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【 CASE REPORT 】

Transudative Pleural Effusion Associated with Extramedullary Hematopoiesis

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Abstract:
The authors report a case of transudative pleural effusion associated with extramedullary hematopoiesis due to the presence of a myeloproliferative neoplasm, which was unclassified. A 71-year-old man presented with right pleural effusion during an exacerbation of thrombocytosis. The pleural effusion was transudative, although there was no history of cardiac failure or hypoalbuminemia, and treatment with diuretics failed. Extramedullary hematopoiesis was diagnosed in bilateral paravertebral soft tissue and the liver on ^{111}In bone marrow scintigraphy. The administration of hydroxyurea simultaneously reduced peripheral blood platelet count and pleural effusion within 2 weeks. The possible cause of transudative pleural effusion in association with extramedullary hematopoiesis is discussed.

Key words: myeloproliferative disorders, transudate, bone marrow scintigraphy, hydroxyurea

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Introduction

Extramedullary hematopoiesis (EMH) is an ectopic tissue with hematopoietic function at sites other than the bone marrow, either due to hematopoietic dysfunction or increased blood cell destruction. EMH occurs in association with congenital hemolytic anemia, thalassemia, myeloproliferative diseases such as myelofibrosis and polycythemia vera. EMH can develop in the liver, spleen, thymus, central nervous system, lymph nodes, lungs, and/or paravertebral region. Pleural effusion or hemothorax may occur in cases of intrathoracic paravertebral EMH (1-3).

The present article describes a case of pleural effusion, which developed in a patient with myeloproliferative neoplasm, unclassifiable (MPN-U), intrathoracic and hepatic EMH, and was controlled with pharmacotherapy for MPN-U.

Case Report

A 71-year-old man was admitted to the authors' hospital for dyspnea and bilateral pleural effusion. He was diagnosed with MPN-U based on increased levels of hematocrit (60.7%) and low levels of serum erythropoietin (<0.6 mIU/mL) thus suggestive of polycythemia vera, however, neither a Janus kinase 2 V617F mutation or Philadelphia chromosome was present and a bone marrow biopsy could not be performed due to the lack of the patient's consent; he had been followed up for 5 years without any medication. Bilateral pleural effusion appeared 15 months before this admission. He was treated with diuretics and chest tube drainage of the right pleural effusion 2 months before admission, when his peripheral white blood cell count was 34.4×10^9/L, red blood cell count $10{,}760\times10^9$/L, and platelets 340×10^9/L (Fig. 1). On admission, physical examination revealed decreased respiratory sounds, and redness and swelling of the skin in the right chest. Peripheral blood tests revealed an in-

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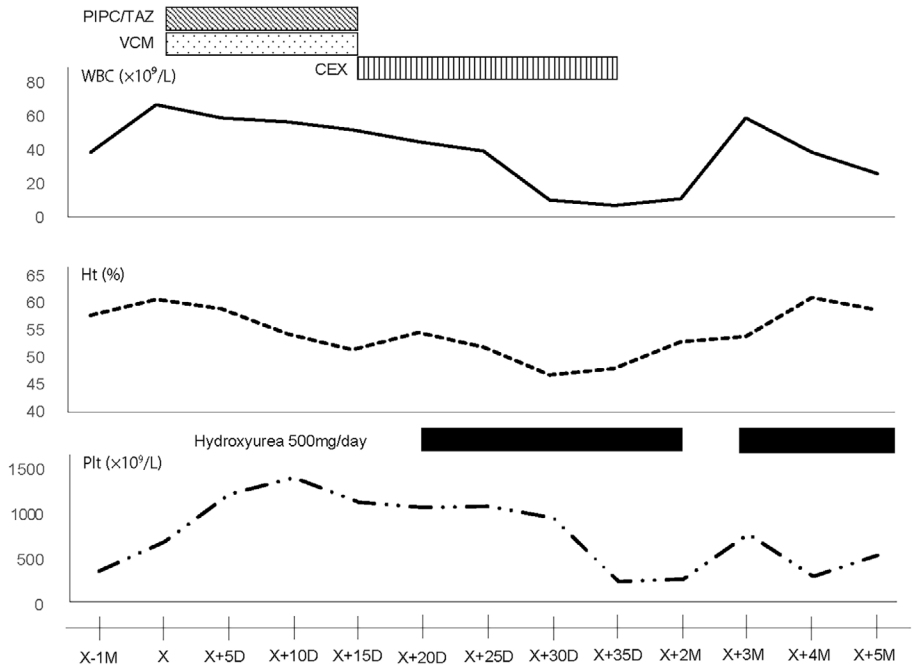

