

Original Article

Aberrant phenotypes in Kikuchi's disease

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Abstract: Initial reports emphasized the immunophenotypic similarities between benign and malignant T cell populations, while some previous studies indicating that aberrant T-cell antigen loss is a good marker for detecting malignant T-cell proliferation. Recently, we found a very interesting and thought-provoking phenomenon: In benign disease-28 of 38 (73.7%) cases of Kikuchi's disease also showed aberrant phenotypes with loss of pan-T cell antigens, which makes the differential diagnosis between Kikuchi's disease and T cell lymphoma more challenging. In our study, 38 cases of Kikuchi's disease and 30 cases of reactive lymphoid hyperplasia (RLH) were studied by EliVision immunohistochemical staining. As well as TCR gene rearrangement using PCR was negative in 10 tested cases of the Kikuchi's disease. Among these cases, the most common antigen deficiency was CD5 (22 cases), then CD7 (11 cases), CD2 (8 cases) and CD3 (2 cases). Compared with proliferative and xanthomatous types of Kikuchi's disease, antigens tended to be lost in necrotizing type. Based on follow-up data, a correlation was not found between the occurrence of aberrant phenotypes and prognosis. In RLH, obvious pan-T cell antigen loss was also not found. In conclusion, this is the first study to demonstrate distinct patterns of antigen loss in Kikuchi's disease, suggesting that T cell antigen loss is not reliable as an auxiliary diagnostic standard for T cell lymphoma.

Keywords: Kikuchi's disease, histiocytic necrotizing lymphadenitis, T cell lymphoma, pan-T cell antigens, differential diagnosis

Introduction

Up till the present moment, we focus mainly on the tumor diseases, in fact, non-neoplastic diseases also have research value and can not be replaced, especially when these two kinds of disease difficulties in the differential diagnosis. As T cell lymphomas are much less common than B cell malignancies, few comprehensive studies have been made. The good news is recent studies have suggested that the expression of aberrant T cell phenotypes, that is, four pan-T cell antigens, CD2, CD3, CD5 and CD7 lost in malignant T cell proliferations and thus may help to differentiate between benign and malignant disease [1-8].

However, in the premalignant disease - lymphomatoid papulosis (LyP) also existed the loss of pan-T cell antigens [9]. Whether other benign lymphoid diseases appear antigen loss phenomenon? To date, abnormal T-cell antigen expression in benign lymphadenopathies has never been documented. In our study, we intermittently found T cell antigen loss in cases of

Kikuchi's disease. This is the first study to demonstrate distinct patterns of antigen loss in Kikuchi's disease.

We studied 38 cases of Kikuchi's disease and 30 cases of RLH by EliVision immunohistochemical staining to evaluate T cell antigen loss situation and to verify the effectiveness which as an auxiliary diagnosis index to the T cell malignant lymphoma. Since the disease with loss of antigens, whether it can be similar to lymphoma with clonal expression? In keeping with this hypothesis, these diseases were verified by PCR to be polyclonal.

Material and methods

Subjects

Thirty-eight cases of Kikuchi's disease were chosen for study and biopsies from the department of pathology in Beijing Friendship Hospital between April 2007 and February 2012. Study inclusion was based on definite diagnosis and the integrity of clinical data. In addition, 30 cases of RLH were included as a control group.

Pan-T-cell antigens lost in Kikuchi's disease

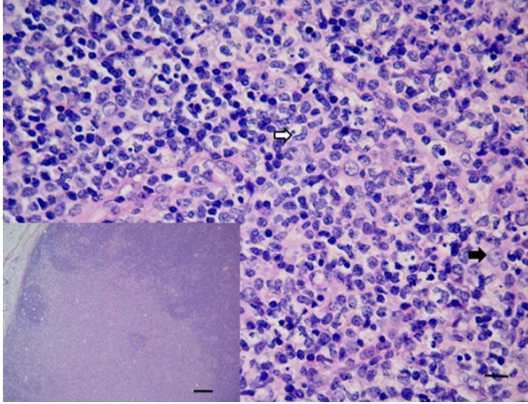


Figure 1. Lymph node, cryostat section. At low power, patchy pale lesions of histiocytic necrotizing lymphadenitis are observed in the paracortical area of the node (Bar = 100 μ m). At higher magnification, lesions are composed of histiocytes with round or irregular nuclei with associated characteristic karyorrhectic debris (white arrow). Immunoblastic cells are present (black arrow) with diffuse proliferation of transformed lymphocytes (Bar = 50 μ m).

