Idiopathic Myelofibrosis with Refractory Massive Ascites

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Abstract

A 55-year-old woman presented with massive refractory ascites in the course of idiopathic myelofibrosis. The ascites was exudative, and a cytological examination revealed granulocytes of varying maturity, erythroblasts, and megakaryocytes with trisomy 8. The ascites was assumed to have developed from peritoneal extramedullary hematopoiesis. An abnormal karyotype in the cells in the ascitic fluid, which was the same abnormality as in peripheral blood, helped to prove extramedullary hematopoiesis in this case, which can be an aid in making a differential diagnosis in cases of ascites associated with myelofibrosis. (Internal Medicine 42: 525-528, 2003)

Key words: symptomatic massive ascites, idiopathic myelofibrosis, extramedullary hematopoiesis, megakaryocyte, trisomy 8

Introduction

Idiopathic myelofibrosis (IM) is a myeloproliferative disorder in the spectrum of clonal hemopathies. Its clinical features are characterized by broad fibrosis and osteosclerosis of the bone marrow, extramedullary hematopoiesis with marked splenomegaly, and leukoerythroblastic anemia.

Abdominal fullness is not uncommon among patients with IM, and it is usually associated with the mass effect of splenomegaly. Ascites occurs in 2–10% in IM (1–4). We describe a case of IM with symptomatic massive refractory ascites due to peritoneal extramedullary hematopoiesis.

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creased again. She was readmitted to our hospital in December 2000.

The white-cell count was 45,280/μl with 5% blasts on readmission. Ascitic examinations showed an extreme increase in the cell count (33,760/μl), which was comprised of hematopoietic cells such as granulocytes in all stages of maturation, and erythroblasts. Chromosomal analysis of the cells in the ascites with the G-banding method showed trisomy 8 in 19 out of 20 cells analyzed, an abnormality which was also identified in her peripheral blood cells (Fig. 3 lower right).

We administered hydroxyurea and ranimustin, but with no response. In addition, massive pleural effusion appeared. She died of respiratory failure and ventriculogenic arrhythmia on the 75th day of her hospitalization. Blasts in the peripheral blood were 4 % when she died.

Her autopsy revealed massive ascites, which amounted to 2,100 ml, diffuse intestinal wall thickness and hepatosplenomegaly. Extramedullary hematopoiesis was confirmed in the spleen and liver. Myeloblasts, which were positive for myeloperoxidase and CD15 antigens by immunostaining, had infiltrated into various organs including the liver, spleen, pleura, peritoneum, greater omentum, and so on (Fig. 4). Her
bone marrow was almost completely replaced by the myeloblasts (Fig. 1 right).

**Discussion**

Patients with symptomatic massive ascites caused by peritoneal extramedullary hematopoiesis have been reported previously, but are limited in number (6–11). Kumar and Naylor (6) reported that the pleural or peritoneal fluid from 5 out of 3,279 patients contained megakaryocytes, and three of them were IM patients. Two of the patients underwent autopsies, and the foci of ectopic hematopoiesis was found on the serous surface (11).

Silverstein et al also discussed the mechanism of ascites in IM (12). Two of three patients with massive ascites had documented portal hypertension and one was found to have megakaryocytes in his ascitic fluid. The etiology of ascites in IM is assumed to be result from three major sources. The first is portal hypertension accompanied by ectopic hematopoiesis in the liver and spleen. The second is thrombosis of the portal vein. The third is ectopic metastasis of hematopoietic tissue in the peritoneum. In our case, mild esophageal varices (F1) were observed by esophagogastroduodenoscopy, which shows some correlation to portal hypertension as one of the etiologies for the ascites. A computed tomographic scan of the abdomen showed no evidence of thrombosis of the portal vein.

Peritoneal extramedullary hematopoiesis is usually proven by peritoneal biopsy. Ascitic cytology is also a reliable means since peritoneal extramedullary hematopoiesis is proven in autopsy in such cases. Other cases had the peritoneal tissue which was predominantly fibrous and contained only a few hematopoietic cells (2). Unfortunately, we did not have the opportunity to perform a peritoneal biopsy. The blasts infiltrating the peritoneum recognized at autopsy suggest that the ectopic hematopoiesis on the serous surface might have been replaced by the blasts with its rapid progression. The marked existence of blasts in the vascular structures of the peritoneum might suggests that the leakage of the blood component to the ascites at the time of leukemic transformation just before death. However, the longstanding course of refractory ascites with various immature hematopoietic cells without blasts, and no other apparent course of the ascites strongly suggests the ascites to be due to extra-medullary hematopoiesis in the peritoneum.

A computed tomographic scan sometimes shows the mass of extramedullary hematopoiesis (13), but not in the present case.

To date, no report has been discussed the karyotypic analysis of cells from ascites in IM. The present case had trisomy 8 of the cells in ascites which clearly showed the utility of the method to confirm peritoneal hematopoiesis. Although peritoneal biopsy is a gold standard method as a diagnostic procedure for the peritoneal hematopoiesis, additional cytogenetic analysis of the cells in the ascites might be useful.

The patient’s ascites responded temporarily to high-dose corticosteroids, but cytotoxic agent administration was not effective. Hirayama et al also reported that corticosteroid administration was effective for pleural effusion in a patient with IM (14).

Leukemic transformation occurs in approximately 20 percent of patients during the first 10 years after the onset of the disease (15). The present case is ranked in the high risk group on the LILLE scoring system for predicting survival in IM (16). Reilly suggested that an abnormal karyotype is an indicator of poor prognosis in addition to age and anemia (17), but this was denied by a multivariate analysis according to Tefferi (18) and Okamura (19). They conclude trisomy 8 is a poor-risk factor, but the presence of an abnormal karyotype in general does not carry an adverse prognosis. Novel strategies, including hematopoietic stem cell transplantation, should be considered for idiopathic myelofibrosis, especially for those with a poor prognosis.

**References**