Figure 1. **Peripheral blood cell counts during the treatment. The white blood cell count (WBC; ×10⁹/L, solid line), hematocrit (Ht; %, dotted line), and platelet count (Plt; ×10⁹/L, two-dot chain line) in the peripheral blood during the treatment are presented. Hydroxyurea, 500 mg once daily, was started on day 20 after the admission (X), with a rapid decrease in white blood cell count, hematocrit, and platelet count. Self-discontinuation of medication in an outpatient setting was accompanied by a temporary increase in peripheral blood cells. PIPC/TAZ: piperacillin/tazobactam, VCM: vancomycin, CEX: cefalexin**

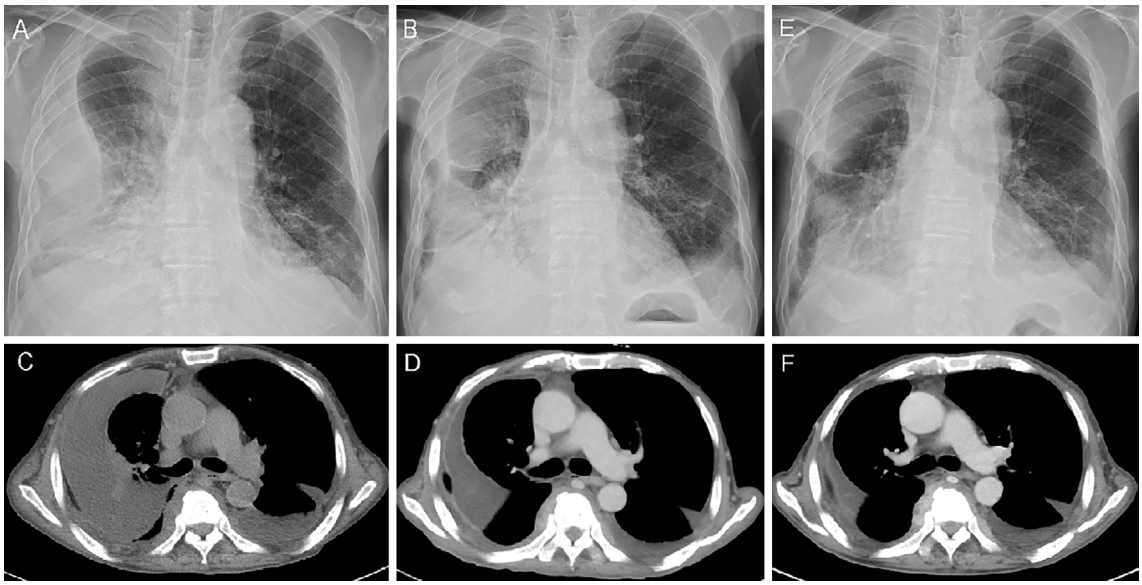

Figure 2. **Radiographic findings before and after treatment with hydroxyurea. Chest radiograph and thoracic computed tomography (CT) scan before hydroxyurea treatment (A, C), and 2 weeks (B, D) or 3 months (E, F) after the administration of hydroxyurea. CT revealing uniformly enhanced soft-tissue density in the paravertebral region (D, F).**

creased white blood cell count of 67.2×10⁹/L, a red blood cell count of 9,880×10⁹/L, a platelet count of 694×10⁹/L, with a serum albumin level of 2.2 g/dL and a brain natriuretic peptide level of 174 pg/mL. Thoracic computed tomography (CT) revealed right-dominant bilateral pleural effusion and atelectasis in the right lung, and bilateral paravertebral mass presenting with strong contrast enhancement (Fig. 2). Abdominal CT suggested the presence of chronic liver disease with an irregular hepatic surface and a blunt liver edge, although a patent paraumbilical vein was not ob-