Immunohistochemistry and clinical scoring

Biopsies were routinely processed, formalin-fixed, paraffin-embedded and continuous sectioned at 3 μ m thickness. Sections were stained with the following monoclonal antibodies: anti-CD3 (1:100; clone SP7), anti-CD2 (1:40, clone AB75), anti-CD5 (clone 4C7), anti-CD7 (clone 7C03), anti-CD20 (1:200, clone L26), anti-CD68 (1:30, clone TGB04 + TGB05), anti-Ki-67 (1:200, clone MIB-1), anti-CD163 (1:100, clone 10D6), anti-CD123 (1:100; clone BR4MS). Antigen retrieval was performed by boiling in EGTA, pH 9. All antibodies were purchased from Maixin, Fuzhou, China. At the same time with the substitution of PBS as negative control.

Formalin-fixed RLH serial sections were immunostained for CD2, CD3, CD5 and CD7 as a positive control. Serial sections were immunostained for CD2, CD3, CD5 and CD7 in the same lesion area, and a scoring system was established to evaluate size, number, and cellular density of T cell clusters, which were semiquantitatively graded in each microscopic field at 400 \times magnification (negative, +, ++, and +++). The following scores were assigned: < 5% positive cells were negative, \geq 5% positive cells were positive, 5-25% positive cells were +, 26-50% positive cells was ++ and > 50% positive cells were +++. Among which, + and ++

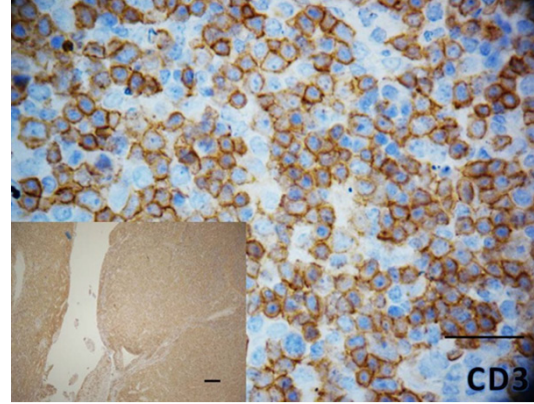


Figure 2. Immunohistochemical staining of Kikuchi's disease. The majority of lesional cells are positive for CD3 in a low-power view (Bar = 100 μ m). At higher magnification, 80% of lesional cells are positive for CD3 (Bar = 50 μ m).

were considered as T cell antigen loss (-) and +++ was considered as no antigen loss (+).

Analysis of clonal gene rearrangement

Take 4~8 paraffin sections of 5~10 μ m thick, dewaxed by xylene and then extract DNA. Using BIOMED-2 multiplex PCR amplification system to carry on TCRB, TCRG and TCRD gene rearrangement. PCR amplification was adopted 25 μ l reaction system, among which including the template DNA 1~5 μ l, four kinds of dNTP 0.1 mmol/L, primer 1 mmol/L, Taq enzyme 0.5 U. Through 10% polyacrylamide gel electrophoresis and ethidium bromide staining, the 5~10 μ l PCR products were observed under UV penetration colorimeter. Thereinto, β 2 globin primer as internal control, the PCR amplified products of the reactive lymphoid hyperplasia DNA and the template-free DNA as negative control, the lymphoma tissue sample known in advance have monoclonal rearrangement as positive control.

Statistical analysis

Data were analyzed using continuity correction χ^2 tests with SPSS 16.0 software.

