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Original Article

Histiocytic necrotizing lymphadenitis diagnosed by conventional cytology and liquid based cytology

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Abstract: Histiocytic necrotizing lymphadenitis (HNL; Kikuchi-Fujimoto disease) is a rare benign disorder. The diagnosis of HNL is established on recognizing the characteristic histologic findings from biopsy of the enlarged lymph nodes. Though diagnosis of HNL by fine-needle aspiration (FNA) was reported, the characteristic fine-needle aspiration cytologic features with conventional cytology and a liquid based cytology test (LCT) have not been well documented. In this study, 42 cases of suspicious necrotic lymph nodes were subjected to cytology and biopsy diagnosis. The lymph nodes were aspirated using a 10 mL disposable syringe with the percutaneous ultrasound guided. Samples were used for conventional cytology and LCT. Among 42 cases of suspicious necrotic lymph nodes, 37 of cases were histologically confirmed as HNL; 3 of cases were hyperplasia of lymphoid tissue; 1 case was tuberculosis of lymph node, and 1 case was classical Hodgkin lymphoma (nodular sclerosis type). 31 out of 37 (83.8%) cases of HNL were diagnosed by conventional cytology, 33 out of 37 (89.2%) were diagnosed by LCT. Our results indicate that no significant difference on accuracy rate between conventional cytology and LCT, but LCT has its advantages in the diagnosis of HNL.

Keywords: Histocytic necrotizing lymphadenitis, conventional cytology, liquid based cytology test

Introduction

Histiocytic necrotizing lymphadenitis (HNL), also known as Kikuchi-Fujimoto disease, is a benign and self-limited disease and was first described in Japan by Kikuchi and Fujimoto in 1972 as a subacute necrotizing lymphadenitis of unknown etiology [1-3]. HNL affects preferentially the Asian population with a female predominance. HNL usually manifests as isolated cervical lymphadenopathy accompanied by fever and night sweats. However, in some patients, the only presenting symptom may be a fever of unknown origin [4]. HNL is characterized morphologically by nodal paracortical and cortical patchy necrotic areas with prominent karyorrhectic and karyolytic debris and associated mononuclear cell response composed of histiocytes, phagocytic macrophages, lymphoid cells, foamy histiocytes, and a striking population of mononuclear cells with plasmacytoid morphology [5-8].

The diagnosis of HNL is established on recognizing the characteristic histologic findings from biopsy of the enlarged lymph nodes. Though diagnosis of HNL by fine-needle aspiration (FNA) was reported before [9, 10], the characteristic fine-needle aspiration cytologic features, especially the difference between traditional smear and LCT have not been well documented. HNL is a self-limiting disorder and most often requires supportive care only. The biopsy is of time consumption and brings patient about mental stress. It would be most desirable if the diagnosis could be established on the clinical findings and morphologic diagnosis of FNA of the lymph node rather than by lymph node biopsy. In the present study, the suspicious necrotic lymph nodes on the body surface were aspirated using a 10 mL disposable syringe (21-gauge needles) with the percutaneous ultrasound guided. Samples were used for conventional smear, and the needle residual specimens were injected into fixed solution for

