Langerhans Cell Histiocytosis Presented as Generalized Vesiculo-Pustules in a Neonate

-A Case Report

Yu-Fen Lee  Ding-Dar Lee  Han-Nan Liu

A one-month-old female baby had been noted to have multiple vesicles and pustules over the head, face, trunk and four extremities since she was one-week-old. Under the impression of disseminated herpes virus infection, intravenous acyclovir was given after admission. Serum herpes simplex virus and varicella zoster virus enzyme-linked immunosorbent assay test and virus culture were all fruitless, although herpes simplex virus-1 was vaguely identified in direct fluorescent staining of lesion scrapings. Unfortunately, new lesions still continued popping out despite treatment. Dermatologist was then consulted, and Tzanck smear as well as skin biopsy were performed. The histopathological exam showed Langerhans cell histiocytosis. Skull x-ray film showed expansile osteolytic lesion over the left parietal area and the chest x-ray increased reticulonodular infiltration in both lung fields. There was no abnormal finding in the long bone survey or abdominal sonography. In summary, we report a case of neonatal Langerhans cell histiocytosis presenting as generalized vesiculo-pustules. It should be differentiated from herpes virus infection in the clinical setting. (Dermatol Sinica 27: 176-180, 2009)

Key words: Langerhans cell histiocytosis, Vesiculo-pustules, Tzanck smear

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare disease of unknown cause characterized by the proliferation of a distinct cell type that is S-100 and CD1a positive containing cytoplasmic Langerhans granules. The reactive versus neoplastic nature of the LCH is debated. It includes four main clinical forms: Letterer-Siwe disease, Hand-Schuller-Christian Disease, eosinophilic granuloma and Hashimoto-Pritzker disease. It is a disorder with a broad clinical spectrum of severity. Here, we report an unusual case of LCH displaying generalized vesiculo-pustules in a neonate with specific Tzanck smear finding and false-positive result of direct fluorescent staining of herpes simplex virus-1 (HSV-1).

CASE REPORT

A female fullterm baby had been well until she was one-week-old. Multiple vesicles and pustules over the head, face, trunk and four extremities were noted. She was admitted to our pediatric ward under the im-
pression of herpes virus infection at age of one month. She was afebrile with stable vital signs, and no organomegaly was present. The laboratory data showed a white blood cell count of 11300/mm$^3$ (N/L/E 42.2/37.7/2.3), hemoglobin 11.3 g/dl, platelets 398000/mm$^3$, C-reactive protein <0.1 mg/dl, alanine aminotransferase/aspartate aminotransferase 50/56 U/L, direct bilirubin/total bilirubin 0.1/0.5 mg/dl, alkaline phosphatase 339 U/L and GGT 59 U/L. Intravenous acyclovir 40mg q8h was given. Serum HSV enzyme-linked immunosorbent assay (ELISA) test, serum varicella zoster virus (VZV) ELISA test and virus culture showed negative result, although HSV-1 was vaguely identified in direct fluorescent staining of lesion scrapings. New lesions continued to appear despite intravenous acyclovir treatment. Cutaneous examination revealed multiple 2-4 mm vesicles, tiny pustules, crusted papules and erosions over the scalp, face, trunk and extremities, including the palms and soles (Fig. 1A, 1B, 1C). Central umbilication could be seen in some of the skin lesions (Fig. 1D). Tzanck preparation from the skin lesions demonstrated large epithelioid-appearing cells, but no multinucleated giant cells were found. The nuclei were oval and had longitudinal grooves. (Tzanck smear, original magnification x1000)

(B) There was focal spongiosis with eosinophils exocytosis in the epidermis. Besides, loose aggregates of large cells, some of which showed infolded, vesicular nuclei, were seen in the epidermis and the papillary dermis. Few mitoses were also seen. In the upper dermis, there was a mild perivascular inflammatory cell infiltrate composed of eosinophils and lymphohistiocytes. (H&E, original magnification, x400)

(C) These large cells were weakly positive for S-100 protein. (original magnification x400)

(D) These large cells were strongly positive for CD1a. (original magnification x400)
for S-100 protein and strongly positive for CD1a (Fig. 2C, 2D). The results of histopathological and immunohistochemical exam confirmed the diagnosis of LCH. The patient was referred to pediatric oncologist. Skull x-ray film showed an expansile osteolytic lesion over the left parietal area and the chest x-ray increased reticulonodular infiltration in both lung fields (Fig. 3A, 3B). There was no abnormal finding in the long bone survey or abdomen sonography. Chemotherapy was suggested but the patient’s parents want to seek for second opinion.

