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LETTER TO THE EDITOR

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Cytological features and immunohistochemical findings related to lymphomatous effusion in an angioimmunoblastic T-cell lymphoma patient: Case report

To the Editor,

The course of an angioimmunoblastic T-cell lymphoma (AITL) is diverse, but overall, it is aggressive and has a poor prognosis.[1] Serous effusions, including pleural, pericardial, and peritoneal effusions, are a common condition in patients with a malignant lymphoma.[2] It has also been reported that a patient with AITL experienced pleural effusions before biopsy lesions were found.[3] It is a general belief that immunohistochemical analysis with a cell block technique is usually effective for the diagnosis of malignant lymphoma in serous effusions. However, to the best of our knowledge, cytological features and immunohistochemical findings related to lymphomatous effusion caused by AITL are not well known.

A 67-year-old woman complained of cough, sputum, and left shoulder to back pain, and was referred to our hospital because of suspected pneumonia. One month later, severe malaise and swelling of the cervical, axillary, and inguinal lymph nodes were observed. The serum level of soluble interleukin-2 receptor was as high as 2030 U/ml, and computed tomography revealed generalized lymphadenopathy. A cervical lymph node biopsy showed that medium-sized to large atypical lymphoid cells with a clear cytoplasm proliferated with effacement of normal architecture (Figure 1A,B). Vascular proliferation with endothelial cell swelling and foci of plasma cell infiltration was also observed. Immunohistochemically, atypical lymphoid cells were positive for CD3 (Figure 1C) and negative for CD20 (Figure 1D). In addition, atypical lymphoid cells stained with follicular helper T (TFH) cell markers, such as CD10 (Figure 1E), programmed death receptor-1 (PD-1) (Figure 1F) and BCL6, were observed. CXCL13 was partially positive (Figure 1G) and ICOS was negative for these cells. A small number of lymphoid cells were positive for EBV by in-situ hybridization for EBV-encoded RNA (EBER) (Figure 1H). Marked proliferations of follicular dendritic cell meshwork with immunoreactivity for CD21 (Figure 1I) were observed entrapping the blood vessels. The patient was diagnosed with AITL.

Chest computed tomography performed 12 days after a cervical lymph node biopsy revealed abundant pleural effusions on both sides. A cytological examination of the right pleural effusion showed atypical lymphoid cells mixed in many plasma cells, histiocytes, and mesothelial cells (Figure 2A). The atypical lymphoid cells were medium-sized to large with prominent nucleoli (Figure 2B). May-Grünwald-Giemsa staining also showed atypical lymphoid cells with irregular shaped nuclei and basophilic cytoplasm (Figure 2C). There were various cells consisting of plasma cells, histiocytes, mesothelial cells, and immunoblastic cells in the background. The cytologic findings indicated a progression of malignant lymphoma into the thoracic cavity, although the subtype with AITL could not be confirmed. We subjected the pleural effusion to immunohistochemical analysis. Cell block sections prepared from the right pleural effusion revealed that lymphoid cells with irregular shaped nuclei presented with plasma cells, histiocytes, and mesothelial cells (Figure 3A). Atypical lymphoid cells were almost all immunoreactive for CD3 (Figure 3B) and also positive for TFH-cell markers CD10 (Figure 3D), PD-1 (Figure 3E), CXCL13 (Figure 3F) and BCL6. The expression of CXCL13 had a perinuclear dot-like pattern in a small number of atypical lymphoid cells. CD20 was negative for atypical lymphoid cells (Figure 3C), although it was considered positive for immunoblastic cells. A few lymphoid cells were seen that were positive for EBV by in situ hybridization for EBER. The patient was diagnosed with pleural effusion due to the involvement of AITL. THP-COP therapy consisting of pirarubicin (tetrahydropyranyl adriamycin), cyclophosphamide, vincristine, and prednisolone was employed. As a result, the lymph nodes shrank, and the pleural effusion disappeared in computed tomography.

