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Case Letter (493/500 words)

Dear Editor,

Cutaneous alternariosis is a phaeohyphomycosis caused by *Alternaria* species and occurs predominantly in immunocompromised patients, as *Alternaria* species are only weakly pathogenic.[1-3] Various antimycotics, such as amphotericin B or itraconazole, are known systemic antifungal therapies. However, treatment of alternariosis remains challenging.[1-4] Organ transplantation accompanied with immunosuppressive treatments is an important risk factor for alternariosis as it may increase its incidence rate.[4] Post-transplantation patients often have difficulty withstanding systemic antifungal therapy; amphotericin B potentially causes renal toxicity, and itraconazole can interact pharmacologically with immunosuppressive treatments.[1] To our knowledge, there are two cases in English literature.[1,4] Torres-Rodríguez et al. reported a case of subcutaneous alternariosis treated with persistent thermotherapy without antifungal treatment.[1] Suda et al. reported a case of cutaneous alternariosis initially treated with itraconazole (200 mg/day p.o.), which was later switched for voriconazole (400 mg/day

p.o.). Skin lesions regressed following combination therapy with thermotherapy; however, the patient suffered from rotary vertigo and liver damage due to antifungal therapy use.[4] Here, we present the first case of cutaneous alternariosis was safely and successfully treated using thermotherapy combined with terbinafine hydrochloride 1% cream safety in a patient who underwent kidney transplantation.

Following kidney transplantation for diabetic nephropathy, a 54-year-old woman received tacrolimus (0.10 mg/kg/day), mycophenolate mofetil (1 g/day), and methylprednisolone (60 mg/day). One year after transplantation, she observed a red papule on her right forearm without previous trauma and subjective symptoms, which grew to form a protruding, irregular, 5 × 7 cm large, reddish plaque over a period of 1 year (Fig. 1a). Serum β-d-glucan levels were within the normal range. Histopathologic analysis with hematoxylin-eosin (H&E) staining displayed the presence of numerous spherical bodies and infiltration of inflammatory cells, mainly lymphocytes and histiocytes, in the dermis (Fig. 1b and c). Grocott staining revealed several spores and hyphae in the dermis (Fig. 1d and e). Fungal cultures of the biopsy specimen produced colonies with the morphology of *Alternaria* species, i.e., brown-olivaceous colonies and

conidia with transverse and longitudinal or oblique septa (Fig. 1f and g). Considering the side effects of systemic antifungal therapy in immunosuppressed individuals and the progressive enlargement and depth of alternariosis, we applied thermotherapy combined with terbinafine hydrochloride 1% cream. Disposable adhesive heat pads at 50–55°C were applied for 12 h/day every day, and terbinafine cream was administered once a day. After 6 months of this combination therapy, the plaque had completely resolved (Fig. 1h). Histopathologic analysis with H&E and Grocott staining revealed no fungal structures and cultures of biopsy samples exhibited no fungal growth. No relapse was detected over an 8-month follow-up.

Granted the mechanism of this combination therapy remains unclear, it could nevertheless accelerate the treatment period compared to thermotherapy alone; the combination therapy took 6 months and the thermotherapy alone took 1 year.[1] Note that metastatic/disseminated infection should be excluded especially in heavily immunocompromised patients prior to use of local therapy.[5] This combination therapy could be a safe and effective treatment option for cutaneous alternariosis, especially in post-transplantation patients.

1

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Figure legends

Figure 1. Clinical and histopathological features of the patient

(a) An irregular 5 × 7 cm large brown-reddish plaque on the right forearm growing over a period of 1 year.

(b and c) Histopathological analysis showing spherical bodies with infiltration, primarily of lymphocytes and histiocytes, in the dermis (H&E, hematoxylin eosin staining, original magnification × 40; scale bar = 200 □m [b], original magnification × 400; scale bar = 20 □m [c]).

(d and e) Grocott staining revealing numerous spores and hyphae in the dermis (original magnification × 40; scale bar = 200 □m [d], original magnification × 400; scale bar = 20 □m [e]).

(f and g) Microscopic analysis of the plaque morphology showing a circular, gray-olivaceous and powdery colony of pigmented branched septate hyphae and conidia with transverse septa and longitudinal septa that grew at 35°C, 5 days after inoculation on a potato dextrose agar plate (original magnification × 400; scale bar = 20 □m).

(h) The plaque on the right forearm disappeared after 6 months of combination therapy.

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Figure1, Harada et al.