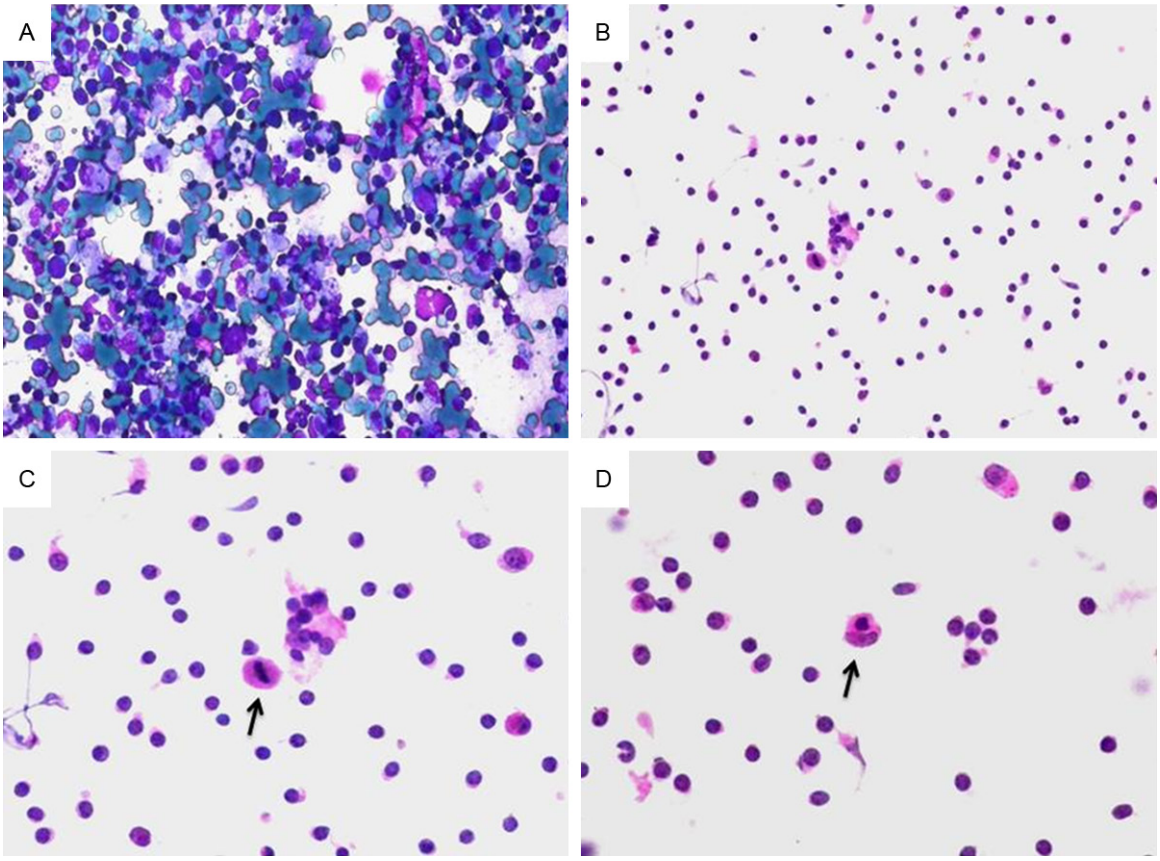

Figure 1. Cytologic features of histiocytic necrotizing lymphadenitis. A: Conventional smear slide shows the background is not clear compared with. B: LCT slide with a clear background. C: Karyokinesis (arrow). D: Crescentic histiocyte (arrow).

cells. The cellular slide was prepared by LCT and immunohistochemical staining. We compared the diagnosis of conventional cytology and LCT by fine-needle aspiration with that of biopsy.

Materials and methods

Patients

Between September 2010 and December 2012, 42 cases of suspicious necrotic lymph nodes were subjected to biopsy and cytology diagnosis. Thirty patients were female, while other twelve patients were male. The mean age was 30.6 years (range from 3-71 years). All patients were presented with lymphadenopathy, 39 patients had cervical lymphadenopathy, 2 patients had in axillary lymphadenopathy, and one patient had thigh lymphadenopathy. Partial patients had irregular fever. All patients had superficial lymph nodes with a vary size, unilateral or bilateral, single or multiple, and the texture is medium.

Preparation of fine-needle aspiration conventional smear and LCT

The aspirates were obtained using a 10 mL disposable syringe (21-gauge needles) with the percutaneous ultrasound guided. For each case, both conventional cytology and liquid-based cytology were performed. The air-dried smears were prepared and stained with Wright-Giemsa stains. After samples were used for conventional smear, the needle residual specimens were injected into fixed solution for cells. The cellular slide was prepared by a LCT by using the ThinPrep system (Cytyc Corporation, Boxborough, USA) according to the manufacturer's instruction.

