Cardiac Tamponade in the Blastic Crisis of Chronic Myelogenous Leukemia

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A 36-year-old man with Philadelphia chromosome-positive chronic myelogenous leukemia (CML) developed hemorrhagic pericarditis with tamponade as a terminal manifestation of the blastic crisis. Cardiac tamponade should be kept in mind as an uncommon cause of death of CML patients. Based on a literature review, symptomatic pericarditis in patients with CML blast crisis suggests imminent death. This is in contrast to long-term survival for patients in the chronic phase.

(Key Words: chronic myelogenous leukemia, blastic crisis, hemorrhagic pericarditis, cardiac tamponade, imminent death)

INTRODUCTION

Although pericardial effusion has been frequently observed at postmortem examination in blastic crisis of chronic myelogenous leukemia (CML), cardiac tamponade as a clinical manifestation is very rare (6). Only fourteen cases of cardiac tamponade in the blastic crisis and chronic phase of CML have been documented in the literature since 1950. In this report, we describe a patient with Philadelphia chromosome-positive CML in whom cardiac tamponade due to hemorrhagic pericarditis developed in the terminal stage of blastic crisis. This patient, 1 of a total of 37 adult CML patients in blastic crisis who died in Tokai University Hospital during the 15-year period between 1978–1990, was the first to succumb to cardiac tamponade.

CASE REPORT

A 36-year-old man was admitted on January 13, 1988, to Tokai University Hospital for evaluation of abdominal distention and fever. On physical examination, a blood pressure of 122/76 mmHg, temperature of 37.9°C and regular pulse rate of 84/min were noted. The lungs were clear, and heart sounds were normal. There was no pathologic adenopathy. The liver edge was palpable 3 cm beneath the right costal margin. The spleen edge was palpable 4.5 cm beneath the navel. Initial laboratory evaluation revealed a hemoglobin (Hb) of 5.4 g/dl, platelet count of 63,400/mm³, and white blood cell (WBC) count of 99,900/mm³ with 38% blasts. Serum chemistry revealed an increase of LDH to 750 μ/l and ALP to 313 μ/l (normal ranges: 127–230 and 40–119 μ/l, respectively). A bone marrow aspirate revealed an increase to 41.6% of blasts with maturation arrest. The blasts expressed CD 38 (Leu 17), HLA-DR and myeloid-associated antigens of CD 13 (My7) and CD 33 (My9). A karyotypic study revealed the Philadelphia chromosome in the metaphase of bone marrow cells. The leukocyte alkaline phosphatase score was 4 (control: 276). A chest roentgenogram was unremarkable. An electrocardiogram (ECG) revealed no abnormalities. The patient was diagnosed as having myeloid blastic crisis of CML. An iliac bone marrow biopsy revealed fibrosis and an increase in immature myeloid cells. The patient was treated with combination chemotherapy, using methotrexate, cytara- bine, vindesine and prednisolone. A temporary decrease in the number of blood blasts after
chemotherapy and subsequent rises were repeated. Blasts persisted in comprising more
than 90% of the leukocytes in the blood. In mid-June, persistent fever (40°C) developed.
Blood, urine and throat cultures and chest X-ray results were negative, but the patient
was treated empirically with sulfactam/cefoperazone, amikacin, sulfamethoxazole/trimethoprim, isoniazid, rifampicin and miconazole. *Pseudomonas aeruginosa* and
*Acinetobacter anitratus* were demonstrated by sputum culture on June 27. The fever fell after
the administration of imipenem/cilastatin, treatment to which these pathogens were
sensitive. Orthopnea, jugular venous distention and sinus tachycardia developed in early July,
1988. Central venous pressure (CVP) began to rise at the same time. Follow-up chest roent-
genograms revealed a prominent increase in the size of the cardiac silhouette. An ECG revealed
low voltage, suggesting pericardial effusion and a horizontal decrease of the ST segments with
T inversion, suggesting myocardial damage. The QT interval was also prolonged. An
echocardiogram revealed a large pericardial effusion with evidence of left ventricular dys-
function. Gradual increase in the pericardial effusion led to cardiac tamponade. On August
3, 1988, two months after the appearance of the pericardial effusion, the patient died from
cardiac failure. Disseminated intravascular coagulation was not detected. A final blood
examination was as follows: Hb of 5.3 g/dl, a platelet count of 25,000/mm³, and a WBC
count of 57,600/mm³ with 1% segmented neutrophils, 1% bands, 1% lymphocytes, 1% 
promyelocytes and 96% blasts. A pericardiocentesis was performed immediately after
death and serosanguineous fluid was removed. The pericardial effusion was exudative in
nature; there were 7,625 WBC/mm³ consisting of 94% blasts, 1% lymphocytes and 5% 
erythroblasts. Cultures of the pericardial fluid were negative for bacteria, fungi and acid-fast 
bacilli. A pericardial biopsy was not performed. The clinical course from May to August, 1988,
is shown in Figure 1.

