycline (200 mg) for acne. Three weeks later, after the *S. brevicaulis* infection was confirmed, he was prescribed a daily dose of itraconazole 200 mg and doxycycline 200 mg. After 3 months on the regimen, because there were improvements in his condition but also signs hepatotoxicity (liver enzymes elevation), itraconazole was stopped and replaced with indomethacin. Improvement in the lesions was maintained with doxycycline 200 mg + indomethacin 75 mg for the following 8 months, as granulomatous indurations at the submental area had notably regressed, leaving only hypertrophic scars (Fig. 1C). In the ninth month of follow-up, there was no recurrence of the lesions. Upon examination, we found fewer erythematous indurations. These scars were found to be keloidal scars instead of those caused by cutaneous granulomas.

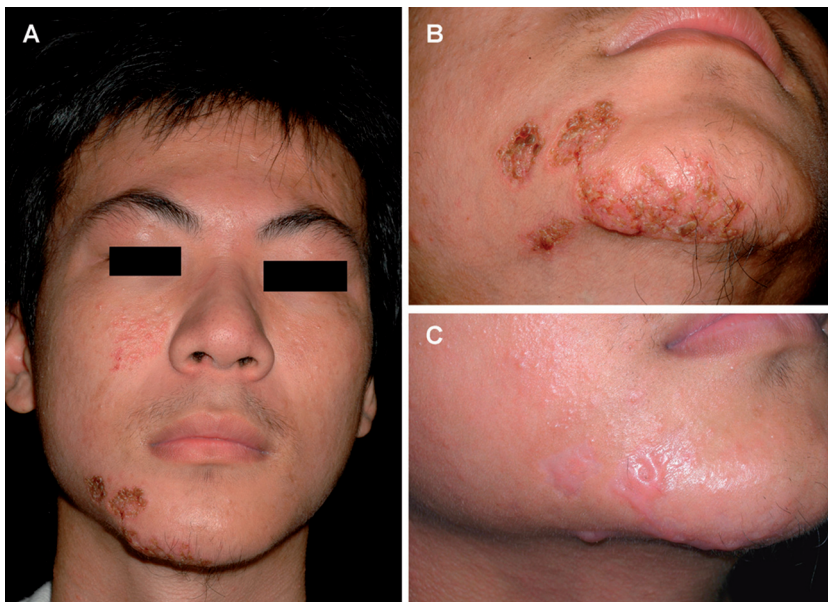


Fig. 1. (A, B) Cutaneous *Scopulariopsis brevicaulis* infection presenting as granulomatous nodules on the right submental area. The initial lesions were flesh-coloured papules with a greasy appearance on the right cheek. (C) The nodules regressed 8 months later, leaving only hypertrophic scars.

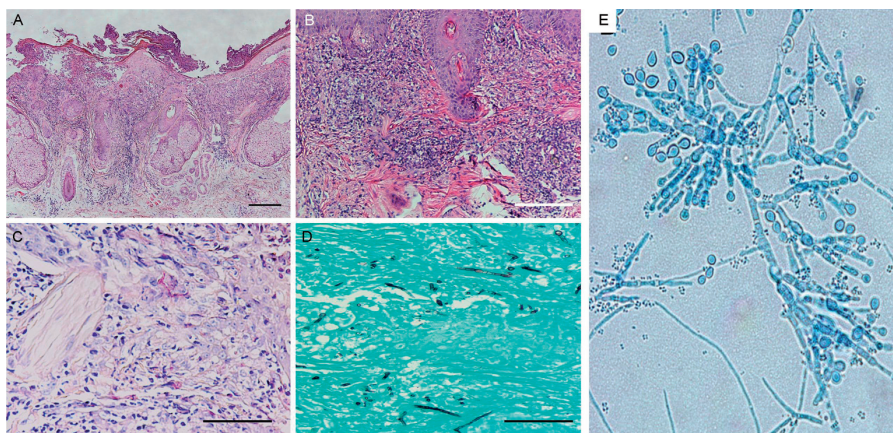


Fig. 2. (A, B) Biopsy specimen showed heavy granulomatous inflammation with hyphae. (H&E stain). Hyphae and spores were further enhanced by (C) Periodic acid-Schiff (PAS) stain and (D) Grocott's Methenamine Silver (GMS) stain. (Bar = 200 µm in each figure). (E) Hyalined and septated hyphae with conidiophores terminating in groups were characteristic features of *S. brevicaulis* in this study.

DISCUSSION

The spectrum of severe human mycoses includes the formation of fungus balls in preformed pulmonary cavities (1), keratitis (2), post-traumatic endophthalmitis (3), disseminated skin lesions in patients with AIDS (4), granulomatous subcutaneous infections (5), invasive hyalohyphomycosis (6), pneumonia in leukaemic patients (7), endocarditis related to valvuloplasty or prosthetic valves (8), and even fatal disseminated infection following bone marrow transplantation (9).

Only a meticulous investigation, including the growth of colonies in culture, microscopic identification of morphology and polymerase chain reaction (PCR) sequencing, will make the accurate diagnosis of *S. brevicaulis* possible. Initially, the surface of the colony is usually white and glabrous, but it may become powdery light brown with a light tan periphery. *Scopulariopsis* spp. resemble *Penicillium* spp., but have shorter and sometimes simpler conidiophores; the conidium-bearing cells are annellides rather than phialides and may be more cylindrical. The conidia are larger, rough, and uniquely shaped and can be identified by as they are cut off at one end (10).

Several authors have reported that *S. brevicaulis* is resistant to amphotericin B, flucytosine, and azole compounds (11, 12). Similarly, a recent 5-year retrospective multicentre study of nail infections has reported *Scopulariopsis* to be treatment-resistant, with only 18% of cases documented to benefit from treatment (12). Debridement or excision of necrotic tissue and antifungal chemotherapy is often the treatment of choice (7). The prognosis depends mainly on the patient's immune status and the feasibility of surgical debridement (9).

The patient's atopic diathesis complicated his infection. The reason for this may be that atopy, in which overactive Th2 cells induce immediate hypersensitivity responses to antigen, inhibits or overpowers the ability of the Th1 cells to maintain a delayed type hypersensitivity response. The predominance of Th1 over Th2 type cytokines correlates with protection against various mycoses (13). Thus, the reduction in Th1 cells makes the patient more susceptible to fungal infection.

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