Results

Clinical features

Among the 38 cases of Kikuchi's disease, patients included 22 females and 16 males with a mean age of 24.6 years (median = 23

Pan-T-cell antigens lost in Kikuchi's disease

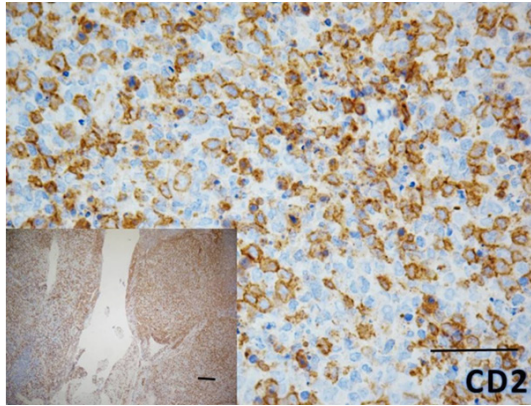


Figure 3. Immunohistochemical staining of Kikuchi's disease. The majority of lesional cells are positive for CD2 in a low-power view (Bar = 100 μ m). At higher magnification, 60-70% of lesional cells are positive for CD2 (Bar = 50 μ m).

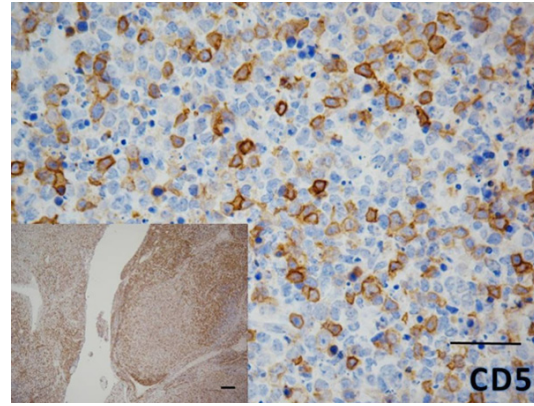


Figure 4. Immunohistochemical staining of Kikuchi's disease. The majority of lesional cells are negative for CD5 in a low-power view, but lymphocytes are positive for CD5 around the lesions (Bar = 100 μ m). At higher magnification, 30-40% of lesional cells are positive for CD5 (Bar = 50 μ m).

years; range, 4-53 years). Based on clinical information, all 38 patients presented with persistent fever and lymph node enlargement, 30 patients experienced body temperatures higher than 39°C and six patients between 38-39°C with fever durations between 10 days to 2 months, with a mean time of 26.5 days and a median time of 28 days. The sites of involvement included cervical lymph nodes (33 cases), supraclavicular lymph node (one case), hilar lymph node (one case), submaxillary lymph nodes (one case), celiac lymph node (one case), axillary lymph node (one case). All 30 cases of RLH involvement sites were cervical lymph nodes.

Morphological features

Morphological findings from all 38 cases were similar and characterized by nodal paracortical and cortical patchy lesions with karyorrhectic nuclear debris and associated mononuclear cell response composed of histiocytes, lymphoid cells, and a large population of mononuclear cells with plasmacytoid (**Figure 1**). The presence of plasma cells and neutrophils is not a feature of Kikuchi's disease. Although the cellular composition of lesions varied depending on the age of the lesion, karyorrhectic debris and numerous mononuclear cells were identified in all lesions, some of which were extensive. The latter included phagocytic (tingible body macrophages) and non-phagocytic (crescentic) mononuclear cells, as well as foamy cells, plasmacytoid mononuclear cells, and

small and larger lymphocytes. In four cases, lesional cells extended into the perinodal fibroadipose tissue. Furthermore, we divided the 38 patients into three pathologic types: proliferative (PT) type, necrotizing (NT) type and xanthomatous (XT) type, according to the histological features described by Kuo [10]. Approximately 80% of cases were in both PT and NT types. Among these cases, NT types were 60.5% (23 cases), PT types were 31.6% (12 cases) and XT types were 8% (three cases).

