

# Increasing Numbers of Mast Cells in Skin Lesions of Hyperpigmented Mycosis Fungoides with Large-Cell Transformation

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Dear Editor:

Mycosis fungoides (MF) is a common type of cutaneous T-cell lymphoma. In recent years, several reports have been published on an uncommon and rare form of MF: hyperpigmented MF<sup>1-4</sup>. Herein, we report a case of hyperpigmented MF and discuss the mechanisms of "hyperpigmentation."

A 55-year-old Japanese man presented at the dermatological outpatient clinic of our hospital for widespread, pruritic, hyperpigmented plaques. The lesions, which first appeared nearly 15 years ago, gradually developed; they were diagnosed as MF, and were subsequently treated with topical corticosteroids and/or radiation with narrow-band ultraviolet B (UVB). However, no therapeutic response was observed and small nodular lesions developed. On physical examination of the patient, we observed hyperpigmented plaques with no atrophy on the face, trunk, and extremities (Fig. 1A). We found small nodules on the back. Blood cell count, urinalysis, and serum chemistry were within normal limits. Anti-human T-cell leukemia virus type I antibody was negative. Computed tomography scan from the neck to the pelvic area was normal. Histopathological analysis of skin specimens collected from a hyperpigmented plaque on the buttocks revealed slight acanthosis with atypical lymphocytic infiltration within the epidermis and upper dermis, containing some inflammatory cells and abundant melanophages (Fig. 1B). Rearrangement of the T-cell receptor ( $\beta$  chain) was detected using reverse transcriptase polymerase chain re-

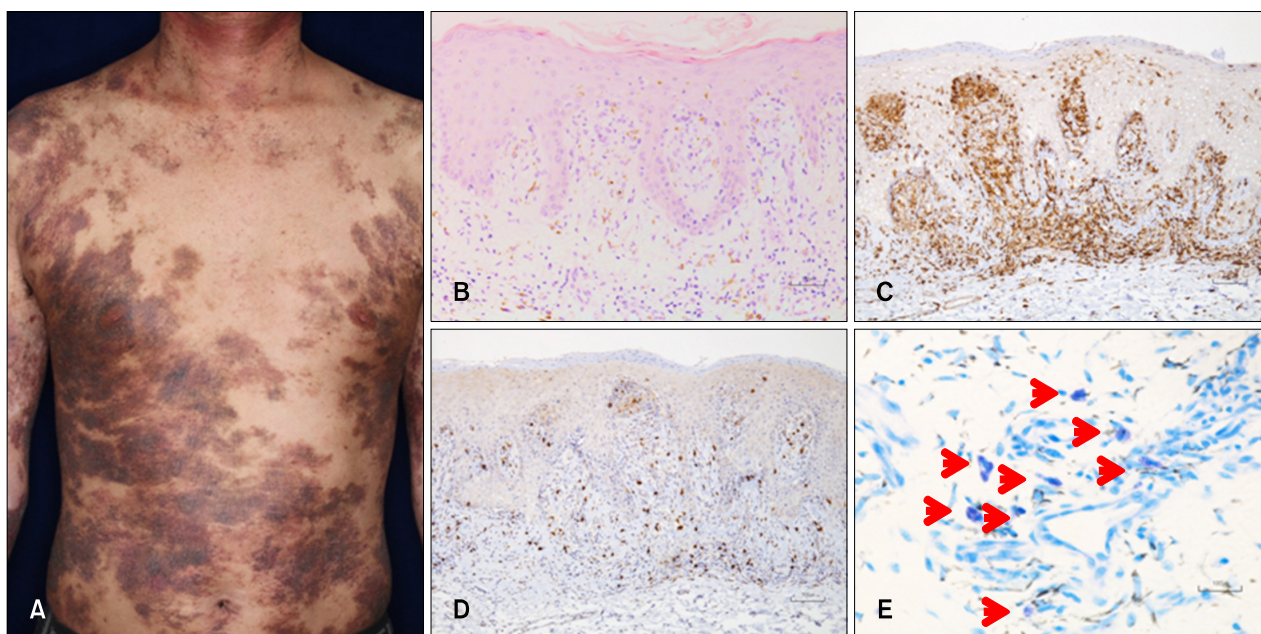
action method, but not Southern blot analysis. Immunohistochemically, most of the atypical lymphoid cells were CD4-positive (Fig. 1C and D). We diagnosed the lesions as MF, particularly, hyperpigmented MF. After X-ray irradiation to the nodules on the back, oral retinoid plus long-wave UVA therapy was started. Although CD30 (+) large-cell transformation was found during the therapeutic course, the patient's general health and skin improved over time.