**DISCUSSION**

The following causes of pericardial effusion in CML patients have been described. In most
cases, leukemic cell infiltration of the pericardi-
um has been the cause of the effusion. As a rare
cause, infectious pericarditis due to bacterial,
fungal, tubercular, or viral agents may occur
in the background of pancytopenia after chemotherapy in the blastic crisis of CML (11).
Shih et al (13) have reported a patient in the
chronic phase of CML who developed
pericardial extramedullary hematopoiesis such as
myeloid metaphasia. This was proven by
in-vitro assays of the pericardial fluid for
granulocyte-macrophage and erythroid progen-
itor cells. Leukocytosis may cause plugging of
blood vessels, and marked thrombocytosis may
be occasionally associated with thrombotic
episodes. Both leukocytosis and thrombocyto-
sis can lead to vascular occlusion with tissue
hypoxia and subsequent damage, followed by
hemorrhage into the pericardium. Other
reports (1, 12, 16, 17) revealed that adminis-
tration of daunorubicin, high-dose cyclophos-
phamide or cytarabine can induce pericarditis,
frequently with neutrophil infiltration in the
effusion. In summary, the several possible
causes of pericardial effusion in leukemic
patients are: (i) leukemic cell infiltration, (ii)
infection, (iii) bleeding, (iv) antileukemic drugs
and (v) extramedullary hematopoiesis. We were
unable to isolate an infectious agent from our
patient's pericardial fluid. The patient had
been receiving antibacterial, antifungal and
antitubercular therapy before the episode.

Tubercular pericarditis is a difficult diagnosis
to prove, but the negative pericardial fluid
culture and fall in fever after the administra-
tion of imipenem/cilastatin argue against this
etiology. The WBC differential of the pericar-
dial effusion, paralleled the blood count, includ-
ing the more than 90% blasts. This finding is
different from that in cytarabine-induced
pericarditis (our patient did receive low-dose
cytarabine therapy) which is consistent with
acute inflammation including neutrophils but
no leukemic blast cells. The hemorrhagic effu-
sion present in the patient likely was secondary
to refractory thrombocytopenia and tissue
hypoxia due to vascular occlusion induced by
marked leukocytosis and subsequent damage.
We believe that vascular destruction due to
myopericardial infiltration of leukemic blast
cells also contributed to this effusion.

A total of 15 cases of CML with cardiac
tamponade, including this case, are summa-
### Table 1a Chronic phase CML with pericardial effusion

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Sex</th>
<th>Pericardial effusion</th>
<th>Period from effusion to death</th>
<th>Year*</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28/F</td>
<td>bloody</td>
<td>24 months</td>
<td>1941</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>18/M</td>
<td>bloody</td>
<td>24 months</td>
<td>1949</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>58/F</td>
<td>bloody</td>
<td>12 months</td>
<td>1950</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>38/M</td>
<td>?</td>
<td>10 months</td>
<td>1965</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>28/M</td>
<td>?</td>
<td>9 months</td>
<td>1966</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>35/M</td>
<td>bloody</td>
<td>1.5 months</td>
<td>1971</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>45/M</td>
<td>bloody</td>
<td>24 months</td>
<td>1986</td>
<td>13</td>
</tr>
<tr>
<td>9</td>
<td>48/F</td>
<td>bloody</td>
<td>10 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Year when pericardial effusion developed.

### Table 1b Blastic crisis CML with pericardial effusion

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Sex</th>
<th>Pericardial effusion</th>
<th>Period from effusion to death</th>
<th>Year*</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>34/M</td>
<td>yellow</td>
<td>10 hours</td>
<td>1968</td>
<td>11</td>
</tr>
<tr>
<td>11</td>
<td>60/M</td>
<td>yellow</td>
<td>24 hours</td>
<td>1971</td>
<td>11</td>
</tr>
<tr>
<td>12</td>
<td>52/F</td>
<td>bloody</td>
<td>2.5 months</td>
<td>1974</td>
<td>9</td>
</tr>
<tr>
<td>13</td>
<td>41/M</td>
<td>yellow</td>
<td>a few hours</td>
<td>1978</td>
<td>10</td>
</tr>
<tr>
<td>14</td>
<td>23/M</td>
<td>yellow</td>
<td>1.5 months</td>
<td>1980</td>
<td>14</td>
</tr>
<tr>
<td>15</td>
<td>36/M</td>
<td>bloody</td>
<td>1 month</td>
<td>1988</td>
<td>our case</td>
</tr>
</tbody>
</table>

*Year when pericardial effusion developed.
rized in Tables 1a and 1b. In the 9 cases of chronic phase CML (Table 1a), the pericardial effusions, probably induced by leukemic cell infiltration, responded to irradiation, systemic chemotherapy and/or pericardiocentesis. These cases survived for a mean of 12 months (7 weeks to 24 months). Therefore, cardiac tamponade in these cases does not seem to be a factor in the poor prognosis. In 4 of 5 blast crisis CML (Table 1b), excluding the one case of bacterial pericarditis, leukemic cell infiltration caused the effusion. These patients did not respond to systemic chemotherapy or pericardiocentesis. Two cases (#11 and #13) died within 24 hours, and the remaining 3 cases survived for 1, 1.5 and 2.5 months, respectively. Therefore, the appearance of pericardial effusion in CML blastic crisis indicates imminent death. Although cases 5 and 9 in the chronic phase and case 13 in the blastic crisis were well-controlled hematologically by systemic chemotherapy, leukemic cell infiltration resulting in pericardial effusion and tamponade occurred. It is probable, based on clinical observations, that the infiltration is present for a long time with an acceleration of the process during periods of exacerbation and as the disease advances.

REFERENCES
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