Immunohistochemical and PCR features

In all Kikuchi's disease cases, T cells strongly expressed CD3 and were negative for CD20 and macrophage-associated markers. CD2, CD5 and CD7 expression varied among cases. A relatively similar distribution pattern of CD68, MPO and CD163 expression was observed in all cases, which identified a population of macrophages (70-100%). Plasmacytoid mononuclear cells were positive for CD123. Ki-67 expression was dependent on the age of the lesion, which was diffusely detected in 50-80% of surrounding lesional cells. The amplification gene TCRB, TCRG and TCRD of ten cases of Kikuchi's disease, in the relevant position of BIOMED-2 PCR receptor gene rearrangement primers designed system did not appear positive bands, indicates that no clonal rearrangement.

Lost or deficient expression of pan-T cell antigens was observed in 28/38 cases (73.7%). The most common T-cell antigen lost was CD5

Pan-T-cell antigens lost in Kikuchi's disease

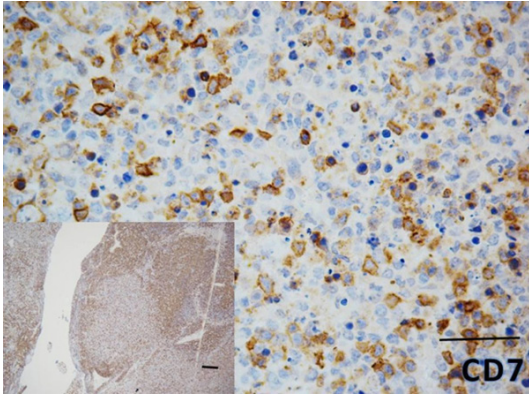


Figure 5. Immunohistochemical staining of Kikuchi's disease. Immunostaining the same lesion area of the same case shows lesional cells are infrequently positive for CD7, indicating antigen lost (Bar = 100 μ m). At higher magnification, lesional cells positive for CD7 are obviously decreased compared with that of CD3 and CD2 positive cells (Bar = 50 μ m).

(14/28 cases, 50%), including CD5+ for eight cases, CD5++ for six cases, followed by loss of CD7 (2/28 cases, 7%) with CD7+, then loss of CD2 (1/28 cases, 4%) with CD2++. There was also loss of CD2 and CD7 (2/28 cases, 7%) with CD2++ and CD7++, lack of CD5 and CD7 (4/28 cases, 14%) with CD5+ and CD7+, lack of CD2 and CD5 (2/28 cases, 7%), with CD2++ and CD5+, lack of CD2, CD7 and CD5 (1/28 cases, 4%), with CD2++, CD7++ and CD5+, lack of CD2, CD5 and CD7 and partial loss of CD3 (2/28 cases, 7%), with CD2++, CD3++, CD5+ and CD7++ (**Figures 2-6**). Among these cases, the most common aberrant pattern of T-cell antigen loss was CD5 (23 cases), then CD7 (11 cases), CD2 (8 cases) and CD3 (two cases). Among the 38 cases of Kikuchi's disease, 22/23 cases were in NT types, 5/12 cases were in PT types and lost one or more antigens, three cases in XT types and only one case loss CD5. Statistical analysis revealed a significant difference between lost expression of pan-T cell antigens and histological phase-NT ($P = 0.027$, Fisher exact probability test), namely the loss of pan-T cell antigens mostly in NT types. In the RHL control, there was no significant difference of CD2, CD3, CD5 and CD7 expression.

Two groups of comparisons

Statistical analysis revealed a highly significant difference between the 38 cases of Kikuchi's disease and 30 cases of RHL ($P < 0.05$) for antigen loss, further confirming the significance of

detecting the loss of pan-T cell antigens in Kikuchi's disease.

