Diagnosis of Nodal Langerhans Cell Histiocytosis by Fine Needle Aspiration Cytology

Li-Yu Lee, MD; Chung-Jan Kang[1], MD; Yi-Yueh Hsieh, MD; Swei Hsueh, MD

Langerhans cell histiocytosis (LCH) is a rare disease and disease confined to the lymph nodes is even more uncommon. Fine needle aspiration (FNA) cytology of LCH of the lymph nodes has rarely been described.[1-5] A case study of LCH of the lymph nodes in a 23-year-old man is presented. FNA smears showed high cellularity composed of many isolated Langerhans cells (LCs) with nuclear grooves admixed with numerous eosinophils, lymphocytes, giant cells, macrophages, and neutrophils. Further immunohistochemical study of the excised lymph node sections revealed that the histiocytes were positively stained with CD1a. The presence of LCs with nuclear grooves and eosinophils suggests the possibility of LCH. FNA cytology is a valuable method for diagnosis. *(Chang Gung Med J 2005;28:735-9)*

Key words: histiocytosis, Langerhanscell, fine needle aspiration, lymph nodes.

Langerhans cell histiocytosis (LCH) is a rare disease affecting predominantly children and young adults, but it can be found in any age group. The estimated incidence is about 5 per million, with most cases occurring in childhood.[6] In the past, the disorder was referred to as histiocytosis X. It was subdivided into three variants--- eosinophilic granuloma, Hand-Schuler-Christian disease and Letterer-Siwe syndrome--- as originally proposed by Lichtenstein in 1953.[7] These three conditions are now believed to represent different expressions of the same basic disorder. Therefore, the Writing Group of the Histiocyte Society, which proposed that the diagnostic terms be made specific and inclusive, coined the term LCH.[8]

LCH is considered a neoplasm of the mononuclear phagocytic immunoregulatory system of unknown etiology. The disease is characterized by a clonal proliferation of a special kind of histiocyte of the antigen-presenting dendritic type called the Langerhans cell (LCs).[9]

The unifocal form of LCH (solitary eosinophilic granuloma) usually involves the bone. The multifocal unisystem form of LCH (Hand-Schuler-Christian disease) almost always occurs in the bone. The multifocal multisystem form of LCH (Letterer-Siwe syndrome) involves many organs, including the bone, skin, liver, spleen, and lymph node. Lymph node involvement may be an associated feature of LCH, but isolated nodal LCH is rare.[10,11] Recently, only a few cases of LCH have been reported using fine needle aspiration (FNA) cytology.[1,11,14-18] This paper describes an uncommon case of LCH of the lymph nodes with a definitive FNA cytodiagnosis which was confirmed by immunohistochemical study.

CASE REPORT

A 23-year-old man visited our ENT clinic in February 2004 because of an extremely tender left neck nodule, which had persisted for approximately one month. Two firm, tender, slightly movable 1.0 x 1.0 x 1.0 cm left cervical lymph nodes were found on physical examination. The patient had no fever or loss of body weight. There was no evidence of

From the Department of Pathology; [1]Department of Otolaryngology, Chang Gung Memorial Hospital, Taipei.
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Correspondence to: Dr. Swei Hsueh, Department of Pathology, Chang Gung Memorial Hospital. No. 5, Fushing St., Gueishan Shiang, Taoyuan, Taiwan 333, R.O.C. 333. Tel.: 886-33281200 ext. 2737; Fax: 886-33280147; E-mail: swei@cgmh.org.tw

hepatosplenomegaly. The initial clinical impression favored reactive lymphadenitis. Sonography of the neck showed bilateral multiple hypoechic nodules, with more nodules located on the left side. FNA cytology was performed on the enlarged neck node which had been detected by the patient.

Papanicolaou smears revealed high cellularity in the aspirate, which was composed of a mixture of abundant, predominantly dissociated histiocytes and eosinophils. They were accompanied by various numerous neutrophils, lymphocytes, macrophages, and multinucleated giant cells (Fig. 1). The histiocytes were large cells with abundant, pale blue cytoplasm and round to oval, vesicular nuclei. Prominent nuclear indentations and grooves (with a coffee bean appearance) were observed in the mononucleate histiocytes and multinucleate giant cells. Occasional mitoses were seen. The eosinophils were of the natural type and showed bilobular nuclei and numerous large, eosinophilic granules. The cytologic findings were suggestive of LCH. An excisional biopsy was done for histologic confirmation.

