Bone marrow necrosis in a patient with non-Hodgkin lymphoma

Dilek ARGON¹, Mustafa ÇETİNER¹, Cafer ADIGÜZEL¹, Işık KAYGUSUZ¹, Tülin F. TUĞLULAR¹, Tülay TECİMER², Mahmut BAYIK¹

¹ Department of Hematology, Marmara University Medical Faculty, ² Department of Pathology, Marmara University Medical Faculty, Istanbul, TURKEY

Turk J Haematol 2004;21(2): 97-100

Received: 31.10.2003  Accepted: 23.03.2004

ABSTRACT

Bone marrow necrosis is a rare but ominous finding in various malignant and nonmalignant disorders. It is usually a postmortem diagnosis, but with the advent of modern imaging methods and clinical suspicion, bone marrow necrosis can be diagnosed as antemortem, especially in malignant disorders. We report a 60-years old man with newly diagnosed non-Hodgkin lymphoma presenting with anemia and very high level of alkaline phosphatase. On bone marrow biopsy, it was noted with extensive BMN characterized by cellular debris with indistinct cellular margin and abnormally eosinophilic staining cytoplasm. Despite the prompt institution of aggressive chemotherapy, one week later, liver function tests gradually deteriorated and the patient succumbed. Given the high mortality rate, when the bone marrow necrosis is suspected especially in a patient with malignancy, disease specific treatment and vigorous supportive measures should be immediately commenced.

Key Words: Bone marrow necrosis, Hematologic malignancy.

ÖZET

Non-Hodgkin lenfomalı bir hastada kemik iliği nekrozu


Anahtar Kelimeler: Kemik iliği nekrozu, Hematolojik malignite.
INTRODUCTION

Although it has been described sixty years ago, little is known on bone marrow necrosis (BMN) in medical practice[1]. The first antemortem definition was made by Nies in patients with acute leukemia in 1965[2]. BMN is defined as necrosis of myeloid tissue and medullary stroma in large areas of the bone marrow (BM)[3]. This clinicopathologic entity is completely different from both avascular bone necrosis in which there is no destruction of spicular architecture and marrow aplasia in which there is only a loss of myeloid tissue not reticular structure[4,5]. By now, about 270 cases have been reported in the literature. Table 1 lists all causes of BMN that has reported so far. Malignancy which constitutes 90% of cases is the most common underlying disorder of BMN[3,6]. Up to 10% of patients with BMN have nonmalignant disorders. As shown in Table 1, there is a wide variety of disorders causing BMN.

The most important diagnostic sign is bone pain[7]. The pain is acute, intense and usually located in lower back. It is more evident in malignant disorders. More than half of patients with BMN present with fever[7]. Embolization of fat and necrotic marrow to lung are the other rare but life-threatening complications of BMN[8]. Among the laboratory findings, various cytopenias, leukoerythroblastic differential count, and increased levels of lactic dehydrogenase (LDH) and alkaline phosphatase (AP) are the most prominent features[9]. In BM examination, it is noted that the cells lose their normal staining pattern and have irregular shape and margin on cytology[3]. It is usually required to aspirate the marrow from multiple sites to obtain enough material[10]. The combination of gelatinous transformation and necrosis is the hallmark of BM biopsy[11]. Adjunctive to clinicopathologic diagnose, BM scintigraphy with Technetium and indium is a highly sensitive method. Magnetic resonance imaging is another useful noninvasive diagnostic tool, though its sensitivity not superior to scintig-
palpable bilaterally. There was no cyanosis, jaundice, dyspnea or edema. His past medical history was significant for coronary heart disease. He was taking a vasodilator, an angiotensin converting enzyme inhibitor and aspirin. He had no history of surgical intervention.

Complete blood cell analysis revealed mild anemia with normocytic normochrom appearance (Hb: 9.9 g/dL), and lymphocytosis. Erythrocyte sedimentation rate was 22 mm/h. In biochemical analysis the most prominent finding was the increased level of AP (2758 mg/dL). LDH and transaminase levels also had increased minimally. All the other biochemical parameters were normal.

At the end of first part of diagnostic work-up, the patient was thought to have a kind of lymphoma and referred to surgery unit for excisional biopsy of one of the enlarged cervical nodes. Cervical node biopsy revealed diffuse large B-cell lymphoma. Then, the patient underwent bone marrow biopsy and thoracoabdominal and cervical axial computerized tomography (CT) for staging purpose. CT scan of body revealed mediastinal and paraaortic lymphadenomegalies in addition to peripheral enlarged nodes. BM aspiration resulted in dry-tap. On examination of BM biopsy, it was noted extensive BMN characterized by cellular debris with indistinct cellular margin and abnormally eosinophilic staining cytoplasm (Figure 1).

At the completion of diagnostic studies, the patient was diagnosed to have stage IVB diffuse large B-cell lymphoma and treated with aggressive chemotherapy. Despite chemotherapy, one week later, liver function tests gradually deteriorated and the patient succumbed.

**DISCUSSION**

Although the survival of BMN depends on the underlying disorder, the ultimate prognosis is poor[14]. Table 2 lists survival rates in various disorders[3]. In hematologic malignancy, especially leukemias, most of the patients with BMN in whom achieved complete remission usually relapse early[15,16]. BMN in solid tumors reflects widespread metastasis including bone marrow and bad outcome. Despite the notorious outcome, some authors have reported resolved patients with chemotherapy and supportive measures even if, rare. For this reason, when an underlying pathology is detected, vigorous supportive care together with special treatment must be started including transfusion of blood components, adequate antibiotic treatment, hydration, oxygenation and alkalinization to permit a time for spontaneous recovery of the normal hematopoiesis. Given the complex pathophysiology of BMN, some novel therapies such as anti tumor necrosis factor (TNF)-α antibodies and various cytokines may be promising modalities in future.

**Table 2. Survival rates in BMN**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>n</th>
<th>Median survival (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>35</td>
<td>4</td>
</tr>
<tr>
<td>AML</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>MPD</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Solid tumors</td>
<td>18</td>
<td>5 weeks</td>
</tr>
<tr>
<td>Infections</td>
<td>5</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
<td>2.5 weeks</td>
</tr>
</tbody>
</table>

MPD: Myeloproliferative disorders.
REFERENCES


Address for Correspondence:
Dilek ARGON, MD
Doğancilar Halkdersanesi Sokak, No: 27/1
81160, Üsküdar, İstanbul, TURKEY
e-mail: d_argon@hotmail.com

Bone marrow necrosis in a patient with non-Hodgkin lymphoma

Argon D, Çetiner M, Adgüzel C, Kaygusuz I, Tugular TF, Tecimer T, Bayık M.