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-1예 보고-

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Cytologic Features of Ascitic Fluid Complicated by Small Cell Variant T-cell Prolymphocytic Leukemia -A Case Report-

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T-cell prolymphocytic leukemia (T-PLL) is a rare, mature T-cell lymphoproliferative disorder with a post-thymic mature T-cell phenotype. The disease is characterized by rapidly rising lymphocytosis, lymphadenopathy, and splenomegaly. The clinical course is usually aggressive and progresses with frequent skin lesions and serous effusions. In 25% of cases, leukemic cells are small and tumor cells may not have a discrete nucleolus under light microscopy. Although the presence of characteristic cytoplasmic protrusions or blebs in tumor cells is a common morphologic finding in the peripheral blood film irrespective of the nuclear features, small cell variants lacking the typical nuclear features can cause diagnostic problems in clinical cytology. Furthermore, the small leukemic cells can share some cytologic findings with lymphocyte-rich serous effusions caused by non-neoplastic reactive lymphocytosis as well as other small lymphocytic lymphoproliferative disorders. Here, we describe the cytological findings of ascitic fluid complicated by small cell variant T-PLL in a 54-year-old man, the cytology of which was initially interpreted as small lymphocytic malignancy such as small lymphocytic lymphoma/chronic lymphocytic leukemia.

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Key Words : Leukemia, Prolymphocytic, T-cell, Cytology, Ascitic fluid

INTRODUCTION

T-cell prolymphocytic leukemia (T-PLL) is an aggressive mature T-cell lymphoproliferative disorder (LPD) characterized by proliferation of small-to-medium prolymphocytes with a post-thymic T-cell phenotype, and most patients present with rapidly rising lymphocytosis, hepatosplenomegaly, and generalized lymphadenopathy.[1-4] In 25% of cases, leukemic prolymphocytes are small and do not have a visible nucleolus under light microscopy, and are designated small cell variant T-PLL.[5,6]

We describe the cytomorphology of ascitic fluid complicated by small cell variant T-PLL, with an

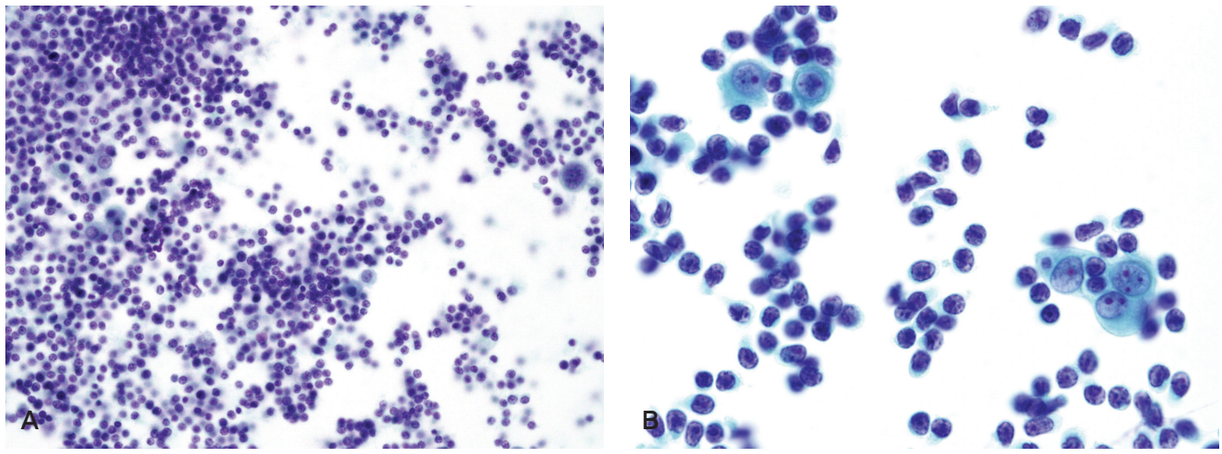

Fig. 1. Cytology of ascitic fluid: (A) The smear is moderately cellular with monomorphous population of small lymphocytes in clear background with a small number of reactive mesothelial cells. (B) Some lymphoid cells exhibit prominent nucleoli and asymmetrical cytoplasmic elongations. (Papanicolaou stain).

emphasis on differential cytodiagnosis of ascitic fluid showing aberrant small lymphocytes.