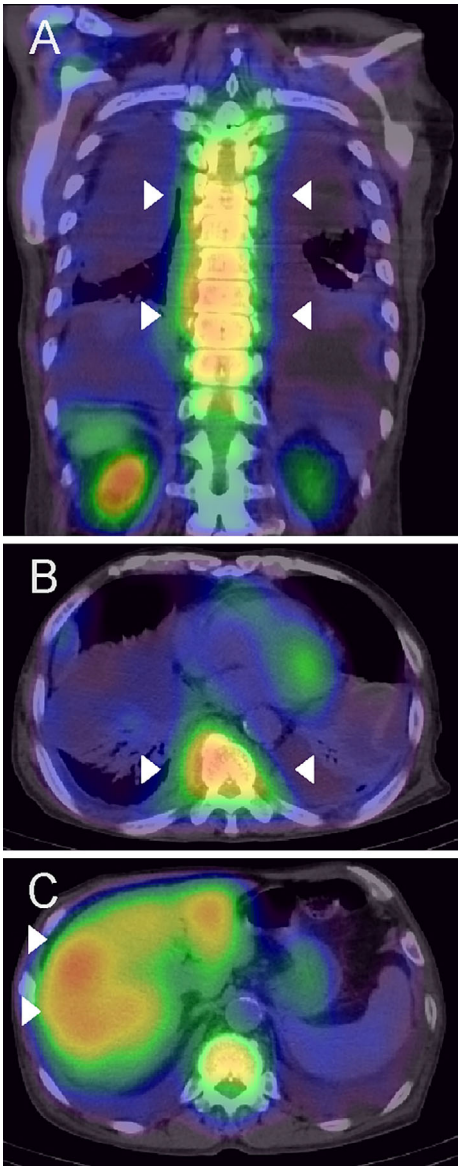

Figure 3. **^{111}In bone marrow scintigraphy. ^{111}In accumulation in the bone marrow was observed in the paravertebral soft tissue at the levels of Th5-Th10 (A, B; arrowhead) and in the liver (A, C).**

served. Right pleural effusion was pale, bloody, and transparent, with total protein concentration of 2.3 g/dL (5.4 g/dL in serum) and a lactate dehydrogenase level of 207 IU/mL (859 IU/mL in serum). No microorganisms or tumor cells were found in the pleural effusion. ^{111}In bone marrow scintigraphy revealed an extramedullary accumulation in the paravertebral mass and the liver (Fig. 3).

Antibiotic treatment improved the skin lesion in the chest without any reduction of pleural effusion. The platelet counts thereafter further increased to $1,400\times10^9$/L at day 10, and hydroxyurea, 500 mg once daily, was started on day 20 (Fig. 1). Two weeks later, platelet count decreased to 260×10^9/L, and the right pleural effusion was also reduced without any change in the size of EMH (Fig. 1, 2). The pleural effusion further decreased within 3 months (Fig. 2), and thereafter continued to be reduced for 5 months since the treatment with hydroxyurea was introduced.

Discussion

We encountered an individual with MPN-U who presented with intrathoracic and hepatic EMH and transudative pleural effusion. The volume of pleural effusion increased during deterioration of the underlying disease, while it decreased after administering appropriate treatment for MPN-U.

It has been reported that intrathoracic EMH sometimes presents with pleural effusion, and in all cases except for a case accompanied by cardiac failure (1-3), the effusion is exudative based on the criteria described by Light et al. (4). The exact mechanism by which exudative pleural effusion occurs in the presence of EMH is unclear; however, it may be due to inflammation caused by friction between the EMH lesion and the visceral pleura. In the present case, however, the pleural effusion which was examined repeatedly was transudate without any clinical manifestation of cardiac failure.

Although EMH complicated by transudative pleural effusion is rare, transudative ascites is often observed in the cases with EMH in the liver and other abdominal organs (5). In these cases, ascites is possibly associated with portal hypertension, which develops in 10-20% of cases with myeloproliferative disorders due to increased portal blood flow and intra-portal thrombi (6, 7). Although a detailed assessment of portal hypertension was not performed in this case, abdominal CT revealed an irregular hepatic surface and a blunt liver edge suggestive of liver cirrhosis and ^{111}In bone marrow scintigraphy suggested the presence of EMH in the liver. The cause of transudative pleural effusion in the present case might therefore have been the pleuroperitoneal influx of transudative ascites caused by MPN-U-related portal hypertension.

The appropriate choice for the treatment of EMH in the paravertebral region remains controversial; irradiation, surgical resection, drug therapy, and pleurodesis for pleural effusion can be performed (2, 3, 8). EMH is radiosensitive and treated with low-dose irradiation (7.5-30 Gy) (9, 10), although the recurrence rate is relatively high (19-35%) (11). Combined radiation therapy and laminectomy can provide more reliable decompression effect in cases with spinal cord compression symptoms. Pleural effusion can also be controlled with the intrathoracic injection of cisplatin and dexamethasone, or pleurodesis with tetracycline or bleomycin. In this case, however, we treated the patient with the oral administration of hydroxyurea because pleural effusion increased in association with a worsening of thrombocytosis, and a previous case report demonstrated that the oral administration of hydroxyurea and busulfan rapidly reduced transudative ascites (12). As expected, pleural effusion, as well as peripheral blood platelet count, decreased rapidly, with no change in the size of EMH. This clinical response to hydroxyurea further supports the hypothesis that transuda-

tive pleural effusion in the present case was derived from ascites caused by portal hypertension.

Conclusion

There are several mechanisms by which pleural effusion can accumulate in cases with myeloproliferative disorders and EMH. If the effusion is transudative, it is important to consider the possibility of portal hypertension and pleuroperitoneal migration of ascites. In these cases, pleural effusion can be controlled with hydroxyurea and other drugs targeting the underlying myeloproliferative disorders.

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

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