Gross examination of the biopsy specimen revealed a tan to yellow lymph node measuring 1.3 x 0.7 x 0.7 cm. Microscopic examination showed partial effacement of the lymph nodal architecture by a polymorphic population of cells, including histiocytes, eosinophils, lymphocytes, giant cells, macrophages, and neutrophils. Numerous eosinophil microabscesses were found admixed with sheets of large mononuclear and multinuclear histiocytes (Fig. 2). On high magnification, the histiocytes revealed abundant pale cytoplasm and elongated grooved and cleaved nuclei with a delicate chromatin pattern, inconspicuous nucleoli, and thin nuclear membrances. Occasional mitoses were noted, averaging one per 20 high power (X 40) fields. The biopsy was diagnosed as LCH. Immunohistochemically, the membranes of the LCs were positive for CD1a (Fig. 3).

The patient subsequently received clinical staging for LCH. The complete blood count was within

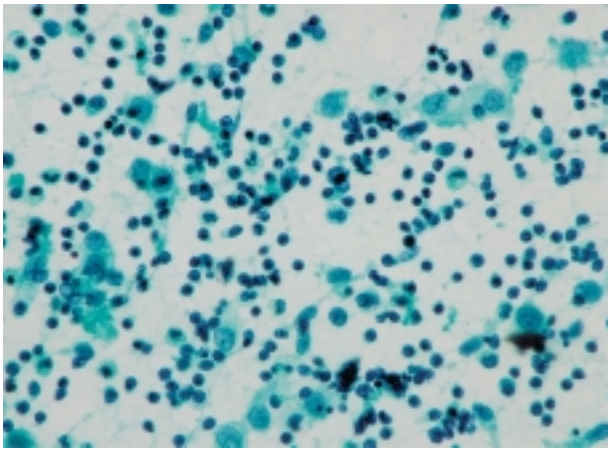

Fig. 1 FNA smear reveals loosely clustered Langerhans cells with prominent nuclear grooves, accompanied by many eosinophils. (Papanicolaou stain, original magnification, x 400).

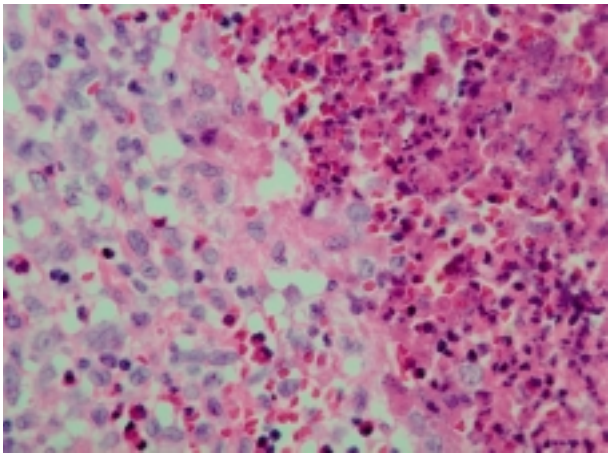

Fig. 2 An eosinophil microabscess is found admixed with sheets of large mononuclear and multinuclear histiocytes. (H & E stain, original magnification, x 400).

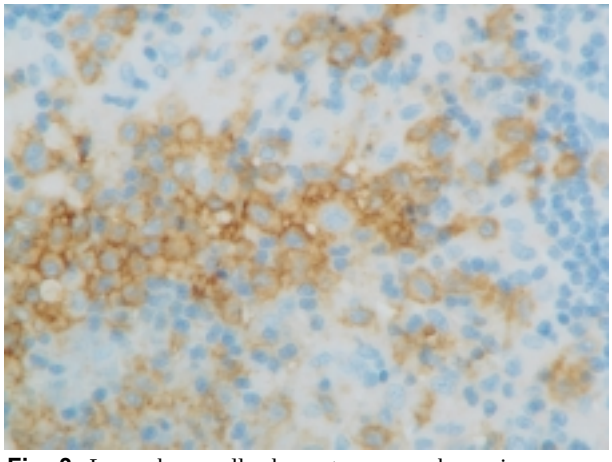

Fig. 3 Langerhans cells show strong membrane immunoreactivity for CD1a. (immunoperoxidase, original magnification, x 400).

normal limits. No other systemic involvement was found after series studies. He was alive and well one month postoperatively and has had regular follow-up in the out-patient clinic without any further treatment.

