Successful Hematopoietic Reconstitution with Granulocyte Colony-Stimulating Factor in a Patient with Hypoplastic Acute Myelogenous Leukemia

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We describe a 68-year-old Japanese male with hypoplastic acute myelogenous leukemia (AML) who achieved complete hematological reconstitution following granulocyte colony-stimulating factor (G-CSF) administration. The patient had pancytopenia and the bone marrow was hypocellular with 19 to 36% peroxidase-positive blasts without morphological abnormalities suggestive of myelodysplasia. After receiving G-CSF as a supportive therapy for pneumonia, the blood count became normal and the bone marrow was normocellular with less than 5% of blasts. Without subsequent chemotherapy, he relapsed as a form of overt leukemia and died of pneumonia. Chemotherapy may be necessary to maintain remission in hypoplastic AML after hematopoietic reconstitution by G-CSF.

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Key words: hypoplastic leukemia, granulocyte colony-stimulating factor (G-CSF), hematological reconstitution

Introduction

Hypoplastic acute myelogenous leukemia (AML) is a syndrome that includes pancytopenia and hypocellular marrow with an evident increase of leukemic blast cells in a proportion of 15-75% of marrow nucleated cells (1, 2). This disease mainly affects the elderly and accounts for 5-7% of de novo AML (3). The patients typically lack a preceding history of myelodysplasia. Median survival without therapy is 6 to 9 months and most patients die of infectious episodes (2, 3). Recently, the beneficial effects of hematopoietic growth factors have been reported in the treatment of hypoplastic AML (4-7). However, it remains unclear whether post remission chemotherapy is recommended for the patients who have achieved remission by granulocyte colony-stimulating factor (G-CSF). In this report, we describe a case with hypoplastic AML who achieved hematopoietic reconstitution after G-CSF injection and discuss the pertinent literature.

Case Report

A 68-year-old Japanese male was referred to the hospital because of pancytopenia on April 11, 1991. He did not have a history of receiving chemoradiotherapy. No lymphadenopathy nor hepatosplenomegaly was observed on physical examination. The white-cell count was 1,900/µl, hemoglobin concentration (Hb) 6.1 g/dl and platelet (PLT) count 53x10³/µl. Repeated bone marrow aspirates showed hypoplastic marrow (less than 25% cellularity on a clot section) with 19 to 36% of blasts which were positive for peroxidase reaction. Erythroid series did not exceed 50% of marrow cells and morphological abnormalities suggesting myelodysplasia were not present. Chromosomal analysis of the bone marrow cells revealed a normal karyotype. Because the patient was asymptomatic and did not have severe neutropenia, the patient had been placed on careful observation without chemotherapy. On September 9, 1991, he was admitted because of pneumonia involving the left lower lobe. The white-cell count was 400/µl, Hb concentration 5.6 g/dl and PLT 19x10³/µl. The bone marrow aspirate again revealed hypoplastic marrow with 20% of blasts. Subcutaneous
G-CSF Induced Remission in Hypoplastic AML

NCC (/µl)  
14,900 57,000 116,500
Blasts  
(%) of ANC
G-CSF  
100 µg daily
250 µg daily every other day
250 µg weekly

Figure 1. Hematological changes after G-CSF treatment. NCC: nucleated cell count, ANC: all nucleated cells.

Discussion

There are two possibilities concerning the beneficial effects of G-CSF on hematopoietic reconstitution in hypoplastic AML. First, G-CSF may have induced differentiation of leukemic cells (8, 9). It has been recently reported that G-CSF can induce apoptosis and differentiation of myeloid leukemic cells in vitro (10). This is unlikely in the present case, however, because readministration of G-CSF did not bring about beneficial effect when the patient relapsed. Second, G-CSF may have stimulated residual normal hematopoietic stem cells to reconstitute normal hematopoiesis. It has been reported that G-CSF acts on not only myeloid progenitor cells but pluripotent hematopoietic stem cells (11, 12). de Bock et al reported that the lack of growth of marrow cells in patients with hypoplastic AML could be explained by the presence of humoral inhibitory factors for hematopoiesis and decreased production of hematopoietic stimulatory factors from peripheral blood mononuclear cells (13).
Table 1. Reported Cases of Hypoplastic AML with Successful Remission Induction by G-CSF

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Author</th>
<th>Age/Sex</th>
<th>Chromosome</th>
<th>Prior chemotherapy</th>
<th>Maintenance therapy</th>
<th>CR duration (months)</th>
<th>Re-induction therapy at relapse</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toki et al (4)</td>
<td>51/M</td>
<td>N.D.</td>
<td>AraC+Vitamin D</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>2</td>
<td>Muroi et al (6)</td>
<td>67/M</td>
<td>N.D.</td>
<td>DVP</td>
<td>Chemotherapy</td>
<td>48</td>
<td>–</td>
<td>CR</td>
</tr>
<tr>
<td>3</td>
<td>Hayatsu et al (7)</td>
<td>54/M</td>
<td>47, XY, +8</td>
<td>No</td>
<td>G-CSF alone</td>
<td>2</td>
<td>Chemotherapy</td>
<td>CR</td>
</tr>
<tr>
<td>4</td>
<td>Yanagisawa et al (14)</td>
<td>70/M</td>
<td>Normal</td>
<td>No</td>
<td>None</td>
<td>2</td>
<td>No</td>
<td>Relapse, Alive</td>
</tr>
<tr>
<td>5</td>
<td>Present case</td>
<td>68/M</td>
<td>Normal</td>
<td>No</td>
<td>G-CSF alone</td>
<td>2</td>
<td>Chemotherapy +G-CSF</td>
<td>Died</td>
</tr>
</tbody>
</table>

CR: complete remission, N.D.: not described, DVP: Daunomycin, Vincristine, Prednisolone.

However, analyses of the clonality in hematopoietic tissues and assay for G-CSF receptor on blast cells will be necessary to clarify the mechanisms by which G-CSF contribute to the hematopoietic reconstitution in hypoplastic AML.

There have been only four reports describing successful remission induction with G-CSF administration in patients with hypoplastic AML, known to date (4, 6, 7, 14). The remission duration appears to be quite short in patients who were not given cytotoxic agents after obtaining remission (Table 1; present case and cases 3 and 4). One reported case maintained remission for more than 48 months with post remission chemotherapy. Intensive chemotherapy has been reported to be successful in some patients with hypoplastic leukemia (5, 15). Chemotherapy may be feasible and reasonable in hypoplastic AML following the reconstitution of apparently normal hematopoiesis with G-CSF.

References