Immunohistochemical staining of LCT slides

The immuohistochemical staining of LCT slides were carried out. Briefly, antihuman CD31, CD20, CD68, and CD123 monoclonal antibodies (R&D Systems, Minneapolis, U.S.) at a dilution of 1:200 were used as the primary anti-

Table 1. 42 cases of patients diagnosed with conventional cytology and LCT

Methods	37 cases of HNL (%)	5 cases of non-HNL (%)
Smear	31/37 (83.8%)	1/5 (20%)
LCT	33/37 (89.2%)	2/5 (40%)

Table 2. Comparison characteristics between conventional cytology and LCT

Characteristics	smear	LCT
Loss of cells	yes	no
Number of cells	small	large
Background	dirty	clean
Slide quality	low	high
Cellular structure	more distinct	distinct
Immuohistochemical staining	no	yes

body. The incubation was at 4°C overnight, followed by washing with PBS. The slides were incubated with secondary antibody (Dako, Ely, U.K.) for 30 minutes at room temperature. Signals were developed with 3, 3'-diaminobenzidine for 5 minutes and counterstained with hematoxylin.

Results

Both of conventional smear and LCT of HNL displayed a heterogenous pattern showing small and large lymphoctyes, reactive histocytes, and transformed lymphocytes. The cytological features was characterized by a polymorphous lymphoid cell population along with abundant karyorrhectic debris in the background and many histiocytes, which were small sized and usually had an eccentrically placed round to oval or a crescentic nucleus with or without ingested nuclear debris (**Figure 1**). Some of the transformed lymphocytes were large blasts with morphologic features similar to the plasmacytoid monocytes, while others were large cells with purplish cytoplasm that resembled the immunoblasts. Mitoses were uncommon. There were few or no polymorphonuclear leukocytes, plasma cells, or epithelioid cells. Cell degeneration and cell debris were the most conspicuous features. Histocytes with phagocytosis of karyorrhectic debris were seen. Many mononuclear histiocytes with round or oval nuclei and no phagocytic material in their cytoplasm were also present.

Among 42 cases of suspicious necrotic lymph nodes subjected to biopsy and cytology diagnosis, 37 cases were confirmed as HNL by biopsy. Other 5 cases included 3 cases of lymphoid hyperplasia, one case of lymph node tuberculosis, and one case of classical Hodgkin's lymphoma. **Table 1** shows the results of conventional and liquid based cytology in diagnosis of 42 cases.

Discussion

HNL is a well-established non-neoplastic disorder of unknown cause with characteristic clinical findings and affected lymph nodes, particularly those in the neck showing lesions with karyorrhectic nuclear debris and proliferating mononuclear cells, and has a self-limiting clinical course [1, 2, 6]. The diagnosis of HNL is routinely established on recognizing the characteristic histologic findings from biopsy of the enlarged lymph nodes, because of no specific symptoms or laboratory findings for HNL. Microscopically, HNL is characterized by nodal paracortical and cortical patchy necrotic areas with prominent karyorrhectic debris. These necrotic areas are surrounded by mononuclear cells composed of histiocytes, phagocytic macrophages, lymphoid cells, foamy histiocytes, and plasmacytoid dendritic cells. The biopsy is of time consumption and brings patient about mental stress. Cytologic diagnosis of HNL by fine needle aspiration has been investigated [9-11]. A polymorphous lymphoid cell population with abundant karyorrhectic debris and histiocytes, many of which are crescentic, are characteristic fine-needle aspiration cytologic features of HNL. In absence of typical cytologic features, these cases may be confused with tuberculous lymphadenitis, lymphoma, and reactive hyperplasia of lymph node in FNA material.

Liquid-based cytology has been used in cervical cytology diagnosis for many years [12, 13]. It plays an important role in cervical carcinoma screening [12, 14]. Some researchers introduced LCT to fine needle aspiration cytology of lymph node recently [15, 16]. Till now, we do not find researches on the diagnosis of HNL by using LTC.