With our AITL patient, the diagnosis of lymphomatous pleural effusion was easily and rapidly realized with cytology and immunohistochemical analysis using cell block sections. Patients with lymphomatous effusion of diffuse large B-cell lymphoma, which was the most common malignant lymphoma, have a poor prognosis.[4] Clarifying whether the serous effusion that develops in malignant lymphoma is reactive or neoplastic is of critical importance. Although detailed cytologic findings of lymphomatous effusion induced by AITL have not been widely reported, Yamagata et al. described the appearance of plasma cells showing several cell sizes or two nuclei in a pleural effusion.[5] However, no atypical plasma cells were found in this patient. The characteristic morphology and expression of TFH-cell markers are

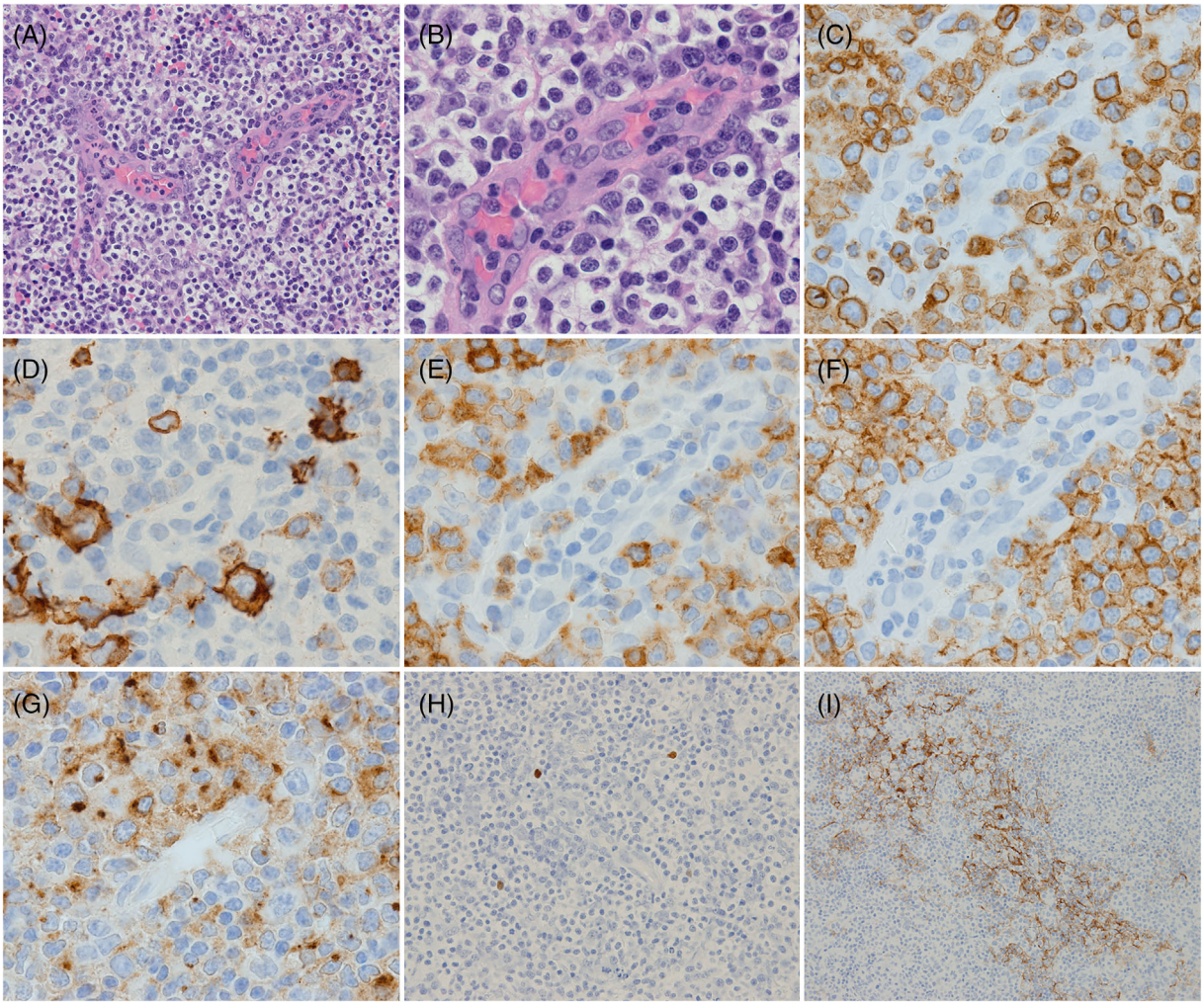

FIGURE 1 Images of cervical lymph node biopsy. (A) Atypical lymphoid cells were aggregated surrounding blood vessels with swollen endothelial cells. (B) Medium-sized to large lymphoid cells with abundant clear cytoplasm