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Cytologic Features of Langerhans' Cell Histiocytosis

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=Abstract=

Langerhans' cell histiocytosis (LCH), known for histiocytosis X, is a clinicopathologic entity characterized by proliferation of Langerhans' cells (LCs) throughout the body including the reticuloendothelial system, bone, and skin. LCs is currently considered as a distinct type of histiocytic cells, not primarily phagocytic in nature.

Recently, we could make the diagnosis on cytologic specimen in a 3 month-old-boy and a 3 year-old-boy. The cases were diagnosed on scraping smear from the skin and fine needle aspiration cytology from the lymph node, respectively.

The characteristic cytologic features of Langerhans' cells were noted in the nuclei, namely eccentric, indented, elongated, and grooved nuclei. The cells also had abundant and acidophilic cytoplasm. The cytologic diagnoses were confirmed on the biopsies from the skin and lymph node, respectively.

Key words : Langerhans' cell histiocytosis, Histiocytosis X, Skin scraping smear, Fine needle aspiration cytology, Lymph node, Skin

INTRODUCTION

The term Langerhans' cell histiocytosis, known for histiocytosis X, has been applied to a specific, although remarkably variable, clinicopathologic entity characterized by the proliferation of Langerhans' cells[1,2]. The Langerhans' cells are presently

regarded as a distinct type of histiocytic or reticular cells, but not primaily phagocytic in nature[3,4]. Langerhans' cell histiocytosis has been described showing distinctive cytologic features, which led to make the diagnosis of this disorder possible.

We described specific architectural features on cytologic materials from two cases of Langerhans' cell histiocytosis. The cytologic diagnoses were later confirmed on histologic sections.

CASE PRESENTATION

1. Case 1

A 3 month-old-boy presented with diffuse erythematous maculopapular rashes throughout the body. The body had fever, hepatosplenomegaly, and papable inguinal lymph nodes. Leukopenia, anemia, and thrombocytopenia were present. Bone marrow examination showed an increased number of histiocytes. Scraping smears and punch biopsy from the skin rash were interpreted as Langerhans' cell histiocytosis.

2. Case 2

A 3 year-old-boy was transferred to this hospital because of multiple cradle cap on the scalp, sore throat, and hepatosplenomegaly. Anemia and cervical lymphadenopathy were elucidated. Aspiration cytology and punch biopsy from the cervical lymph nodes showed findings consistent with Langerhans' cell histiocytosis. Immunohistochemical study was processed on the aspiration cytology smear.

CYTOLOGIC FEATURES

Both cytologic smears from the skin scraping and lymph node aspiration showed essentially identical cytologic features. There were sheets or individually scattered LCs admixed with lymphocytes and eosinophils (Fig. 1). The smears were cellular with an abundance of histiocytes (Fig. 2). The cytoplasm of LCs were abundant, amphophilic, and often finely vacuolated. The cell border was indistinct. The nuclei were oval or kidey-shaped and showed prominent grooves and folds that traversed them in all directions. The chromatin pattern was vesicular. The nucleoli were inconspicuous (Fig. 3). Immunohistochemical stainings for S-100 protein and OKT-6 on the lymph node aspirate showed a moderate degree of immunoreactivity.

HISTOPATHOLOGIC EXAMINATION

1. Case 1

On the examination of skin biopsy, there was a band-like infiltrate of histiocytes in the upper dermis. The histiocytes composing the infiltrate appeared as large, rounded cells with abundant, slightly eosinophilic cytoplasm. The nucleus is usually eccentric in location and indented or kidney-shaped (Fig. 4). Electron microscopic examination revealed numerous, rod-like tubular structure with regular periodicity and a dilated terminal end, characteristic of Birbeck granules (Fig. 5).

2. Case 2

Sections from the lymph node biopsy showed sinuses expanded by an infiltrate of histiocytes characterized by an abundant amphophilic cytoplasm and oval-to-irregulary elongated nuclei with vesicular chromatin. The nuclei had prominent linear grooves arranged in a haphazard fashion.

Fig. 1. Sheets and individually scattered Langerhans' cells admixed with lymphocytes and eosinophils (Skin Scraping ; H-E, ×200).