Follow-up results

More than 28 cases (80%) were followed up after 2 months to 4 years, including the 23 cases with lost pan T-cell antigens. Among them, two cases (subjects 5 and 9) underwent recurrence after 2 years, after spontaneous remission lasting one month, another case (subject 22) experienced seven months protracted course of disease and underwent hormone therapy. The remaining 25 cases (71.4%) did not undergo recurrence. Interestingly, the two cases of recurrence both demonstrated lost CD5 expression, while the other did not lose antigen expression. The remaining cases with antigen loss showed a good prognosis without relapse. We also analyzed whether antigen loss was related to recurrence. Using the Fisher exact probability test with $P = 0.459$, we found that Kikuchi's disease prognosis was independent of antigen loss.

Discussion

A great deal progress has been made in the characterization of CD2, CD3, CD5 and CD7 as pan-T cell antigens, pan-T cell antigens are expressed in normal and peripheral mature T cells, except for CD7 sometimes can loss [11]. Weiss et al. [8] first studied aberrant T-cell phenotypes, and additional studies have suggested an aberrant T-cell immunophenotype that involves the absence of one or more mature T-cell-associated antigens, such as CD1, CD2, CD3, CD5, CD7 CD4 and CD8 [1-8]. Deficient expression of T-cell antigens, morphological changes and clinical features may help to differentiate between benign and malignant disease. Thus, the demonstration of an aberrant phenotype is a valuable supplement to histological assessment to diagnose peripheral T cell lymphoma. However, Varga [9] found that LyP, a disease with benign clinical process and pathological form, also shows diminished expression of CD7 and at least one other T-cell antigen. Clinical follow-up demonstrated that LyP has a 5-20% risk of associated lymphoid malignancy as "pre-cancerous lesions" of the lymphomas [5]. It is still unknown whether antigen loss is similar to that of benign proliferative diseases.

