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Interleukin-12 immunohistochemistry as a diagnostic tool for patch-stage mycosis fungoides

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To the Editor

The histologic diagnosis of early mycosis fungoides (MF) is a challenging task due to a lack of specific markers of malignant cells. Among the most common mimickers of MF are eczematous and psoriasiform dermatoses, such as pigmented purpuric dermatoses, eczema, psoriasis, and pityriasis lichenoides. While the search for specific markers is ongoing, several investigators noted that the variant of T-helper immune response could be a unique feature helping differentiate those cutaneous conditions. Early MF is a Th1-mediated immune process, while eczema and atopic dermatitis are Th2-mediated, and psoriasis is Th17-mediated.^{1,2} Recently, the transcription factors T-bet for Th1 and GATA-3 for Th2 cells were proposed to be useful in differential diagnosis of MF versus contact dermatitis.^{1,3} The follow-up study was unable to reproduce these findings, in that both T-bet and GATA-3 were highly expressed with no significant difference in both MF and spongiotic dermatitis.¹ While those transcription factors defined the lineage of differentiation of T cells, the cytokine milieu truly specifies the immune microenvironment.

To circumvent the controversy of previous studies, we assessed the immunohistochemistry (IHC) score⁴ via staining of IL-12p35 in 5 cases of classic patch MF (all had positive T-cell receptor gene rearrangement), 5 cases of nummular eczema, and 5 cases of psoriasis retrieved from the files of the University of Pittsburgh. The staining protocol was developed using human intestine as a positive control. The normal skin was also stained for comparison. We found a high level of IL-12 in the papillary dermis of patch MF. The staining for IL-12 highlighted dermal dendritic cells and Langerhans cells in the parabasal layer of the epidermis and was significantly more intense in patients with MF in comparison with either psoriatic or eczema lesions (Fig 1).

IL-12 is a crucial cytokine for the maintenance of the unique immune microenvironment where nonmalignant IFN- α - and IFN- γ -producing cytotoxic T cells are intended to control the proliferation of malignant T cells. As the disease progresses, the number of lymphoma cells expand, replacing the nonmalignant population, which accompanies a switch from Th1

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cytokine to Th2 cytokine profile.⁵ Thus, the presence of IL-12 in our samples is an indicator of Th1 microenvironment, which is usually observed in early MF.

In conclusion, we demonstrated an increased level of IL-12 in the patch stage of MF in comparison with similar patches of psoriasis or eczema in a small proof of concept study. Importantly, we chose only cases of classic early MF of patch stage, and, therefore, these data should not be generalized to other stages of this cutaneous lymphoma. We wonder if the staining for IL-12 might have some value in questionable cases of early MF, but these results need to be validated in much larger studies. Cases with equivocal histology would be of interest for future research.

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Fig 1. IL-12p35 staining in mycosis fungoides (MF), psoriasis, and nummular eczema. **A**, Extracellular and intracellular localization of IL-12p35 of dendritic cells in patch stage mycosis fungoides. (Original magnification: $\times 20$; insert $\times 100$.) **B**, IL-12p35 demonstrates sporadic staining of Langerhans cells in psoriatic skin. (Original magnification: $\times 20$.) **C**, Negative IL-12p35 staining in the nummular eczema. (Original magnification: $\times 20$; insert $\times 100$.) **D**, Immunohistochemistry (IHC) score: 5 patients with patch MF, 5 patients with psoriasis vulgaris, and 5 patients with nummular eczema. * $P < .05$; ** $P < .01$.