Extramedullary Hematopoietic Pleural Effusion Accompanied by Follicular Lymphoma

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Abstract

Extramedullary hematopoietic effusion (EHE) is recognized to be an unusual phenomenon accompanied by hematologic disorders. Only a few reports are available of EHE occurring in patients with lymphoma. We herein report the case of a 54-year-old man with follicular lymphoma. Bone marrow aspirates and biopsied specimens showed diffuse invasion of small cleaved atypical lymphoid cells that were positive for CD10, 20, bcl2, immunoglobulin lambda and Bcl-2-IgH rearrangement. The pleural effusion aspirates and a biopsied specimen obtained via thoracoscopy revealed megakaryocytes and immature myeloid cells in addition to lymphoma cells. To the best of our knowledge, this is the first report of EHE accompanied by lymphoma according to the World Health Organization classification.

Key words: extramedullary hematopoietic effusion, extramedullary hematopoiesis, lymphoma


Introduction

Extramedullary hematopoietic effusion (EHE), including pleural, peritoneal and pericardial effusion, is widely accepted to be a rare manifestation accompanied by hematologic disorders and neoplastic diseases (1-5). Due to its rarity, most reports are case reports. On the other hand, two large retrospective analyses of EHE revealed the most common primary diseases associated with EHE to be myelofibrosis (1) and lung cancer (2). Reports of EHE accompanied by malignant lymphoma have been limited thus far and lack detailed clinical data (1, 2). We herein report a case of EHE accompanied by follicular lymphoma (FL).

Case Report

A 54-year-old man with a past history of pneumothorax was admitted to our hospital in July 2012 due to dyspnea. A physical examination revealed systemic lymphadenopathy and hepatosplenomegaly. A chest X-ray revealed marked pleural effusion in the left lung (Fig. 1A). Computed tomography (CT) scans also showed pleural effusion in the left lung, with no evidence of a ground-glass appearance, septal thickening or any nodules in either lung (Fig. 1B). The CT scans also disclosed superficial, mesenteric and post-peritoneal lymphadenopathy in addition to marked hepatosplenomegaly. The laboratory results were as follows: WBC=335×10^9/L, Hb=9.4 g/dL, platelet count=5.2×10^9/L, LDH=190 IU/L and beta2-microglobulin=6.0 mg/L. Many small cleaved lymphoid cells were recognized in the peripheral blood (Fig. 2A). A bone marrow aspirate also revealed diffuse infiltration of small cleaved cells. A flow cytometric analysis of neoplastic cells of CD45 gating was positive for CD10, CD20 and lambda, suggesting that these neoplastic cells reflected mature lymphoid malignancy. A conventional

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cytogenetic analysis showed a normal karyotype, while a fluorescence in-situ hybridization analysis was positive for IgH-Bcl-2 and negative for IgH-cyclin D1. A bone marrow biopsy specimen revealed that neoplastic cells occupied the majority of the bone marrow (Fig. 2B); the neoplastic cells were positive for CD10 (56C6; Nichirei Bioscience Inc., Tokyo, Japan), CD20 (L26; Roche Diagnostics K.K., Tokyo, Japan) (Fig. 2C) and bcl-2 (124; Nichirei Bioscience Inc.) and negative for CD5 (4C7; Nichirei Bioscience Inc.). Therefore, the case was compatible with a diagnosis of low-grade follicular lymphoma according to the World Health Organization (WHO) classification (6). The clinical stage was IV according to the revised Cotswold criteria (7).

The following results were obtained from the pleural effusion specimen: total cell count=7,400/μL, protein level=4.6 g/dL, glucose level=133 mg/dL and LDH level=90 IU/L. The pleural effusion aspirates exhibited many megakaryocytes (Fig. 2D) and immature myeloid cells (Fig. 2E) on May-Giemsa staining, in addition to small cleaved cells. The megakaryocytes were positive for CD61 (Y2/51; Dako, Glostrup, Denmark, data not shown), and the immature myeloid cells were positive for MPO (Fig. 2F). Thoracoscopy revealed a reddish-brown lesion in the left lower parietal pleura (Fig. 1C), and a biopsied specimen showed many megakaryocytes positive for factor VIII (F8/86; Nichirei Bioscience Inc.) (8) (Fig. 2G, H) among lymphoma cells.

After performing pleurodesis and administering four cycles of R-CHOP therapy (9), the patient had no symptoms related to FL and no peripheral involvement was observed, although the planned treatment was not completed.

Discussion

EHE is a rare symptom accompanied by hematologic disorders, malignancy and benign disorders (1-5, 10). Garcia-Riego et al. reported that EHE was recognized in five of 20,793 cases over a period of 21 years (2). The following underlying mechanisms have been considered: 1) a manifestation of myeloproliferative disorders, 2) bone marrow replacement by neoplastic cells or fibrosis, and 3) leakage of marrow through a defective bony cortex, similar to Paget’s disease. Only a few reports are currently available on EHE accompanied by malignant lymphoma (1, 2), and they lack detailed clinical data. Furthermore, the cases were not diagnosed according to the WHO classification.

Many reports are available regarding EHE accompanied by primary or secondary myelofibrosis (2-5), and such pa-
Figure 2. (A) Diffuse invasion of small cleaved lymphoid cells was identified in the peripheral blood (May-Giemsa stain, original magnification ×1,000). (B) Bone marrow biopsied specimen [Hematoxylin and Eosin (H&E) staining, original magnification ×100]. (C) Staining with the CD20 Stain. The majority of cells in the bone marrow were positive for CD20 (original magnification ×1,000). (D) Megakaryocytes were observed with lymphoma cells in the pleural effusion (May-Giemsa stain, original magnification ×1,000). (E) Myeloid blasts were also observed in the pleural effusion (May-Giemsa stain, original magnification ×1,000). (F) Immature myeloid cells were positive for MPO staining (original magnification ×1,000). (G) A biopsied specimen of the left lower parietal pleura. Megakaryocytes were observed among neoplastic cells (H&E staining, original magnification ×630). (H) Staining with factor VIII. The cytoplasm of the megakaryocytes was strongly positive (original magnification ×630).

Patients can develop secondary pulmonary hypertension and left ventricular failure (3-5). The radiological findings, including computed tomography scans, show a ground-grass appearance, septal thickening and cardiomegaly (3). On the
other hand, nodules in the lungs due to extramedullary hematoopoiesis have been reported in patients with myelofibrosis (4) and pneumothorax (10). In the present case, there was no evidence of pulmonary hypertension during the patient’s clinical course, in the radiological findings or associated with the extramedullary hematopoietic nodules. EHE may have been accompanied by FL because megakaryocytes and immature myeloid cells were detected with lymphoma cells in the pleural effusion and a biopsied specimen of the parietal pleura, although the patient had a past history of pneumothorax.

Regarding invasion of lymphoma in pleural effusion (11, 12), a report from the M.D. Anderson Cancer Center Hospital suggested that the most frequent subtype is aggressive lymphoma, including diffuse large B-cell lymphoma (11). As for low-grade FL, three of 29 cases involved invasion into pleural effusion. In the present case, the patient had dyspnea due to pleural effusion, systemic lymphadenopathy and hepatosplenomegaly and a markedly elevated WBC count at diagnosis. Therefore, the present patient may have had FL for a long period of time, and replacement of the bone marrow may be considered to be the primary mechanism of EHE.

In conclusion, EHE is a rare manifestation accompanied by malignant lymphoma. To the best of our knowledge, this is the first report of EHE accompanied by lymphoma according to the WHO classification.

The authors state that they have no Conflict of Interest (COI).

References