Budd-Chiari Syndrome Caused by Hepatic Vein Thrombosis in a Patient with Myeloproliferative Disorder

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We report a 24-year-old Japanese female hospitalized with jaundice and ascites. She exhibited hepatosplenomegaly, severe liver dysfunction, and slight polycythemia with an increase in serum levels of β-thromboglobulin and platelet factor 4. Bone marrow was hypercellular with an increase in progenitor cells. The aggregation response of platelets to ADP and to collagen was markedly increased. Venography revealed narrowed hepatic veins with ‘spider web’ sign. Liver biopsy revealed hepatic congestion. Budd-Chiari syndrome was diagnosed, and was thought to be due to thrombosis related to myeloproliferative disorder. Liver transplant was successful in relieving symptoms.

(Key words: latent myeloproliferative disorder, liver transplantation)

Introduction

Patients with Budd-Chiari syndrome present with hepatomegaly, abdominal pain, and ascites (1). The syndrome is caused by occlusion of the hepatic vein or the inferior vena cava (2). Etiologic factors may include systemic diseases that induce a hypercoagulable state. Primary myeloproliferative disorders (MPD), especially polycythemia vera and essential thrombocytemia, and paroxysmal nocturnal hemoglobinemia (PNH) are the most common causes of thrombogenic hematological disorders (3, 4). In Japan, however, the most common etiology of Budd-Chiari syndrome is idiopathic membranous obstruction of the inferior vena cava (5–7). We present a patient with Budd-Chiari syndrome associated with latent MPD, who demonstrated marked hyperthrombogenesis.

Case Report

A 24-year-old Japanese woman was hospitalized in July 1991 with a complaint of epigastralgia when she was found to have jaundice, hepatosplenomegaly, and a small amount of ascites. She was found to have thrombocytosis, 12 x 10^4/μl, in July 1992. She was referred and admitted to our hospital in September 1992 for further evaluation of persistent jaundice and ascites. There was no medical history of blood transfusion and no family history of liver disease. Physical examination on admission revealed mild jaundice, abdominal distention, hepatosplenomegaly, and dilatation of the abdominal veins. Vascular spiders, palmar erythema, and pretibial edema were absent. Laboratory findings on admission were as follows: red blood cell count, 500 x 10^6/μl; hemoglobin, 15.0 g/dl; hematocrit, 45.2; white blood cell count, 1.13 x 10^4/μl; platelet count, 33.1 x 10^4/μl; total protein, 6.5 g/dl; albumin, 3.8 g/dl; total bilirubin, 4.2 mg/dl; GOT, 43 IU/l; GPT, 30 IU/l; ALP, 393 IU/l; θ-GTP, 75 IU/l; APIT, 59.4 second; and thrombotest, 20%. Renal function was normal. Tests for hepatitis B surface antigen, hepatitis B core antibody, and the second generation antibody to hepatitis C virus were negative. Computed tomography of the abdomen revealed hepatosplenomegaly: the caudate lobe was remarkably swollen (Fig. 1A). Cavernography revealed stenosis of the inferior vena cava (IVC), caused by pressure from the caudate lobe (Fig. 1B). No membranous obstruction was detected. Venography revealed narrowing of the three hepatic veins on the peripheral side. “Spider web” sign was also noted (Fig. 1C). Liver biopsy revealed prominent fibrosis at the periphery and in zone 2 of the lobe; hepatic necrosis was distributed over a wide area. Degeneration of the hepatic cells and deposits of hemosiderin were found, indicating the presence of chronic liver congestion. Budd-Chiari...
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Figure 1. A. Abdominal CT of the patient, demonstrating marked hepatosplenomegaly. B. Cavanography showed stenosis of the inferior vena cava in the area of the liver due to pressure from the caudate lobe. There was no membranous obstruction. C. Venography of the right hepatic vein revealed a narrowing of veins on the peripheral side as well as “spider web” sign.

syndrome caused by hepatic venous thrombosis was diagnosed.