Pan-T-cell antigens lost in Kikuchi's disease

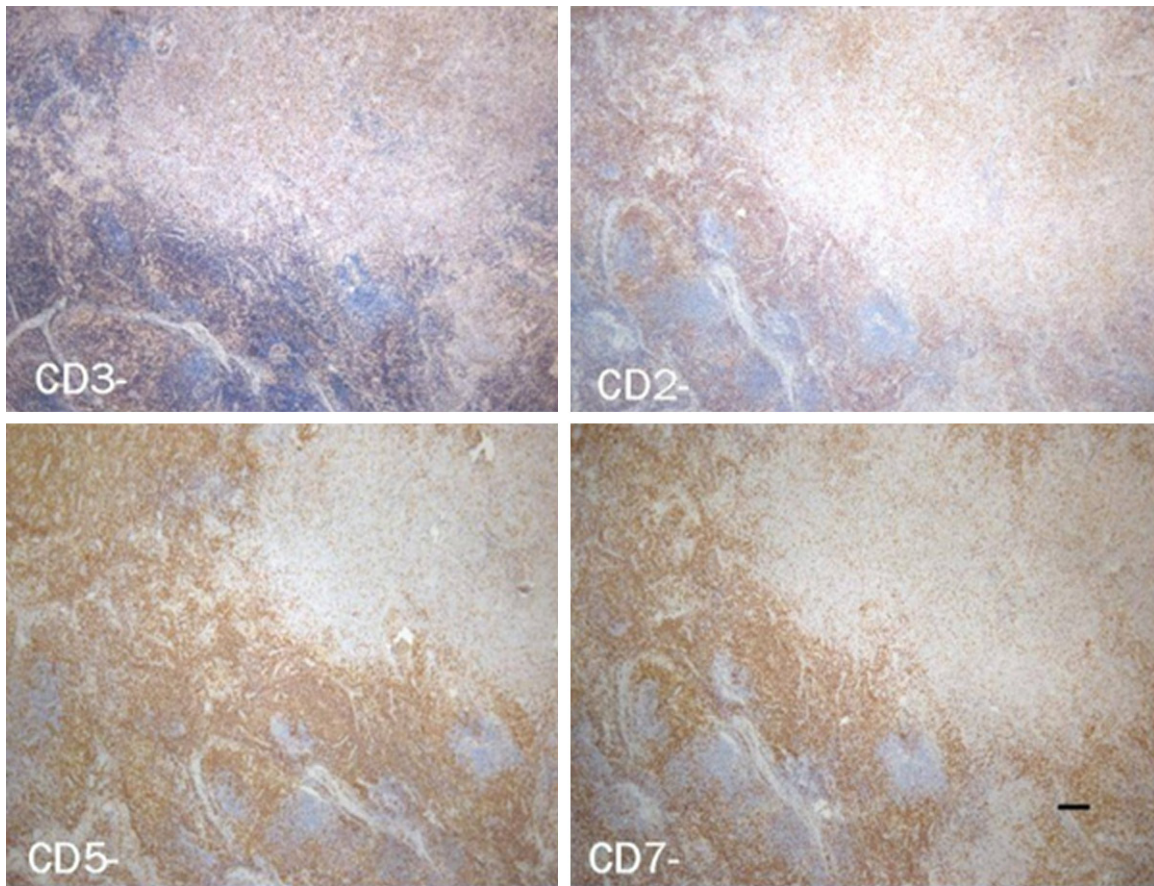


Figure 6. Immunohistochemical staining of Kikuchi's disease. Around lesions, lymphocytes are diffuse and positive for T cell antibodies as an internal control. In contrast, lesional cells of the same case are scattered and negative for CD2, CD3, CD5 and CD7, indicating antigen loss (Bar = 100 μ m).

Kikuchi's disease is a histiocytic necrotizing lymphadenitis and self-limited benign lymphadenopathy with associated fevers and systemic symptoms. It commonly affects Asian adults younger than 40 years of age. Most cases of Kikuchi's disease are diagnosed by typical histological appearance, clinical manifestation and expression of CD68, CD163, MPO and CD123. However, this disease is heterogeneous and frequently presents with diagnostic problems such as distinction from T cell lymphomas. Therefore, a differential diagnosis from lymphoma may be particularly difficult, and some cases of Kikuchi's disease have been misdiagnosed as large cell lymphoma because of atypical features of large lymphoid cells [12, 13]. In the first diagnosis, nearly 60% of Kikuchi's disease cases have been considered as malignant lymphoma according to statistics in Britain, and the misdiagnosis rate is 40% [14]. Because there are fundamental differences between the treatment and prognosis

of malignant lymphoma and other lymph node inflammatory diseases, correct diagnosis is very important.

When Kikuchi's disease and T cell lymphoma are difficult to identify by morphology, pathologists may use diminished expression of T cell antigens to differentially diagnose those lesions. The loss of antigens in one case of Kikuchi's disease led us to further investigate T cell antigen loss in Kikuchi's disease. Therefore, we performed immunohistochemical staining of 38 cases of Kikuchi's disease and 30 cases of RLH to evaluate the significance of T cell antigen loss as an auxiliary diagnosis index.

Statistical analysis showed significant differences between the 38 cases of Kikuchi's disease and 30 cases of RHL (all $P < 0.05$) and confirmed that Kikuchi's disease shows aberrant pan-T cell antigens loss. Among these cases, the most common pan-T cell antigen

Pan-T-cell antigens lost in Kikuchi's disease

lost was CD5 (23 cases), then CD7 (11 cases), CD2 (eight cases) and CD3 (two cases). Obvious antigen loss was not detected in the control group.

