Long Term Complete Remission in Primary Plasma Cell Leukemia

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A 76-year-old female was diagnosed as having primary plasma cell leukemia (PCL), based on abundant atypical plasma cells in the circulation and bone marrow, monoclonal κ light chain in the serum and urine, the immunophenotype of the plasma cells and the lack of preceding multiple myeloma. The patient was treated with melphalan and prednisolone (MP), and complete remission (CR) was achieved; this was maintained for 28 months. The duration of CR in this patient appears to be the longest of those reported in well-documented primary PCL patients who have been treated with MP chemotherapy. (Internal Medicine 34: 251-254, 1995)

Key words: melphalan, prednisolone

Introduction

Plasma cell leukemia (PCL) is a rare condition in which there is malignant proliferation of plasma cells, defined as an absolute circulating plasma cell level greater than 2,000/μl (1). The incidence of PCL has been estimated to be 1.6%-5.0% of all cases of multiple myeloma (1, 2). There are two forms of PCL: primary and secondary. The primary form, which occurs in individuals without preceding multiple myeloma, is estimated to account for 50% to 70% of PCL (1, 3). Most cases of primary PCL involve IgG and light chain-producing cells, and the involvement of IgM and IgA is less frequent (4). Other features of primary PCL are similar to those of multiple myeloma. The response of primary PCL to chemotherapy is usually poor and survival is correspondingly brief (3, 5, 6); there have been only 13 reported patients who survived for more than 12 months with complete remission (CR). Most of these patients were treated with intensive combination chemotherapy. In this report, we describe an exceptional patient with primary PCL, who achieved a long-lasting CR of 28 months with conventional melphalan/prednisolone (MP) chemotherapy, a therapy that is widely used in treating multiple myeloma.

Case Report

A 76-year-old Japanese female was admitted to Saiseikai Ibaraki Hospital in September 1991, because of the sudden onset of low back pain. She had been well until this episode. The results of physical examination were non-specific, except for anemic palpebral conjunctivae. Laboratory examinations revealed a white cell count of 8,800/μl with 28% atypical cells (Fig. 1a), a platelet count of 2.0x10^4/μl, and hemoglobin concentration of 8.9 g/dl. Sternal bone marrow aspirate showed a nucleated cell count of 12.2x10^4/μl with 90% atypical cells (Fig. 1b). The morphological features of circulating atypical cells were almost identical to those of the cells in the bone marrow. The atypical cells were negative for peroxidase and PAS staining. Surface immunophenotype analysis revealed a white cell count of 8,800/μl with 28% atypical cells (Fig. 1a), a platelet count of 2.0x10^4/μl, and hemoglobin concentration of 8.9 g/dl. Sternal bone marrow aspirate showed a nucleated cell count of 12.2x10^4/μl with 90% atypical cells (Fig. 1b). The morphological features of circulating atypical cells were almost identical to those of the cells in the bone marrow. The atypical cells were negative for peroxidase and PAS staining. Surface immunophenotype analysis revealed atypical cells positive for CD38 and plasma cell antigen (PCA)-1, but negative for CD10, CD19, CD20, HLA-DR, immunoglobulins, T cell-, platelet-, and myeloid-associated antigens. Almost all the atypical cells contained κ-light chain in the cytoplasm. Cytogenetic examination of the bone marrow cells gave the normal karyotype, although the cell type of the dividing cells remained unclear. Immunoelectrophoresis showed the presence of monoclonal κ-light chain both in the serum and urine. Urinary protein was 2.6 g/day, indicating mostly (95%) monoclonal κ chain.

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Received for publication June 6, 1994; Accepted for publication October 28, 1994
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Internal Medicine Vol. 34, No. 4 (April 1995)
Serum immunoglobulin concentrations were low; levels of IgG, IgA, and IgM were 310, 11, and 25 mg/dl, respectively. Serum levels of urea nitrogen (29.5 mg/dl) and creatinine (3.4 mg/dl) were moderately high. Serum calcium concentration was elevated to 6.1 mEq/L (normal range: 4.2–5.5 mEq/L). Systemic X-ray examination disclosed no osteolytic lesions except for a compression fracture of the fifth lumbar vertebra and general low-grade osteoporosis. From these findings a diagnosis of primary PCL was made.

The clinical course of the patient is shown in Fig. 2. She was treated with oral MP chemotherapy, consisting of 6 mg melphalan and 40 mg prednisolone, for 4 consecutive days. This MP chemotherapy was repeated every 4 weeks. Following the first cycle, the serum calcium level returned to normal. After 2 courses, the atypical plasma cells disappeared both from peripheral blood and bone marrow; subsequently a CR was achieved and this was associated with relief of the low back pain. At this time, the monoclonal kappa chain was undetectable in both serum and urine. After 4 courses of MP chemotherapy, serum immunoglobulins had recovered to normal levels; from that time, the chemotherapy was administered every 3 months, and the CR was maintained for 28 months. On April 18, 1994, recurrence of PCL was noted. Soon after the recurrence, a decrease of serum IgG concentration and reappearance of Bence Jones protein were observed.