So far, the etiology of hyperpigmentation in certain MF cases is not clear. Pavlovsky et al.<sup>4</sup> reported that hyperpigmented MF was characterized by a predominantly CD8-positive phenotype. Those authors speculated that CD8-positive tumor cells could have stronger cytotoxicity and affect neighboring cells such as melanocytes or basal keratinocytes, thereby causing interface changes and marked melanin incontinence, leading to the clinical appearance of hyperpigmentation<sup>4</sup>. However, in the present case, CD4-positive cells were dominant; therefore, hyperpigmentation cannot be attributed to this hypothesis. Yamamoto et al.<sup>1</sup> reported the association of mast cell number with hyperpigmented MF. Melanocytes are strongly stimulated by stem cell factor (SCF), which also activates the mast cells. Increasing numbers of mast cells in the skin with lesions and an upregulation of SCF in sera of hyperpigmented MF cases were found<sup>1</sup>. Thus, we compared the numbers of mast cells in the skin with lesion with normal skin controls and non-pigmented MF cases. Mast cell counts were averaged from three random fields

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**Fig. 1.** (A) Clinical manifestation. Hyperpigmented plaques on the trunk. (B) Histology of the lesional skin of a hyperpigmented plaque. Slight acanthosis with atypical lymphocytic infiltration within the epidermis and upper dermis, containing abundant melanophages (H&E,  $\times 100$ ). (C, D) Immunohistochemical analysis ( $\times 100$ ). (C) CD4 staining and (D) CD8 staining. (E) Mast cells in lesional skin. Red arrowheads indicate mast cells (toluidine blue,  $\times 400$ ).

**Table 1.** Mast cell counts in skin

Variable	Cells/HPF
Present case	43.67
Mycosis fungoides	
1	19.33
2	19.67
Normal human skin	
1	8.67
2	6.67
3	11.67

Values are presented as number. HPF: high-power field.

(cells/high-power field) in toluidine blue-stained skin specimens (Fig. 1E). As shown in Table 1, compared with normal and non-pigmented MF skin, the numbers of mast cells clearly increased in skin lesions of hyperpigmented MF. Unfortunately, we did not examine the serum levels of SCF. However, the increasing numbers of mast cells

suggest the existence of similar underlying mechanisms as reported by Yamamoto et al.<sup>1</sup>

## REFERENCES

1. Yamamoto T, Katayama I, Nishioka K. Role of mast cell and stem cell factor in hyperpigmented mycosis fungoides. *Blood* 1997;90:1338-1340.
2. Lee JS, Yun SJ, Lee JB, Kim SJ, Won YH, Lee SC. A case of hyperpigmented mycosis fungoides: a rare variant. *J Eur Acad Dermatol Venereol* 2007;21:983-985.
3. Erbil H, Sezer E, Koseoglu D, Filiz N, Kurumlu Z, Bülent Taştan H, et al. Hyperpigmented mycosis fungoides: a case report. *J Eur Acad Dermatol Venereol* 2007;21:982-983.
4. Pavlovsky L, Mimouni D, Amitay-Laish I, Feinmesser M, David M, Hodak E. Hyperpigmented mycosis fungoides: an unusual variant of cutaneous T-cell lymphoma with a frequent CD8+ phenotype. *J Am Acad Dermatol* 2012; 67:69-75.