To the Editor:

Allogeneic bone marrow transplantation (BMT) has been performed on a very small number of patients with chronic lymphocytic leukemia (CLL). 1 The main factors that preclude wider use of BMT in CLL have been advanced age, absence of universally recognized criteria for BMT, and difficulty in eradicating the neoplastic clone. However, in younger patients with a compatible donor and poor prognostic features, BMT is now considered a potentially useful therapeutic approach. 2 Recently the European Bone Marrow
Transplantation Group (EBMTG) reported the results of allogeneic BMT in 17 CLL patients.\(^2\) In this series, all clinical and hematologic manifestations of CLL, particularly lymphocytosis, disappeared in the first 4 weeks after BMT. We report here a case in which a delayed complete response was finally achieved despite persistent lymphocytosis lasting 28 weeks after BMT.

A 46-year-old woman was diagnosed in February 1989 of typical B-cell CLL in stage B (I) according to the International Workshop in CLL staging system.\(^4\) She was treated every 2 to 3 weeks with prednisone (40 mg/m\(^2\)/d on days 1 through 4) plus chlorambucil (0.4 mg/kg/d on days 5 and 6), receiving a total of 15 courses. According to standard response criteria,\(^5,6\) she achieved partial remission. The patient was off therapy and doing well during 1 year but finally progression occurred with the following features: absolute lymphocyte count in peripheral blood over 100 x 10\(^9\)/L; 84% of lymphocytes in BM aspirate; a diffuse biopsy pattern, and bilateral cervical, axillary, and inguinal lymph node enlargement. She was again considered stage B (I). On June 7, 1991, BMT was performed with unmanipulated marrow from her HLA-identical, mixed lymphocyte culture nonreactive brother (cell dose 3.93 x 10\(^8\)/kg). The preparative regimen consisted of cyclophosphamide (60 mg/kg on days -6 and -3, etoposide (200 mg/m\(^2\)/d on days -6 and -9, and total body irradiation (12 Gy from day -4 to day 0). Short-course methotrexate and cyclosporine were administered as graft-versus-host disease (GVHD) prophylaxis. On day 13 after BMT, leukocyte counts reached the nadir (1.9 x 10\(^9\)/L). She developed cutaneous grade I acute GVHD and was treated with prednisone from day 14 to day 56. No other remarkable complications occurred during the immediate post-BMT period and she was discharged on day 21.

A progressive lymphocytosis (absolute lymphocyte count > 5 x 10\(^9\)/L) was observed in the following weeks (see Fig 1). White blood cell (WBC) count on day 28 was 21.9 x 10\(^9\)/L, with 75% lymphocytes, and reached a maximum of 35.4 x 10\(^9\)/L on week 6. From week 8 to week 16, the patient presented clinical and serologic evidence of cytomegalovirus (CMV) disease and was treated with gancyclovir (7.5 mg/kg/d for 3 weeks) plus intravenous anti-CMV hyperimmune Ig (500 mg/kg every other day for 10 days). During this period, lymphocyte counts increased to achieve 17.4 x 10\(^9\)/L. At that time, the BM proportion of lymphocytes with typical B-CLL immunophenotype was 44%. Peripheral blood lymphocyte count increased again and persisted over 5 x 10\(^9\)/L until week 27.

Table 1. Peripheral Blood and BM Status After BMT

<table>
<thead>
<tr>
<th>Wks After BMT</th>
<th>0</th>
<th>2</th>
<th>3</th>
<th>10</th>
<th>17</th>
<th>23</th>
<th>32</th>
<th>39</th>
<th>59</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM (%)</td>
<td>84</td>
<td>55</td>
<td>35</td>
<td>44</td>
<td>46</td>
<td>58</td>
<td>22</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>PB (x 10(^9)/L)</td>
<td>43.5</td>
<td>2.3</td>
<td>4.6</td>
<td>5.9</td>
<td>8.5</td>
<td>5.7</td>
<td>2.9</td>
<td>2.1</td>
<td>2.1</td>
</tr>
<tr>
<td>CD5 (%)</td>
<td>80</td>
<td>85</td>
<td>86</td>
<td>72</td>
<td>82</td>
<td>86</td>
<td>80</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CD19 (%)</td>
<td>66</td>
<td>90</td>
<td>62</td>
<td>70</td>
<td>—</td>
<td>32</td>
<td>11</td>
<td>12</td>
<td>—</td>
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<tr>
<td>Slg-lambda (%)</td>
<td>38</td>
<td>—</td>
<td>52</td>
<td>16</td>
<td>65</td>
<td>37</td>
<td>5</td>
<td>10</td>
<td>—</td>
</tr>
<tr>
<td>Biopsy pattern</td>
<td>D</td>
<td>—</td>
<td>D</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>N</td>
<td>N</td>
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<tr>
<td>Karyotype</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>46,XY</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>46,XY</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: D, diffuse; N, nodular; PB, peripheral blood.
minute chromosomes, frequent chromosomal breaks) in the remaining 22 metaphases. Data on morphologic, immunologic, and histologic examinations performed during the follow-up are shown in Table 1. A nodular pattern on BM biopsy, otherwise consistent with complete remission, is currently the only abnormal finding.

Persistent lymphocytosis with subsequent complete remission after BMT in CLL has not been previously reported. This atypical behavior of lymphocytosis observed in our patient demonstrates that, although its biologic significance is unknown, long-lasting monoclonal lymphocytosis after BMT in CLL does not necessarily indicate a therapeutic failure. Cases of long-lasting persistence after BMT of biologic features of active disease with subsequent complete response have been reported in other hematologic malignancies such as multiple myeloma. In our case, the slowly progressive evolution to a status of complete remission may be caused by the gradual disappearance of a nonproliferative leukemic clone irreparably damaged by the conditioning regimen. Results of peripheral blood karyotypic analysis support this interpretation. On the other hand, the therapeutic relevance of a graft-versus-leukemia effect is another probable explanation.

The role of BMT as a treatment for CLL is not fully established because of the lack of certainty about its eradicating ability. Nevertheless, an increasing utilization of both allogeneic and autologous BMT in CLL patients is to be presumed, and thus a better knowledge of atypical patterns of response after BMT could be of aid for the optimal management of CLL transplanted patients.

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