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Two cases of cutaneous sporotrichosis in continental/microthermal climate zone: global warming alert?

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Sporotrichosis is commonly encountered in tropical and subtropical areas, but rarely in continental/microthermal climate zones as defined by the Köppen–Geiger Climate Classification.[1] We report two cases of cutaneous sporotrichosis in Hokkaido, an island in the continental/microthermal climate zone in Japan.

Patient 1 was a 55-year-old Japanese woman, who presented in 2009 with a 6-month history of two dark-red, crusted, infiltrated skin lesions measuring about 10 mm and 2 mm, respectively, on the left upper eyelid (Fig. 1a). She was working as a farmer in Hokkaido and had never lived in any other part of Japan. Histopathological examination of haematoxylin and eosin-stained specimens showed a prominent epidermal hyperplasia and abundant inflammatory infiltration in the dermis. Periodic-acid–Schiff (PAS) and Grocott's methenamine silver (GMS) stains revealed a few round and budding yeast-like cells scattered in the dermis, occasionally within a giant cell. Cultures of the tissue sections of lesion on Sabouraud dextrose agar and potato dextrose agar grew dark-brown velvety colonies. Slide cultures from the colonies contained septate branching hyphae, with slender, tapering conidiophores arising at right angles. A sporotrichin skin test gave a positive reaction.

Patient 2 was a 55-year-old man, who presented in 2002 with a chronic erosive nodule measuring 20 × 10 mm on the left mandible, which had been present for over 1 year on 2002 (Fig. 1b). He was working as a carpenter in Hokkaido, and had never lived in any other part of the country. Histopathological analysis found prominent epidermal hyperplasia and a chronic granulomatous inflammatory cell infiltrate. PAS and GMS stained round yeast-like cells scattered throughout the dermis. Cultures of the biopsied tissue samples grown on Sabouraud dextrose agar produced dark-brown velvety colonies. Slide cultures from the colonies contained septate, branching hyphae. Sporotrichin skin test gave a positive reaction.

Cutaneous sporotrichosis is a fungal infection commonly encountered in tropical and subtropical areas.[1] In Japan, > 3500 cases of cutaneous sporotrichosis were reported as of 2001 on Honshu Island, which falls in the temperate/mesothermal climate zone.[2] By contrast, no case reports were reported from Hokkaido in English journals before 2004. Similarly, few cases have been reported in other continental/microthermal climate zone around the world,[3] suggesting that cutaneous sporotrichosis is extremely rare in that zone. This geographical difference in reported cases may be due to the fact that *Sporothrix schenckii,* the pathogenic fungus that causes sporotrichosis, prefers moderate temperatures (around 22 °C).[1] The yearly temperature in Hokkaido

Figure 1 (a) Patient 1. Nodule and papule on the left upper eyelid. (b) Patient 2. Nodule on the left mandible.

averaged for the years 2000–2008 was 9.1 °C, so these results further suggest that *S. schenckii* rarely occurs in Hokkaido. Interestingly, three cases of cutaneous sporotrichosis, including our two, have been reported from Hokkaido in the Japanese literature since 2000, whereas only one case was recorded before 2000. We suggest that the prevalence of cutaneous sporotrichosis in Hokkaido may be increasing as a result of recent global warming.

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The Fas/Fas ligand system, rather than granzyme B, may represent the main mediator of epidermal apoptosis in dermatomyositis

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We read with interest the paper by Grassi *et al.*[1] reporting an immunohistochemical study on cutaneous lesions of lupus erythematosus (CLE) and dermatomyositis (DM). A particularly interesting finding was that the expression of granzyme B (GrB), a pro-apoptotic serine-protease, was higher in CLE rthan in DM lesions. As GrB is mainly expressed by CD8+ lymphocytes, we were puzzled to read that 'in DM, the CD8+ subpopulation represented > 50% of the lymphocytic population'.[1] This finding is in striking contrast to a study in which our research group found that the CD4/CD8 ratio is approximately 2.5 in DM skin lesions.[2] On the other hand, the number of infiltrating CD8+ cells was reported to be similar to that of the CD4+ cells in CLE in both papers.[1,2] As previous studies also reported a similar level of apoptotic phenomena in lesional epidermis in both CLE and DM,[3,4] it is evident that GrB is not likely to represent a major mechanism of cell death in DM lesions.

We report the results from an ongoing study on skin lesions of six patients with DM, five patients with subacute CLE (SCLE) and five patients with discoid CLE (DLE). The sun-protected, clinically healthy skin of the patients served as internal controls, and five healthy donors comprised the control group. Immunohistochemical examination, performed as described previously,[2] included antibodies to Bax, a pro-apoptotic molecule involved in the mitochondrial pathway of apoptosis and activated by GrB; Bcl-2, its antiapoptotic counterpart also belonging to the mitochondrial pathway; Fas and Fas ligand (Fas-L), two key molecules triggering the death receptor pathway of apoptosis; and caspase 3, the final effector of both pathways. The following monoclonal antibodies were used. Bax: 1 : 500 dilution, clone YTH-2D2 (R&D Systems, MN, USA); Bcl-2: 1 : 1000 dilution, clone 124 (Dako, Copenhagen, Denmark); Fas: 1 : 60 dilution, clone GM30 (Novocastra Laboratories Ltd., Newcastle upon Tyne, UK); FasL): 1 : 50 dilution, clone 5D1 (Novocastra); caspase 3: 1 : 50 dilution, clone 5A1 (Cell Signaling, Danvers, MA, USA).

There was higher expression of Bax than of Bcl-2 in patient epidermis (Table 1). Fas was strongly expressed in epidermal sections from patients with DM (Fig. 1a) and CLE, and there was focal positivity in the healthy skin of these patients. Caspase 3 was expressed strongly in all lesional specimens and moderately in the healthy skin of patients.

Table 1 Semiquantitative evaluation of apoptotic molecules in lesional sections and controls.

	DM	DM-HS	SCLE	SCLE-HS	DLE	DLE-HS	HC
Bax	++	++	+++	++	+++	+	+
Bcl-2	+	+	+	+	++	+	+
Fas	+++	+	+++	+	+++	+	−
FasL	++	+	+++	+	++	+	−
Caspase 3	+++	++	+++	++	+++	++	+

DM, lesional epidermis of dermatomyositis; DM-HS, epidermis of sunprotected healthy skin from patients with DM; SCLE, lesional epidermis of subacute cutaneous lupus erythematosus; SCLE-HS, epidermis of sunprotected healthy skin from patients with SCLE; DLE, lesional epidermis of discoid cutaneous lupus erythematosus; DLE-HS, epidermis of sunprotected healthy skin from patients with DLE; HC, epidermis of sunprotected healthy skin from healthy controls. Semiquantitative evaluation of epidermal positivity for Bax, Bcl-2, Fas and caspase 3: −, negative; +, focal; ++, continuous basal; +++, basal and suprabasal. Semiquantitative evaluation of dermal positivity for FasL: −, negative; +, 0–5 cells; ++, 6–10 cells and +++, > 10 cells).