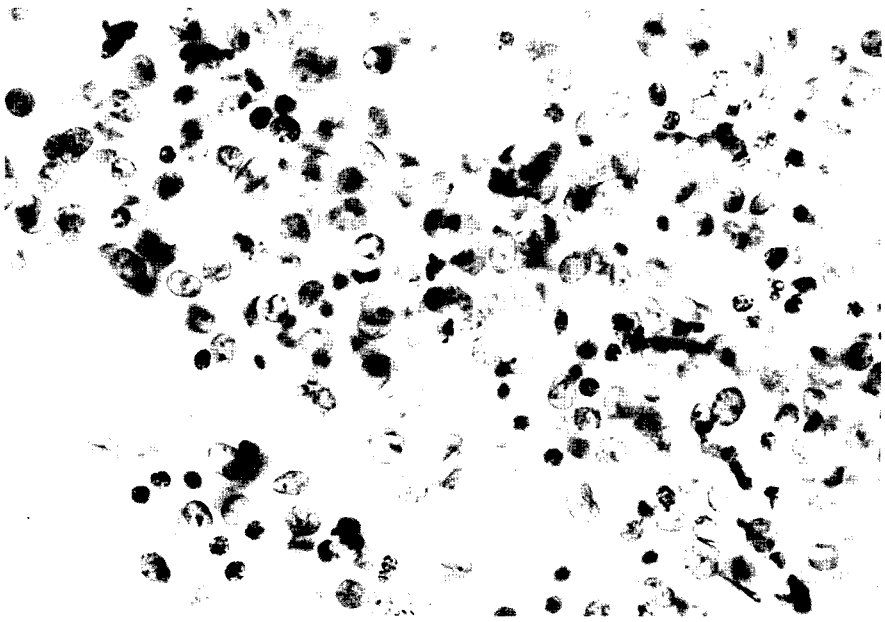

Fig. 2. Cellular smear with an abundance of histiocytes. The histocytes reveal characteristic grooves in the nuclei and ill-defined cytoplasm (Lymphnode ; H-E, ×400).

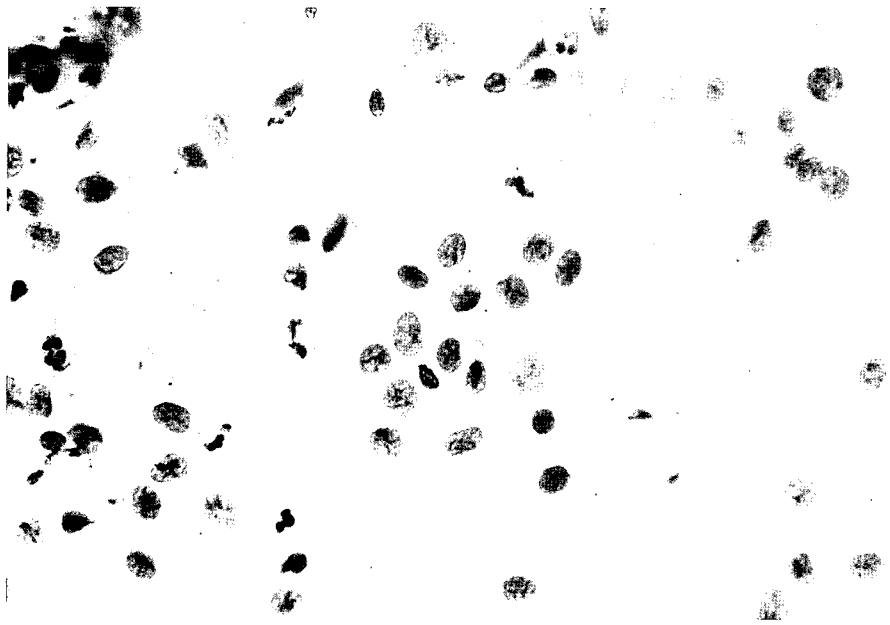

Fig. 3. Prominent nuclear grooves with vesicular chromatin pattern and abundant cytoplasm with indistinct cell border are conspicuous (Skin Scraping ; H-E, ×400).

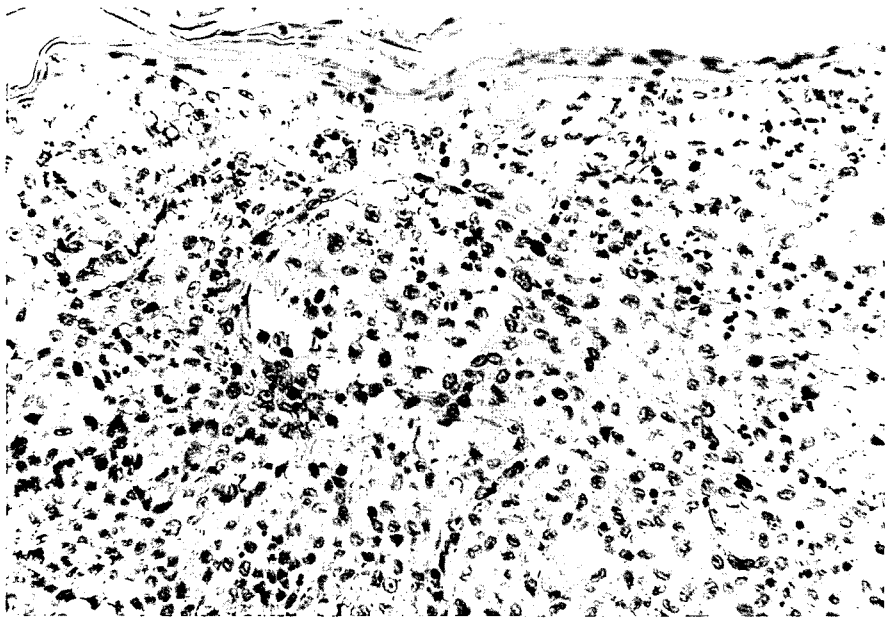

Fig. 4. Infiltrates of histiocytes in the epidermis and upper dermis as well (Skin Biopsy ; H-E, ×200).