were seen (hematoxylin–eosin staining). CD3 (C) was positive and CD20 (D) was negative for atypical lymphoid cells. The immunophenotype of T follicular helper cells, CD10 (E) and programmed death receptor-1 (F), were positive for atypical lymphoid cells. CXCL13 (G) was also partially positive with perinuclear dot-like pattern. (H) A small number of EBV-positive lymphoid cells were observed with EBER in situ hybridization. (I) The CD21 positive follicular dendritic cell meshwork was expanding. A, H, ×400; B–G, ×1000; I, ×200 [Color figure can be viewed at wileyonlinelibrary.com]

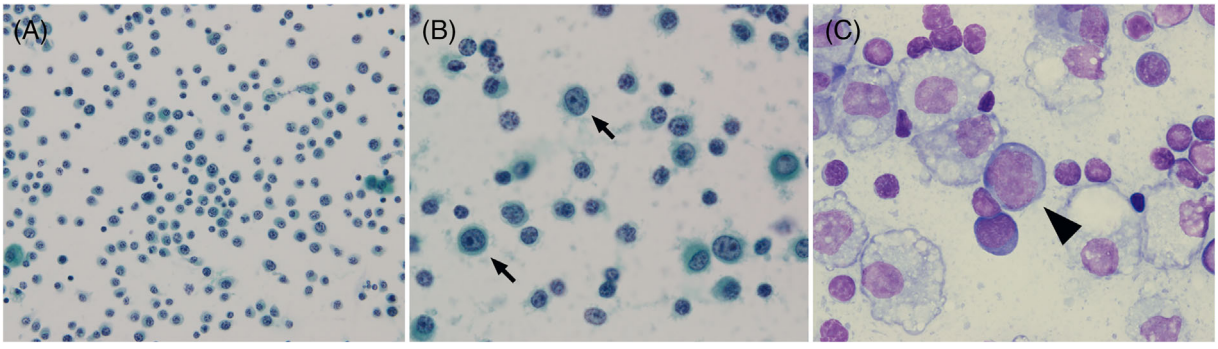

FIGURE 2 Images of pleural effusion cytology. (A) Papanicolaou stain showed atypical lymphoid cells that were present with plasma cells, histiocytes, and mesothelial cells in the background. (B) Medium-sized to large lymphoid cells had prominent nucleoli (arrows). (C) May-Grünwald-Giemsa stain showed irregular shaped nucleus and basophilic cytoplasm (arrowhead). A, ×400; B, C, ×1000 [Color figure can be viewed at wileyonlinelibrary.com]

