Langerhans' Cell Histiocytosis with Proliferation of Immature Langerhans' Cells in the Deep Dermis

Sir,

Langerhans' cell histiocytosis (LCH) embraces disorders previously called histiocytosis X, as the origin of proliferating cells in histiocytosis X (H-X cells) is thought to be Langerhans' cells (LCs) (1). It is known that the characteristic X-bodies, morphologically identical with the Birbeck granules of epidermal LCs, are observed in the cytoplasm of H-X cells. Recently, immunohistochemical studies revealed that H-X cells derived from S-100$^+$/T6$^+$/HLA-DR$^+$ dendritic cells closely resembling LCs (2).

The proliferating cells in LCH, however, differ from typical LCs since they often express CD68 and T4 antigens strongly, and C3b, C3bi, C3d antigen receptors and myelomonocytic antigens weakly. Therefore, it was suggested that the unusual phenotype of H-X cells might be related to their state as "tumor cells" and/or to cell immaturity (3).

We report a case of LCH with proliferation of mononuclear cells, which were thought to be immature cells of LC lineage. To our knowledge, there has been no report similar to our case.

In December 1993, a 9-month-old Japanese boy was admitted to Maebashi Red Cross Hospital with a history of recurrent erythematous eruption on the trunk. He had been suffering from bilateral otitis media. Physical examination revealed a few small hemorrhagic papules on the trunk. Routine laboratory tests revealed anemia (Hb: 8.6 g/dl) and cystic shadow on the chest X-ray and CT scan. On echography and CT scan, neither hepatosplenomegaly nor lymphadenopathy was observed. A skin biopsy from a papule on the breast showed considerable infiltration of histiocytic cells in the papillary dermis. The histiocytic cells presented atypical nuclei and abundant eosinophilic cytoplasm. Notable edema and extravasated erythrocytes were also observed. In the middle dermis,

histiocytic cells were scattered among the collagen bundles. In the deep dermis, a patchy infiltration of mononuclear cells was noted.

Immunohistochemical study was carried out using antibodies against CD45RO (T-cell marker), CD19 (B-cell marker), MAC387 (myeloid/histiocyte marker), CD68 and lysozyme (macrophage marker) and S-100 protein. Most cells in the papillary dermis and the middle dermis were positive for S-100 protein and CD68 antigens. The cells in the deep dermis expressed S-100 protein (Fig. 1) and occasionally CD68 antigen. The cells in the papillary, middle and deep dermis were occasionally positive for lysozyme and completely negative for CD45RO, CD19 or MAC387 antigens.

The pathological examination revealed that $S100^+$, $CD68^+$, $MAC387^-$ large atypical histiocytic cells infiltrated with notable edema and extravasated erythrocytes in the papillary dermis. Although we could not examine CD1 antigen expression in frozen sections or Birbeck granules with electron microscopy, typical morphology on light microscopy and the reasonable immunohistochemical findings indicate that these infiltrating histiocytic cells are of LC lineage. Thus, we diagnosed this patient as LCH. The histopathological findings necessary to make a diagnosis of LCH are a matter of controversy. Some authors assert that the demonstration of either Birbeck granules or CD1 positivity must be established for the diagnosis of LCH (4). In contrast, others claim that in a suitable clinical setting, the typical histopathological features of LCH coupled with the findings of positive S-100 staining are adequate for a definitive diagnosis (5).

As a distinct feature of the present case, we found $S100^+$/$CD68^+$/lysozyme^{+-}/$CD45RO^-$/$CD19^-$/$MAC387^-$ histiocytic cells in the middle dermis and $S\text{-}100^+$/$CD68^{+-}$/lysozyme^{+-}/$CD45RO^-$/$CD19^-$/$MAC387^-$ mononuclear cells in the deep dermis. It is generally accepted that LCs belong to the monocyte-macrophage histiocyte series and are derived from a bone marrow precursor closely related to that of a myelomonocytic lineage. The maturation of LCs and acquisition of CD1 and/or S-100 protein antigen are thought to take place in extravascular compartments (6). Taking our histochemical findings into consideration, the proliferating cells in the middle and deep dermis may have the same origin as the cells in the papillary dermis. Cutaneous indeterminate cells, dermal dendritic cells similar to LCs lacking Birbeck granules, are also commonly located in the superficial dermis (7).

Ruco et al. (8) examined lymph nodes of LCH and demonstrated that $CD1^+$ cells are highly polymorphic. They suggested that the LCH cell population was not homogeneous and that proliferating immature cells committed to LC lineage might also be involved in some cases. Our case may support their speculation and prove the aberrant phenotypic expression of LCH cells (3). The present case may also suggest that the degree of maturation in LCH cells may be related to the depth of the dermis where LCH cells reside and proliferate. Thus, the microenvironment around LCH cells, such as cytokines released from keratinocytes, may affect the phenotypic alteration or maturation of LCH cells.

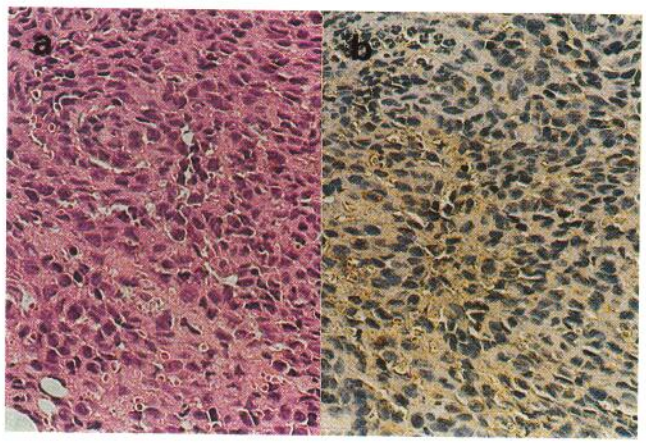

Fig. 1. In the deep dermis, patchy infiltrations of mononuclear cells were observed (*a*) and they were positive for S-100 protein (*b*). original magnification ×200. (*a*) hematoxylin and eosin; (*b*) anti S-100 protein.

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