Hastrup et al. [1] used CD1, CD2, CD3, CD5, CD6, CD7, CD27, CD45RO, CD4 and CD8 to study the loss of T cell antigens in T cell lymphoma, and found that loss of CD7 and loss of three or more pan T-cell antigens were the most common phenotypic abnormalities. CD7 was the most frequent antigen to be reported as lost, followed by CD5. Antigen loss was not significantly associated with the lymphoma histologic type [1]. Similar results have been reported by Al Shanqeety et al. [3], loss of CD2, CD3, CD5 and CD7 was a useful method to diagnose T cell lymphoma, with CD7 or CD7 and CD5 as the most common antigens lost [2]. In our study, the most common abnormality was an absence of CD7, followed by CD5 and CD3, CD2 was the least common antigen to be lost, which is supported by previous reports on T-cell lymphoma [15]. In contrast to previous findings [1-8], in our study, loss of CD7 was observed in only 11 cases, while loss of CD5 was observed in 23 cases. Considering these controversial results concerning antigen loss, we hypothesized that could contribute to the special expression of CD7, which in skin hyperplastic lesions (benign and malignant) does not express [16, 17]. The lesion location of Kikuchi's disease was consistently within the lymphonodes, which may account for the somewhat lower incidence of aberrant CD7 phenotypes observed in our study.

Agnarsson et al. [2] found that CD2 (-) CD7 (+) T-cell lymphoma shows a poorer prognosis than CD2 (+) CD7 (-) T-cell lymphoma. In contrast, our statistical analysis showed there was no immediate relation between antigen loss and prognosis. Based on follow-up data, despite two recurrent cases with CD5 absence, the remaining cases showed loss of CD5 or other antigens and a favorable prognosis without relapse. The patient who underwent hormone therapy didn't loss antigens. Hastrup et al. [1] found that antigens loss is not significantly associated with the lymphoma histological type. While, as we referred above, Kikuchi's disease tends to be misdiagnosed as T-cell lymphoma, hence which was classified based on the method by Kuo et al. [10] to explore the relevance between antigens loss and disease

classification. With the result that antigens loss most commonly found in NT type, PT and XT types without obvious antigen loss. Our study shows that caution should be used during differential diagnosis of T-cell lymphoma and the NT type of Kikuchi's disease, because both diseases involve pan-T cell antigens loss. Therefore, diagnosis should be combined with immunohistochemical staining and clinical history. Only the stability of immunohistochemical staining with comparability is the premise of the experiment. We used serial tissue sections of the reactive hyperplasia lymph node to immunostain for CD2, CD3, CD5 and CD7, to ensure the method was a stable staining technique.

To our knowledge, the expression patterns of pan-T cell antigens in Kikuchi's diseases are not fully characterized. This is the first study to demonstrate distinct patterns of antigen loss in Kikuchi's disease. Our findings show that pan-T cell antigen loss in the lymphatic benign lesion is particularly widespread in NT type of Kikuchi's diseases. Therefore, demonstration of aberrant T cell phenotypes may be a useful supplement to diagnose T cell lymphoma with some potential limitations. We conclude that analysis of the loss of T cell antigen expression cannot separate these two disorders and should be used with caution to identify benign and malignant T cell lesions. Clinical and morphologic features, particularly the presence of abundant karyorrhectic debris along with a paucity of granulocytes, as well as immunohistochemical studies such as the number and growth pattern of plasmacytoid dendritic cells vary to rule out lymphoma, are most helpful in establishing the correct diagnosis. CD123 is a very important auxiliary diagnostic index for Kikuchi's diseases. Kishimoto et al. [18] counted the number of CD123-positive plasmacytoid mononuclear cells (pDCs) in Kikuchi's diseases, RHL, T and B cell lymphomas and Hodgkin's lymphoma to reveal that pDCs more frequently infiltrated Kikuchi's disease with 23.3% compared with those of the other diseases with a mean below 4%. Interestingly, the number of pDCs didn't depend on the age of the Kikuchi's diseases, suggesting that pDCs are excellent indicators for cytologic diagnosis of Kikuchi's disease [18]. Although Kikuchi's disease is a frequent disease, the study of T cell antigens loss can provide useful insights into the differential diagnosis, further research with more patients

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be necessary for the early, no-invasive, and definitive diagnosis for Kikuchi's disease.

Disclosure of conflict of interest

None.