CASE

Clinical Presentation

A 54 year-old male was admitted to the hospital for evaluation of a leukocytosis of 25500×10^9/L, with 71.3% lymphocytes accompanied by ascites, multiple lymphadenopathy, and hepatosplenomegaly. His leukocytosis started 2 months earlier, when he began to complain of facial edema and occasional febrile sensations. Serum LDH was 1189 IU/L. Laboratory tests for viral hepatitis, human immunodeficiency virus (HIV), and human T-cell leukemia virus-1 (HTLV-1) were negative. Peripheral blood film showed an increased number of small-to-medium lymphocytes with condensed chromatin and no visible nucleoli, suggesting chronic lymphocytic leukemia. Straw-colored ascitic fluid was received for cytological evaluation, and diagnosed as small lymphocytic malignancy. Subsequently, diagnostic work-up was performed along with flow cytometry of the bone marrow and an excision biopsy of the inguinal lymph node.

Cytologic Findings in Ascitic Fluid

Smears were markedly cellular with non-cohesive, small, mature lymphocytes in a clean background, with a small number of reactive mesothelial cells (Fig. 1A). In contrast to reactive serous effusion, lymphoid cells in the smears were aberrantly monomorphic with irregular nuclear membranes. Many had a vesicular nucleus with a vague convolution and marginalization of chromatin. Characteristically, some of them exhibited prominent nucleoli and asymmetrical cytoplasmic elongations (Fig. 1B). Cytoplasmic granules or vacuoles were not observed. On the Giemsa-stained smears of the ascitic fluid, most of the lymphoid cells appeared to have eccentric cytoplasmic protrusions or blebs with hand-mirror morphology (Fig. 2). Based on these cytologic findings, a diagnosis of small mature lymphocytic malignancy was given.

Pathologic Findings in Bone Marrow and the Inguinal Lymph Node

More than 40% of the nucleated elements in the bone marrow smear were small lymphocytes with clumped chromatin and scanty basophilic cytoplasm. Flowcytometric evaluation of the bone marrow demon-

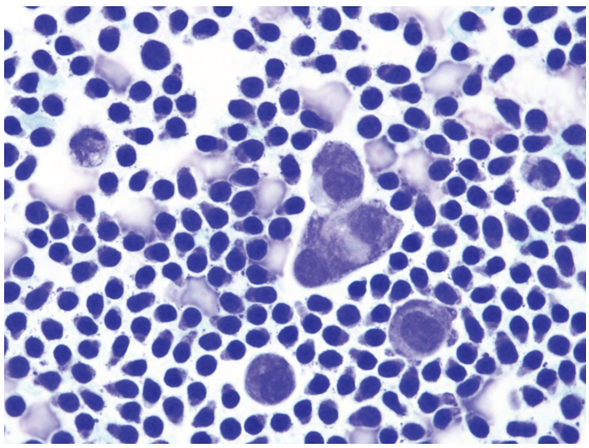

Fig. 2. Giemsa-stained smear of ascitic fluid: Individual lymphocyte shows eccentric cytoplasmic protrusion or blebs giving the appearance of so called hand-mirror morphology (Giemsa).

strated an aberrant T-cell population. Histological sections of the bone marrow biopsy showed diffuse interstitial proliferation of CD3+ small lymphocytes (Figure 3A). Individual lymphocytes had irregular nuclear contours with occasional convolutions and small nucleoli, with CD4+ and CD8- phenotypes. They were positive for CD2, CD3, CD4, CD5, and CD7, but negative for CD8, CD10, CD13, CD19, CD20, CD23, CD33 and TdT.

The excised inguinal node showed effacement of nodal architecture with marked expansion of interfollicular areas infiltrated by monomorphic populations of small mature T-cells with irregular nuclear contours and occasional small nucleoli. Prominent high endothelial venules were frequently observed and often infiltrated by neoplastic cells (Fig. 3B). Mitotic or apoptotic figures were not conspicuous, and the Ki-67 labeling index was about 30～40%. Essentially all infiltrating small lymphoid cells showed diffuse positive staining for CD4 and CD5. They were negative for CD8, CD30, cyclin D1, and ALK1. CD56 immunostaining was patchy and weak in tumor cells (about 5%).

EBER was negative on in situ hybridization performed in histological sections of the bone marrow and inguinal lymph node. PCR analysis of the inguinal lymph node revealed monoclonal rearrangement of T-cell receptor (TCR) gamma chain. PCR analyses for HTLV-1 using histological sections of the inguinal lymph node were negative.