DISCUSSION

The diagnosis of LCH in our patient was made on the basis of FNA smears of the lymph nodes which showed a polymorphic population of cells composed of eosinophils and histiocytes with nuclear groovings.[2] However, the differential diagnoses should include conditions with localized aggregates of LCs such as those observed in association with dermatopathic lymphadenitis (DL), parasitic infection, Kimura's disease, hypersensibility reactions, cat-scratch disease, sinus histiocytosis with massive lymphadenopathy (SHML), and hyperplasic lymph nodes.

In addition, on rare occasions, LCH can associate with a variety of malignant neoplasms in the same node, i.e., malignant lymphoma or metastatic neoplasms.[19] Therefore, further exclusion of malignancies, including Hodgkin's disease (HD), malignant melanoma, papillary thyroid carcinoma, malignant histiocytosis (MH), and other tumor cells with nuclear groovings should also be performed. Malignancies are easily excluded when no malignant cells with obvious cytologic atypia are present on the smear.

Due to the absence of pigment in the histiocytes, the possibility of DL was excluded in our patient. SHML involves primarily the cervical nodes, but its histiocytes are morphologically quite different from those of LCH. In SHML, the histiocytes have abundant cytoplasm, exhibiting hematopoietic phagocytosis and prominent nucleoli. In addition, in SHML, the histiocytes are S-100 protein (+), lysozyme (-), and CD1a (-).[2,5]

LCs reveal characteristic Birbeck granules on electron microscopy. Electron micriscopy is not essential for diagnosis and was not performed in our patient.

LCH exhibits a wide spectrum of clinical behaviors that correlate with the extent of organ system involvement and the age of the patient. The lymph node involvement in LCH can be seen as a part of a systemic disease or as a localized lesion. About two-thirds of lymph node-based lesions are solitary and one-third may involve the adjacent bones. The prognosis of this localized form is very favorable if diagnosed and treated appropriately. The overall survival of patients with unifocal disease is higher than 95%.[20]

In conclusion, when accompanied by a classic clinical presentation, LCH can be easily diagnosed in a FNA smear because of the presence of characteristic LCs and eosinophils. FNA biopsy can serve as a valuable method for diagnosis of LCH.

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局部淋巴結的 Langerhans 氏組織球增加症

李麗玉 康仲然[1] 謝怡悅 薛綏

Langerhans 氏組織球增加症是一種罕見的疾病，尤其只局部發生在淋巴結更加少見。目前許多疾病皆可經由侵襲性小的細針穿刺細胞學抹片來診斷其他疾病。但是，用細針穿刺細胞學抹片來診斷淋巴結的組織球增加症很少被報告過。我們報告一例用細針穿刺細胞學抹片診斷發生在一位 23 歲男性的局部淋巴結的 Langerhans 氏組織球增加症。細針穿刺的細胞學抹片中顯示許多典型單棵有核溝的 Langerhans 氏組織球，混雜一些嗜伊性白血球、淋巴球、巨細胞、吞噬細胞，和中性白血球。進一步免疫化學染色方法顯示 CD1a 對 Langerhans 氏組織球是呈陽性反應。本報告指出在細針穿刺細胞學抹片中若有出現有核溝的 Langerhans 氏組織球和嗜伊性白血球，應該可以診斷出 Langerhans 氏組織球增加症；而細針穿刺細胞學抹片是一種有價值的診斷工具。(長庚醫誌 2005;28:735-9)

關鍵字：Langerhans 氏組織球，細針穿刺細胞學抹片，淋巴結。

長庚紀念醫院　台北院區　病理科系　解剖病理科，[1]耳鼻喉一科
受文日期：民國93年4月5日；接受刊載：民國93年12月24日
通訊作者：薛綏醫師，長庚紀念醫院　病理科系　解剖病理科。桃園縣333龜山鄉復興街5號。Tel.: (03)3281200轉2737; Fax: (03)3280147; E-mail: swei@cgmh.org.tw