**Discussion**

Primary PCL is a rare B-cell malignancy with a very poor prognosis, the median survival of patients with primary PCL being approximately 6.8 months (3). The present patient had a compression fracture of a lumbar vertebra. However, the patient had been well until this episode. Furthermore, no other bone lesion was noted on systemic bone survey. Therefore, it is unlikely that the patient had preceding multiple myeloma. As shown in Table 1 (1–3, 7–18), only 13 patients who survived for more than 12 months with CR have been reported. The majority of these patients were successfully treated with intensive combination chemotherapy. While conventional MP chemotherapy for multiple myeloma has been reported to be ineffective for primary PCL (2, 19), the present patient had a dramatic response to MP chemotherapy, the CR being maintained for 28 months. Patient 1 listed in Table 1 may have responded to MP chemotherapy for 32 months, however, whether the response was CR is unclear. The criteria for response in that study was 50% reduction of leukemic cells. Patient 3 survived for 28 months with MP chemotherapy, however, recurrence of leukemia was observed prior to the patient’s death. Therefore, the duration of CR would have been less than 28 months. The duration of CR in the present patient, therefore, appears to be the longest of these reported in well-documented primary PCL patients who have received MP chemotherapy. In addition, Bence Jones type PCL appeared to be predominant in the long-term survivors with intensive combination chemotherapy but not with MP therapy.

It has been shown that B-cell associated antigens, including CD20, CD21, and HLA-DR, as well as surface membrane immunoglobulin (SmIg), receptors for the Fc fragment of immunoglobulin and complement, are lost before the terminal differentiation into plasma cells (20–23). Cytoplasmic immunoglobulins, and surface CD38 and PCA-1 antigens are expressed in plasma cells but not in mature B-lymphocytes (20). Linden et al reported that 2 of 3 patients with primary PCL showed coexpression of B-cell markers (SmIg, CD19) and plasma cell markers (CD38, PCA-1) (24). Shimazaki et al (25) also reported that primary PCL cells exhibited B-cell associated antigens (CD20, CD10) and SmIg in addition to PCA-1 in 2 of 5 patients. In multiple myeloma, Durie and Grogan (26) suggested that the expression of CD10 antigen which appears in immature B cells, is associated with a high proliferative tendency and drug resistance. Taken together, the expression of B-cell associated markers may be, in part, responsible for the poor prognosis and chemo-resistance in primary PCL and multiple myeloma. The immunophenotype of the leukemic cells in the present patient was similar to that of mature myeloma cells. Furthermore, the nuclear chromatin of both circulating and...
marrow leukemic cells in our patient was fairly condensed. Therefore, it is conceivable that this phenotype may have been related to her good response to MP chemotherapy. MP chemotherapy, therefore, may be worthy of consideration in the treatment of primary PCL presenting the phenotype of mature myeloma plasma cells. Analysis of the outcomes of chemotherapy, including MP in a larger number of patients with primary PCL is required to elucidate the relationship of such therapy to the immunophenotype of leukemic cells.

Acknowledgments: This work was supported in part by the Sasaki Foundation for the Promotion of Leukemia Research.

References

Table 1. Long-Term Survivors of Primary Plasma Cell Leukemia in the Literature

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>M Protein</th>
<th>Treatment</th>
<th>Duration of reported CR (months)</th>
<th>Reference No.</th>
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<tr>
<td>1</td>
<td>32*</td>
<td>F</td>
<td>-</td>
<td>-</td>
<td>32*</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>76</td>
<td>F</td>
<td>BJ(k)</td>
<td>-</td>
<td>28</td>
<td>Present case</td>
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<tr>
<td>3</td>
<td>72</td>
<td>M</td>
<td>IgG</td>
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<td>4</td>
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<td>M</td>
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<tr>
<td>5</td>
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<td>M</td>
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<td>10</td>
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<tr>
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<td>VCR, PDN, sarcolysin peptichemio</td>
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<td>77</td>
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<td>F</td>
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<tr>
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<td>-</td>
<td>32P</td>
<td>14</td>
<td>18</td>
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</table>

For patients other than the MP group, only those who had a complete remission lasting for more than 12 months are listed.


The M2-protocol, consisted of melphalan, cyclophosphamide, carmustine, vincristine and prednisone.

*Whether or not these values indicate the duration of complete remission is unclear. No data (-) indicates that clinical or laboratory information was not available.