DISCUSSION

The leukemic cells of T-PLL are slightly larger than normal lymphocytes, and are characterized by a central

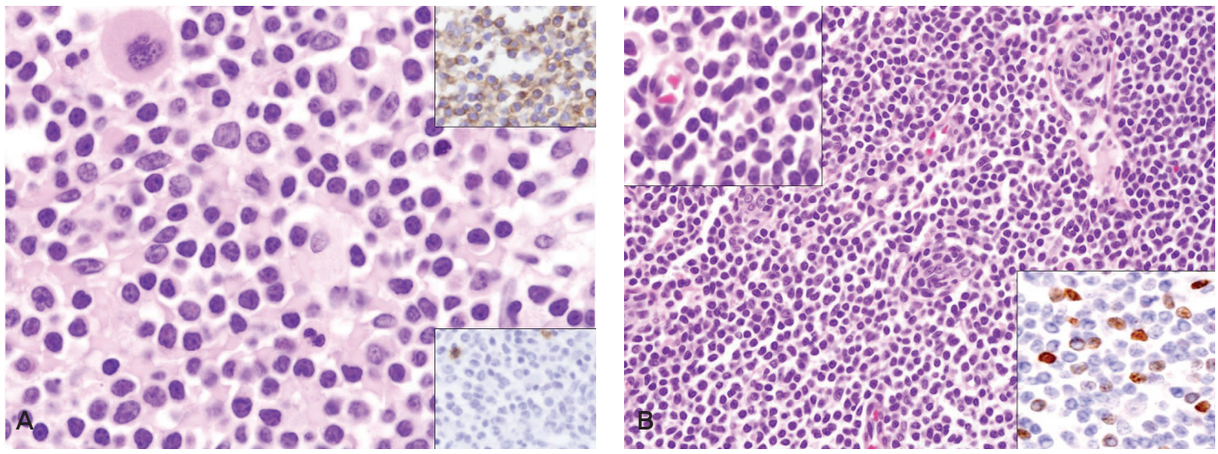

Fig. 3. Bone marrow and inguinal lymph node biopsy: (A) The bone marrow biopsy demonstrates lymphoid cells showing nuclear atypical and irregular nuclear contour with occasional convolution and small nucleolus. They are positive for CD3 and negative for CD20 (upper inset, CD3; lower inset, CD20). (B) The inguinal lymph node is diffusely infiltrated by small-sized monomorphic lymphocytes with small amount of pale cytoplasm with 30～40% of Ki-67 labeling index (right lower inset, Ki67). (H&E, inset; immunohistochemical stain).

distinct nucleolus, irregular nuclear contours, and moderately abundant cytoplasm without cytoplasmic granules or vacuoles.[2-6] However, tumor cells of small cell variant T-PLL lack the characteristic nuclear features of T-PLL, making cytodiagnosis difficult.[5,6]

Based on the clinical history of the patient and the aberrantly monomorphic nature of the small neoplastic lymphoid cells in the clean background, initial cytodiagnosis of ascitic fluid in the present case was small lymphocytic malignancy, although we initially favored chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). However, lymphoma and leukemia seldom involve the body cavity before clinical diagnosis of the disease at other primary sites, such as lymph node, bone marrow, and peripheral blood.[7] In addition, the presence of asymmetric cytoplasmic protrusions is not typical for tumor cells in CLL/SLL. Rapid disease progression along with facial swelling and development of ascites is unusual for CLL/SLL unless prolymphocytic or large cell transformation has occured.[8]

Hand-mirror morphology produced by eccentric cytoplasmic protrusions or blebs on the air-dried Giemsa stain can provide a diagnostic clue in the cytodiagnosis of mature T-cell leukemia.[4-6] This hand-mirror morphology of lymphoid cells was important in diagnosing a case of mature T-cell lymphoma presenting with peritoneal effusion.[9] To the best of our knowledge, the present case is the first report on cytologic findings of ascitic fluid complicated by the small cell variant of T-PLL.

Smears of reactive, mature, lymphocyte-rich effusions caused by tuberculosis are usually highly cellular and rich in T-cells, with relatively clear backgrounds and some reactive mesothelial cells and other inflammatory cells, except in the early stages of acute inflammation or tuberculous emphyema, which show an abundance of neutrophils in a fibrin-rich background.[10,11] The lymphocytes in serous effusion associated with tuberculosis consist of a polymorphous population of small mature T-cells.[12]

In contrast, smears of the ascitic fluid of the present case were characterized by monomorphic populations of small lymphoid cells. In addition, the irregular contours of the nuclear membrane and chromatin clumping in lymphoid nuclei were diagnostic clues to exclude the reactive nature of the lymphocytes.[13]

In conclusion, we describe cytologic findings of ascitic fluid complicated by a small cell variant of T-PLL. Hand-mirror morphology of leukemic cells assists the differential diagnosis of ascitic fluid showing small lymphocytosis.

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