Central Nervous System Relapse after Autologous Peripheral Blood Stem Cell Transplantation in Primary Plasma Cell Leukemia

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Abstract
The usefulness of autologous stem cell transplantation (auto-SCT) has not been established for primary plasma cell leukemia (PCL). After achieving complete remission with chemotherapy, a 61-year-old man underwent autologous peripheral blood stem cell transplantation with a conditioning regimen comprising melphalan 200mg/m² in December 2002. He was discharged on Day 26 in complete remission. PCL relapsed in cerebrospinal fluid 3 months after transplantation. Intra- and extra-thecal plasmacytomas also developed, but no bone marrow relapse was documented. The patient died of disease progression on Day 236 after auto-SCT. Novel therapeutic approaches to PCL are needed.

Key words Melphalan, t(11;14), VAD therapy, Autologous stem cell transplantation, Primary plasma cell leukemia

Case Report
A 61-year-old man was referred to Toyohashi Municipal Hospital in May 2002 due to leukocytosis. He complained of forearm pain but did not display fever, skin eruptions or lymphadenopathy. Survey radiography or scintigraphy did not detect any bone lesions. Computed tomography revealed mild hepatosplenomegaly. Laboratory examination revealed the following results: hemoglobin, 13.8 g/dl; platelet count, 8.3×10¹¹/L; WBC, 30,550/L with 10% peroxidase-negative atypical cells; serum LDH, 653 IU/L; total protein, 6.0 g/dL; and Bence-Jones type-I protein. Bone marrow examination revealed infiltration with 55% atypical cells (Fig. 1). Atypical cells were positive for CD38, CD126 and p53 and negative for CD56 on immunopathological examination of a bone marrow clot. Primary PCL

Introduction
Plasma cell leukemia (PCL) is a rare variant of multiple myeloma (MM).1,2 This disease is defined by circulating plasma cells >2,000/mm² and plasmacytosis accounting for >20% of the white blood cell count (WBC). Primary PCL is defined as plasma cell proliferation first diagnosed in the leukemia phase, and reportedly displays a poor prognosis.1,2 Autologous stem cell transplantation (auto-SCT) is an optimal therapy for MM. In primary PCL, only a small case series has been reported, and the clinical outcome has not been well described.3–5 We report herein the case of a patient with primary PCL who developed central nervous system (CNS) relapse after auto-SCT.
was diagnosed. Cytogenetic analysis revealed a complex karyotype including 43, X, −Y, der(1;22) (q10q10), dup(1)(q21q32), add(5)(q11), del(6)(q?), −10, −13, add(13)(p11), add(15)(p11), −16, +mar1, +mar2. Fluorescent in situ hybridization analysis revealed translocation (11;14) and deletion of 13q14 (RB1) and 17p13 (p53).

Complete remission was achieved after 3 courses of ROAD (vincristine 1.2 mg/m² × 1 day; ranimustine 40 mg/m² × 1 day, melphalan 8 mg/m² × 6 days, dexamethasone 40 mg × 4 days) and 4 courses of VAD therapy (vincristine 0.4 mg/m² × 4 days, doxorubicin × 4 days, dexamethasone 40 mg × 12 days). After successful peripheral blood stem cell collection, the patient underwent autologous peripheral blood stem cell transplantation (auto-PBSCT) with a conditioning regimen comprising melphalan 200 mg/m² in December 2002. Neutrophil engraftment was achieved on Day 10, and he was discharged on Day 26 in complete remission.

Lumbago developed 3 months after auto-PBSCT. Magnetic resonance imaging (MRI) revealed intra- and extrathecal plasmacytomas at the L3 level (Fig. 2). Cerebrospinal fluid (CSF) examination revealed 8,448/µm³ atypical plasma cells, whereas bone marrow examination revealed a normal distribution of cells and serum, and urine M-protein or Bence-Jones protein were not detected in the serum or urine. Intrathecal administration of 15 mg methotrexate and 4 mg dexamethasone was initiated. Atypical plasma cells disappeared after 5 courses of intrathecal administration into CSF. Extrathecal plasmacytomas were treated supportively without chemo- or radiotherapy. The patient did not receive additional intrathecal chemotherapy due to pancytopenia.

The patient complained of lumbago three weeks after the last intrathecal administration, and atypical plasma cells in CSF increased. He died of disease progression on Day 236 after auto-SCT.

**Discussion**

This case indicates that patients with primary PCL could develop CNS relapse and that physicians must be careful in watching for the development of neurological symptoms after auto-SCT. CNS involvement in patients with MM is uncommon. Auto-SCT has become a therapeutic option in MM, although reports of CNS relapse after auto-SCT are limited. Patients with primary PCL are more likely to develop extramedullary involvement. Although we must take into consideration the fact that we only used as a conditioning regimen high-dose melphalan, which fails to penetrate the blood brain barrier into CSF, the frequency of CNS relapse after auto-SCT might be higher in primary PCL than...
References


in MM. There is another concern that the procedure of auto-SCT might induce the risk of CNS involvement. However, information on the association between auto-SCT and CNS involvement is highly limited in MM or PCL. Further investigations are warranted.

The efficacy of auto-SCT for primary PCL has not been established. Our patients relapsed soon after auto-PBSCT. According to the data of The International Bone Marrow Transplant Registry, 2 of 5 patients with PCL died of disease progression within 1 year after auto-SCT. This indicates that auto-SCT has insufficient antitumor effect against primary PCL. Additional novel agents, such as thalidomide or bortezomib, intrathecal chemotherapy before and after auto-SCT and allogeneic SCT might be worth investigating. Further studies are warranted.

The establishment of risk strategies against primary PCL is required. Cytogenetic abnormalities might be useful for identifying high-risk patients with primary PCL, as in MM. Our patient displayed deletion 17q13 and common cytogenetic abnormalities in primary PCL t(11;14), monosomy 13 and abnormality of 1q.9,10 Although abnormality of t(11;14) is reportedly associated with favorable outcomes,9 most abnormalities in our patients are unfavorable.11 Patients with primary PCL display a more complex karyotype than those with MM.12 This is a difficulty in identifying high-risk patients using cytogenetic abnormalities in primary PCL. Further large-scale studies would allow proper interpretation.

In summary, we presented a case involving CNS relapse after auto-SCT in a patient with PCL. PCL displays clinically different characteristics from MM. Novel therapeutic approaches to PCL need to be established.