To clarify the etiology of thrombosis in this patient, serum and bone marrow were examined. There was a marked increase in serum levels of β-thromboglobulin (627 ng/ml; normal range, <52 ng/ml) and platelet factor 4 (281.1 ng/ml; normal range, <20 ng/ml). The aggregation response of platelets to ADP and collagen was markedly activated even at low concentrations of those substances (Fig. 2). Bone marrow was hypercellular with a marked increase in the number of megakaryocytes (Fig. 3). Chromosome analysis of bone marrow cells showed a normal karyotype. In vitro colony assay of bone marrow cells was performed as previously described (8), demonstrating increases in the myeloid and erythroid progenitors (Table 1). These findings suggested that thrombosis might be closely related to hypercoagulability due to myeloproliferative disorder.

The patient’s liver dysfunction deteriorated and she experienced abdominal fullness caused by the ascites. Accordingly, she received an orthotopic liver transplant in April 15, 1993 at Princess Alexandra Hospital in Australia. Surgical findings demonstrated a moderate amount of ascites, a prominent collateral network of veins, an enlarged firm liver with enlargement of the caudate lobe, and splenomegaly. There was no thrombosis in the portal vein or inferior vena cava, but blood clots were observed in the right hepatic vein. Histology of the extirpated liver revealed incomplete fibrous obliteration of the lumen of the right hepatic vein with recanalization. Other hepatic veins were completely obliterated by fibrous tissue. The liver exhibited extensive, but not generalized, cirrhosis, with some areas showing marked congestion, sinusoidal dilatation, and atrophy.
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| (%) Patient (%) Control |
|-------------------------|-----------------------------|
| 100                    | 100                        |
| 80                     | ADP 1/2M                   |
| 60                     | ADP 0.5/2M                 |
| 40                     | ADP 0.1/2M                 |
| 20                     | ADP 0.01/2M                |
| 0                       |                            |

Time: 0 2 4 6 8 10 (min)

Figure 2. Tracing showing platelet aggregation induced by ADP and collagen. A. Patient, tracing for ADP; B. control, tracing for ADP; C. patient, tracing for collagen; D. control, tracing for collagen.

Figure 3. Bone marrow biopsy showing hypercellular marrow and an increase in the number of megakaryocytes (Wright-Giemsa stain, ×400).

Discussion

Hepatic vein thrombosis can lead to Budd-Chiari syndrome. This form of thrombosis can result from thrombogenic condi-
Table 1. In Vitro Colony Assays of Bone Marrow Cells

<table>
<thead>
<tr>
<th>Sample</th>
<th>Growth factors</th>
<th>CFU-E</th>
<th>BFU-E</th>
<th>CFU-G</th>
<th>CFU-M</th>
<th>CFU-GM</th>
<th>CFU-Mix</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Patient BM</td>
<td>PHA-LCM+Epo</td>
<td>81±7.1</td>
<td>78±16.3</td>
<td>65±7.1</td>
<td>53±2.8</td>
<td>25±1.4</td>
<td>4±1.4</td>
</tr>
<tr>
<td>2. Control BM</td>
<td>PHA-LCM+Epo</td>
<td>33±5.7</td>
<td>34±3.5</td>
<td>38±11.3</td>
<td>32±6.4</td>
<td>9±2.5</td>
<td>0</td>
</tr>
<tr>
<td>3. Patient BM</td>
<td>–</td>
<td>0</td>
<td>0</td>
<td>5±2.8</td>
<td>20±2.8</td>
<td>4±0.7</td>
<td>0</td>
</tr>
<tr>
<td>4. Control BM</td>
<td>–</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>16±7.1</td>
<td>1±0.7</td>
<td>0</td>
</tr>
</tbody>
</table>

Light density bone marrow cells obtained from the patient and controls were cultured in the presence of phytohemagglutinin-stimulated leukocyte conditioned media (PHA-LCM) and 2 U/ml recombinant erythropoietin (Epo, Chugai Co., Tokyo, Japan). Colony formation was scored under an inverted microscope on day 14 after culture. Results show the numbers of each type of colony. Results represent the mean±SD of triplicate cultures containing 5 x 10⁴ cells/ml.

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Acknowledgements: We thank Dr. Russel W. Strong, Director of Princess Alexandra Hospital in Australia, for performing the liver transplantation.

References