Fig. 4. Rod-like tubular structures with regular periodicity and with dilated terminal end characteristic of Birbeck granules are present in the cytoplasm around the nucleus (×50,000).

DISCUSSION

LCH was defined as a disease complex characterized histologically by the proliferation of well-differentiated, cytologically benign histiocytes that bear several similiarities to LCs in the normal epidermis[5,6]. The cytoplasm of LCs in the lesions contained characteristic inclusions which resembled Birbeck granules found in the epidermal LCs[7]. S-100 protein was immunohistochemically demonstrated in LCs of LCH, interdigitating reticulum cells in lymph node, and LCs in the epidermis[8]. The present cases showed findings identical to those described in the previous reports. The immunohistochemical and electron microscopic characteristics indicate that LCs in LCH are not phagocytic but reticulohistiocytic in nature[7,8].

Characteristic cytologic features of LCs on smears include abundant, amphophilic, and often feathery cytoplasm with indistinct borders. The nucleus of LC is eccentric in location, oval, elongeted or kidney in shape, and has prominent grooves. The chromatin pattern is finely vesicular. The nucleoli are inconspicuous. The smears from both aspirates of lymph nodes and the skin scraping usually display the abundance of the histiocytes in sheets or individually scattered histiocytes admixed with lymphocytes and eosinophils. These cytologic pattern in conjunction with relevant clinical manifestation allows the definite diagnosis of LCH[7]. Storer et al[9], reported cytologic features of LCs from skin scraping in two cases. They insisted on that their description on skin scraping in LCH was the first. To the best of our

knowledge, the diagnosis of LCH with the skin scraping cytology has not been previously made.

Our examination on LCs in the skin scraping smear revealed cytologic features identical to those found in lymph node aspiration[7]. It was thought that the presence of LCs with characteristic features in the skin scraping smear allowed to arrive the definite diagnosis, as does in the lymph node aspiration smear.

The differential diagnosis of histiocyte-rich aspirates is of particular relevance to the present cases. These include the various hemophagocytic syndromes[10], allergic granulmatosis[11], sinus histiocytosis with massive lymphadenopathy[3], and dermatopathic lymphadenopathy[11]. These entities can be noted in young children and infants. Nevertheless, the various entities may be accurately diagnosed by evaluating the cytologic features of populations aspirated. The hallmark of the various hemophagocytic syndromes is the presence of mature histiocytes exhibiting extensive phagocytosis of red blood cells, other hematopoietic cells, and cellular debris[10]. Sinus histiocytosis with massive lymphadenopathy is a relatively rare syndrome, restricted to children, in which the hallmark is the presence of lymphocytes within the cytoplasm of mature histiocytes, without evidence of cellular destruction. This phenomenon emperiopoesis, is of diagnostic significance[3]. In dermatopathic lymphadenopathy, the characteristic finding is macrophages that have phagocytized melanin and iron pigments. LCs are present. This condition is usually found in the presence of longstanding chronic dermatitis. In allergic granulomatosis, the fine needle aspiration smear shows a population of mature histiocytes and eosinophils. However, these histiocytes do not possess the characteristic cytologic and histologic features of LCH[11].

The cytologic diagnosis of LCH should be considered when the smear is celluar with a large population of distinctive histiocytes accompanying the background population of lymphocytes and eosinophils.

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= 국문 초록 =

Langerhans 세포 조직구증의 세포학적 검색

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저자들은 세포학적 검사로 진단이 가능하였던 2 예의 Langerhans 세포 조직구증의 세포학적 소견을 기술하였다. 한 예는 3 개월된 남아의 구진성 피부병소로 부터 얻은 찰과 도말 표본에서, 다른 예는 3 세된 남아의 종창된 경부림프절의 세침천자 세포학적 표본에서 각각 특징적인 조직구의 도말배경을 관찰함으로써 진단이 가능하였다.

진단적인 세포학적 표본의 검색에서 도말된 세포성분은 풍부하고, 도말배경은 깨끗하였다. 특징적인 조직구는 길죽한 핵의 한쪽이 약간 함몰되고, 긴 구열을 가지며, 핵막은 얇고, 염색질은 섬세하며, 핵소체는 인정되지 않았다. 호산성의 세포질은 풍부하고, 활동적인 탐식작용의 증거는 관찰되지 아니하였다. 특징적인 조직구와 더불어 림프구와 드물게 호산구가 도말배경을 이루고 있었다.