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References

- [1] Hastrup N, Ralfkiaer E and Pallesen G. Aberrant phenotypes in peripheral T cell lymphomas. *J Clin Pathol* 1989; 42: 398-402.
- [2] Agnarsson BA, Vonderheid EC and Kadin ME. Cutaneous T cell lymphoma with suppressor/cytotoxic (CD8) phenotype: identification of rapidly progressive and chronic subtypes. *J Am Acad Dermatol* 1990; 22: 569-577.
- [3] Al Shanqeety O and Mourad WA. Diagnosis of peripheral T-cell lymphoma by fine-needle aspiration biopsy: a cytomorphologic and immunophenotypic approach. *Diagn Cytopathol* 2000; 23: 375-379.
- [4] Borowitz MJ, Reichert TA, Brynes RK, Cousar JB, Whitcomb CC, Collins RD, Crissman JD and Byrne GE Jr. The phenotypic diversity of peripheral T-cell lymphomas: the Southeastern Cancer Study Group experience. *Hum Pathol* 1986; 17: 567-574.
- [5] Jamal S, Picker LJ, Aquino DB, McKenna RW, Dawson DB and Kroft SH. Immunophenotypic analysis of peripheral T-cell neoplasms. A multiparameter flow cytometric approach. *Am J Clin Pathol* 2001; 116: 512-526.
- [6] Nasu K, Said J, Vonderheid E, Olerud J, Sako D and Kadin M. Immunopathology of cutaneous T-cell lymphomas. *Am J Pathol* 1985; 119: 436-447.
- [7] Picker LJ, Weiss LM, Medeiros LJ, Wood GS and Warnke RA. Immunophenotypic criteria for the diagnosis of non-Hodgkin's lymphoma. *Am J Pathol* 1987; 128: 181-201.
- [8] Weiss LM, Crabtree GS, Rouse RV and Warnke RA. Morphologic and immunologic characterization of 50 peripheral T-cell lymphomas. *Am J Pathol* 1985; 118: 316-324.
- [9] Varga FJ, Vonderheid EC, Olbricht SM and Kadin ME. Immunohistochemical distinction of lymphomatoid papulosis and pityriasis lichenoides et varioliformis acuta. *Am J Pathol* 1990; 136: 979-987.
- [10] 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.
- [11] Jaffe ES, Harris N and Stein H. World Health Organization classification of tumour. Pathology and genetics of tumours of hematopoietic and lymphoid tissues. Lyon: IARC press; 2001. pp. 190-235.
- [12] Good DJ and Gascoyne RD. Atypical lymphoid hyperplasia mimicking lymphoma. *Hematol Oncol Clin North Am* 2009; 23: 729-745.
- [13] Hutchinson CB and Wang E. Kikuchi-Fujimoto disease. *Arch Pathol Lab Med* 2010; 134: 289-293.
- [14] Menasce LP, Banerjee SS, Edmondson D and Harris M. Histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto disease): continuing diagnostic difficulties. *Histopathology* 1998; 33: 248-254.
- [15] Shu-hong Z, Xiao-ge Z, Yuan-yuan Z, Yan-ning Z and Shou-Fang H. CD2, CD3, CD5 and CD7 expression in unspecified peripheral T cell lymphoma and reactive lymphoid hyperplasia. *Chinese Journal of Diagnostic Pathology* 2007; 14: 98-100.
- [16] Davis AL, McKenzie JL and Hart DN. HLA-DR-positive leucocyte subpopulations in human skin include dendritic cells, macrophages, and CD7-negative T cells. *Immunology* 1988; 65: 573-581.
- [17] Foster CA, Yokozeki H, Rappersberger K, Koning F, Volc-Platzer B, Rieger A, Coligan JE, Wolff K and Stingl G. Human epidermal T cells predominantly belong to the lineage expressing alpha/beta T cell receptor. *J Exp Med* 1990; 171: 997-1013.
- [18] Kishimoto K, Tate G, Kitamura T, Kojima M and Mitsuya T. Cytologic features and frequency of plasmacytoid dendritic cells in the lymph nodes of patients with histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto disease). *Diagn Cytopathol* 2010; 38: 521-526.