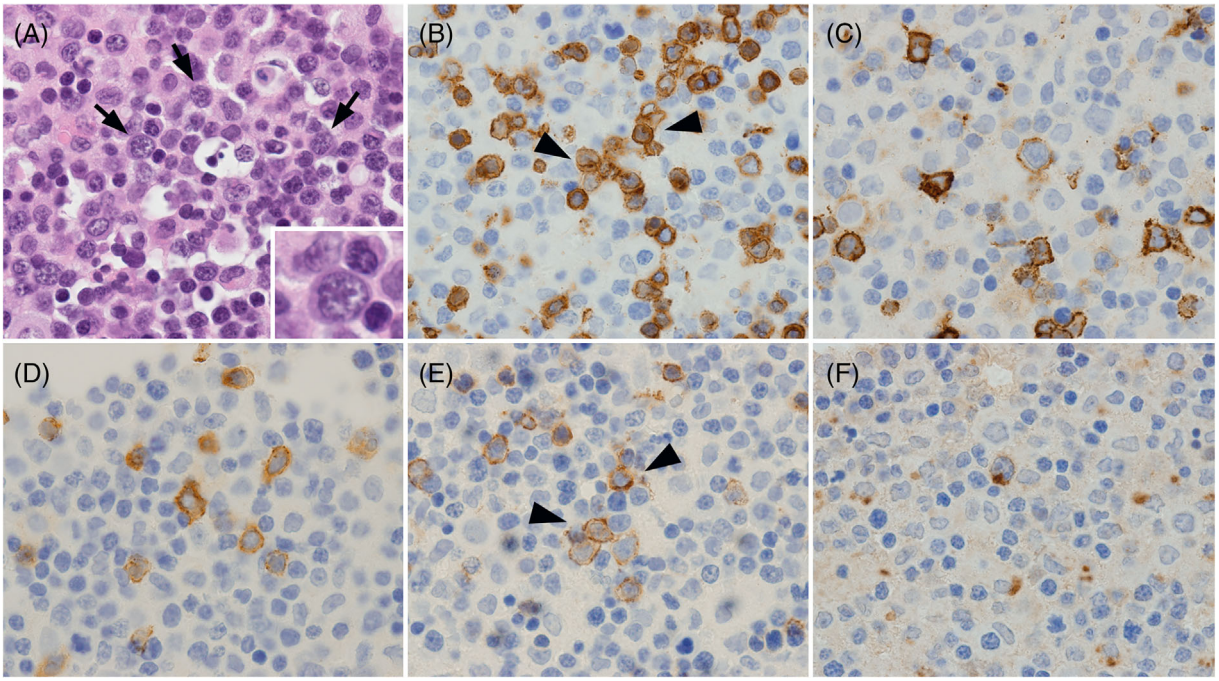

FIGURE 3 Images of cell block sections prepared from the pleural effusion. (A) Lymphoid cells, plasma cells, histiocytes, mesothelial cells and a few atypical lymphoid cells (arrows) were observed (hematoxylin–eosin staining). CD3 (B) was positive for atypical lymphoid cells (arrowheads). CD20 (C) was negative for atypical lymphoid cells, but positive for immunoblastic cells. T follicular helper cells markers, CD10 (D), programmed death receptor-1 (arrowheads) (E) and CXCL13 (F) were positive for atypical lymphoid cells. CD3 (B) and programmed death receptor-1 (E) was demonstrated in the same area in serial sections. A–F, ×1000 [Color figure can be viewed at wileyonlinelibrary.com]

useful for histologic diagnosis.[1] In particular, PD-1 with high sensitivity and CXCL13 with high specificity were useful immunophenotypic markers of neoplastic T cells in AITL.[1,6] In contrast, there were no reports of AITL lymphomatous effusion diagnosed by cell block immunohistochemistry. Our findings related to atypical lymphoid cells immunoreactivity for TFH-cell markers on the cell block sections, and our cytologic findings, were useful for the definitive diagnosis of lymphomatous effusion caused by AITL.

We here report cytological features and immunohistochemical findings of lymphomatous pleural effusion in a patient with AITL.

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CONFLICT OF INTEREST

There are no conflicts of interest regarding the publication of this article.

AUTHOR CONTRIBUTIONS

Haruka Furumai and Kazuyuki Ishida were responsible for the acquisition and interpretation of patient data and manuscript preparation. Yoshimasa Nakazato and Hiromi Machida critically revised the manuscript. Hikaru Kato, Tamiko Nagai, and Hideo Sasaki performed cytological diagnosis and immunohistochemical analyses. Atsuko Takada-Owada and Yuko Kaneko performed cytological diagnoses, histological diagnoses, and immunohistochemical analyses. All the authors approved the final manuscript.

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