In the present study, we used conventional cytology and LTC for diagnosis of HNL with fine-needle aspiration samples. The conventional cytology and liquid based cytology have the similar sensitivity in the diagnosis of HNL

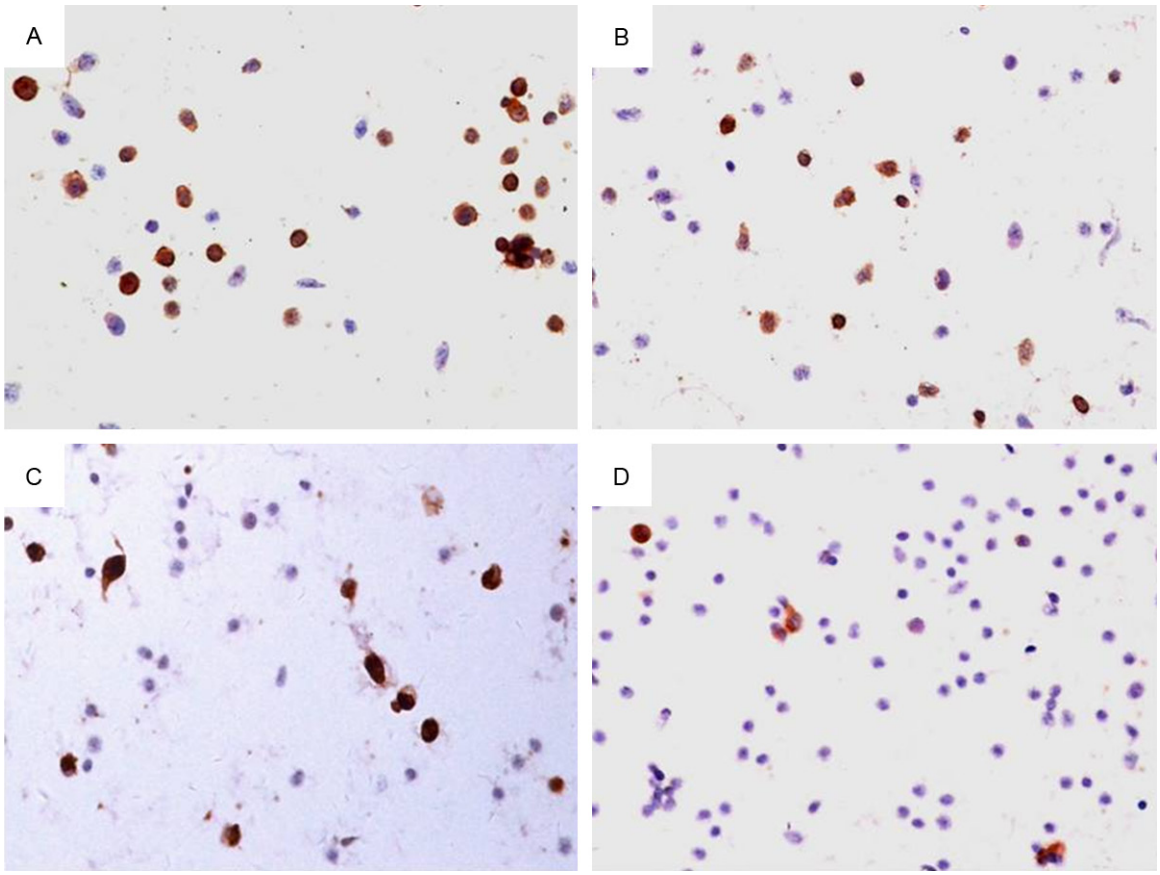

Figure 2. Immunohistochemical staining of LCT slides. A: CD3 with the positive staining of nuclei. B: CD20 with the positive staining of nuclei. C: CD68 with the positive staining of nuclei. D: CD123 with the positive staining of cytoplasm.

(83.8% vs. 89.2%), but liquid based cytology has some advantages. The characteristics of conventional cytology and LTC for diagnosis of HNL are summarized in **Table 2**. For conventional cytology, part of sample is lost when making smear slides. The cells were centrifuged and concentrated in a small field that diameter is 13 mm of slide when making LTC slide, the number of cells in LTC is more than that in smear slide. The slide quality of conventional smear is poor because that cellular layer is not even, which is easy to produce artificial alteration of cells and the cell layer is often thicker. In the LTC slide, the cells distributed evenly and are easy to observe. The antigens in LTC slides are protected and the slides can be used for intensive study including immunohistochemical staining and molecular test. We carried out immunohistochemical staining of CD3, CD20, CD68, CD123 to make a differential diagnosis of HNL and other diseases (**Figure 2**). The structure of nucleus is more distinct in the conventional smear than in LTC. The cost of LTC is increased compared with conventional cytology. Our results indicate that no significant difference on accuracy rate between conventional cytology and LCT, but LCT has its advantages in the diagnosis of HNL.