**DISCUSSION**

Lichtenstein addressed integration of eosinophilic granuloma of bone, Letterer-Siwe disease, Hand-Schuller-Christian disease as a related expression of a single nosologic entity called Histiocytosis X in 1953. Congenital self-healing reticulohistiocytosis was first reported in 1973 by Hashimoto and Pritzker who described a congenital disorder characterized by multiple reddish brown papulonodules limited to the skin that spontaneously healed without sequelae. Now these conditions are designated as LCH. Cutaneous manifestations are very common in LCH and may represent the earliest sign of the disease. Multiple yellowish erythematous translucent papules, 1-2mm in diameter, covered by scales and usually on the trunk and scalp are typical findings. But vesicles and pustules may rarely occur, simulating eczema, miliaria, scabies, varicella, intertrigo, candidiasis, rosacea and folliculitis decalvans. Our case was presented by generalized vesiculo-pustules. The differential diagnosis of neonatal vesiculo-pustular eruption includes erythema toxicum neonatorum, neonatal pustular melanosis, miliaria, congenital candidiasis, perinatal Listaria monocytogenes or herpes simplex infection, infantile acropustulosis, incontinentia pigmeni, neonatal Behcet’s syndrome, and eosinophilic pustular folliculitis. Based on the histopathological finding, the clinical vesiculo-pustules were formed due to spongiosis in this case.

In our case, Tzanck preparation from the skin lesions demonstrated large epithelioid-appearing cells, but no multinucleated giant cells were found. The nuclei were oval and had longitudinal grooves. The same findings were also seen in the previous cases of LCH in the literature. Tzanck preparation of LCH usually revealed dominant epithelioid histiocytes characterized by oval or reniform nuclei and abundant pale amphophilic cytoplasm. The nuclear chromatin was finely distributed. So we may use the Tzanck preparation in the preliminary diagnosis of LCH. The procedure is easy to do, inexpensive and gives a quick result. Besides, it may be helpful for the patients who couldn’t receive skin biopsy immediately or have temporary risk of skin biopsy, for example, severe thrombocytopenia or severe infection.

The possibility of herpes simplex infection was initially impressed in our case because of generalized vesiculo-pustules with umbilication and HSV-1 identified in direct fluorescent staining of lesion scrapings. However, new lesions still continued to appear despite intravenous acyclovir treatment. In 1978, Hodge and others proposed eosinophil
fluorescence in cutaneous infiltrates is a possible source of confusion, but its significance was not clearly addressed. Detlefs and others suggested eosinophils show nonspecific fluorescence in immunofluorescent techniques because the fluorescein isothiocyanate label of the antiserum binds with the basic proteins in the eosinophilic granules. In our case, skin biopsy revealed eosinophils in the epidermis and upper dermis, which might be the cause of the false positive results of immunofluorescent slide tests.

In conclusion, we report an unusual case of LCH presented as generalized vesiculopustules in a neonate with specific Tzanck smear finding and false-positive direct fluorescent staining of HSV-1. The list of differential diagnosis of neonatal vesiculo-pustular eruptions should always include LCH. In this setting, Tzanck preparation may be helpful in making a preliminary diagnosis of LCH. We should keep in mind that eosinophils may confound the results of immunofluorescent slide tests of herpes virus.

REFERENCES
蘭格罕氏細胞組織球增生病在一新生兒以全身性水痘膿樣病灶表現
- 病例報告

李瑜芬  李定達  劉漢南
台北榮民總醫院皮膚部

一位女嬰自出生後一週起，在頭上，臉上，軀幹及四肢出現了許多的水疱及膿疱，因為疑似疱疹病毒感染在滿月時住院並接受靜脈注射acyclovir。雖然單純疹病毒和水痘帶狀疹病毒的血清檢查與病毒培養的結果都是陰性，但是病灶的直接抗體螢光檢查呈現第一型單純疹病毒。治療之後，仍有許多新病灶出現，於皮膚科會診後進行Tzanck 抹片以及皮膚切片檢查。皮膚切片的病理報告為蘭格罕氏細胞組織球增生病。之後的檢查結果包括：頭部\X光檢查發現在左側頂骨處有擴張性的蝕骨病灶；胸部\X光攝影顯示在二側肺野均有網狀結節狀浸潤增加的情形；長骨\X光檢查與腹部超音波掃描皆無異常。總而言之，我們強調以新生兒的全身性水痘膿樣病灶所表現的蘭格罕氏細胞組織球增生病，在臨床上必須與疱疹病毒感染作鑑別診斷。（中華皮誌：27: 176-180, 2009）