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Disclosure of conflict of interest

None.

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References

[1] Ma DD, Hollis RR and Delbridge L. Histiocytic necrotizing lymphadenitis (Kikuchi's disease). Aust N Z J Med 1986; 16: 711-713.

[2] Sterman BM, Benninger MS and Eliachar I. Histiocytic necrotizing lymphadenitis (Kikuchi's disease). Head Neck 1989; 11: 349-352.

[3] Kuo TT. Cutaneous manifestation of Kikuchi's histiocytic necrotizing lymphadenitis. Am J Surg Pathol 1990; 14: 872-876.

[4] Shirakusa T, Eimoto T and Kikuchi M. Histiocytic necrotizing lymphadenitis. Postgrad Med J 1988; 64: 107-109.

[5] Chan JK and Ng CS. Immunohistochemical studies on histiocytic necrotizing lymphadenitis. Pathology 1987; 19: 104.

[6] Kuo TT. Kikuchi's disease (histiocytic necrotizing lymphadenitis). A clinicopathologic study of 79 cases with an analysis of histologic subtypes, immunohistology, and DNA ploidy. Am J Surg Pathol 1995; 19: 798-809.

[7] Felgar RE, Furth EE, Wasik MA, Gluckman SJ and Salhany KE. Histiocytic necrotizing lymphadenitis (Kikuchi's disease): in situ end-labeling, immunohistochemical, and serologic evidence supporting cytotoxic lymphocyte-mediated apoptotic cell death. Mod Pathol 1997; 10: 231-241.

[8] Menasce LP, Banerjee SS, Edmondson D and Harris M. Histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto disease): continuing diagnostic difficulties. Histopathology 1998; 33: 248-254.

[9] Kung IT, Ng WF, Yuen RW and Chan JK. Kikuchi's histiocytic necrotizing lymphadenitis. Diagnosis by fine needle aspiration. Acta Cytol 1990; 34: 323-328.

[10] Hsueh EJ, Ko WS, Hwang WS and Yam LT. Fine-needle aspiration of histiocytic necrotizing lymphadenitis (Kikuchi's disease). Diagn Cytopathol 1993; 9: 448-452.

[11] Mannara GM, Boccato P, Rinaldo A, La Rosa F and Ferlito A. Histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto disease) diagnosed by fine needle aspiration biopsy. ORL J Otorhinolaryngol Relat Spec 1999; 61: 367-371.

[12] Koss LG. Utility of liquid-based cytology for cervical carcinoma screening. Cancer 2000; 90: 67-69.

[13] Sherman ME, Mendoza M, Lee KR, Ashfaq R, Birdsong GG, Corkill ME, McIntosh KM, Inhorn SL, Zahniser DJ, Baber G, Barber C and Stoler MH. Performance of liquid-based, thin-layer cervical cytology: correlation with reference diagnoses and human papillomavirus testing. Mod Pathol 1998; 11: 837-843.

[14] Hutchinson ML, Zahniser DJ, Sherman ME, Herrero R, Alfaro M, Bratti MC, Hildesheim A, Lorincz AT, Greenberg MD, Morales J and Schiffman M. Utility of liquid-based cytology for cervical carcinoma screening: results of a population-based study conducted in a region of Costa Rica with a high incidence of cervical carcinoma. Cancer 1999; 87: 48-55.

[15] Rossi ED, Martini M, Capodimonti S, Lombardi CP, Pontecorvi A, Vellone VG, Zannoni GF, Larocca LM and Fadda G. BRAF (V600E) mutation analysis on liquid-based cytology-processed aspiration biopsies predicts bilaterality and lymph node involvement in papillary thyroid microcarcinoma. Cancer Cytopathol 2013; 121: 291-297.

[16] Garbar C, Remmelink M and Mascaux C. Fine needle aspiration cytology of lymph node: experience of 2 university hospitals with conventional smears and liquid-based cytology. Acta Cytol 2008; 52: 418-423.