Plasma Cell Leukemia Maintaining Complete Remission by Syngeneic Stem Cell Transplantation Combined with Low-Dose Thalidomide Maintenance Therapy

Masahiro Abe, Hisayuki Yokoyama, Yasuo Tohmiya, Yoko Okitsu, Hirotö Ohguchi, Katsura Kohata, Joji Yamamoto, Yasushi Onishi, Kenichi Ishizawa, Junichi Kameoka and Hideo Harigae

Abstract

Plasma cell leukemia (PCL) is a rare variant of multiple myeloma, which is very aggressive and resistant to chemotherapy. We report a case of PCL successfully treated with syngeneic peripheral blood stem cell transplantation followed by low-dose thalidomide. As of March 2009, the patient has maintained CR for 39 months posttransplant. The clinical course of the present case suggests that autologous stem cell transplantation using a graft with reduced contamination of malignant cells followed by low-dose thalidomide maintenance therapy may improve the PCL treatment outcome.

Key words: plasma cell leukemia, syngeneic stem cell transplantation, low-dose thalidomide

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Introduction

Multiple myeloma (MM) is a hematological malignancy characterized by the proliferation of clonal plasma cells. Although novel agents, such as bortezomib and lenalidomide, have been developed for MM, it remains incurable. Plasma cell leukemia (PCL) is a rare MM variant, reported to occur in fewer than 5% of plasma cell neoplasms (1-4). Since PCL is highly aggressive and resistant to chemotherapy, its prognosis is very poor; median survival is reported to be 6-8 months (5). In this report, we describe a patient with primary PCL who has maintained complete remission (CR) for more than 3 years with syngeneic stem cell transplantation (SCT) combined with low-dose thalidomide maintenance therapy.

Case Report

In June 2005, a 37-year-old man, who complained of chest and low back pain, was admitted to Ishinomaki Red Cross Hospital. His white blood cell count was 8,800/mm³ with 42.5% of atypical lymphocytes (plasma cell-like cells). His hemoglobin and platelet counts were 13.2 g/dL and 29.1x10⁴/mm³, respectively. Serum IgG was 310 mg/dL, serum albumin was 4.2 g/dL, and β₂-microglobulin was 2.3 mg/dL. Bence-Jones protein of the κ-type was detected in the urine and serum by immunoelectrophoresis, however, the amount of Bence-Jones protein was below 200 mg/day. His serum creatinine level was normal, and bone marrow was normocellular marrow with 70.4% plasma cells. These cells are positive for CD38 and CD56 and negative for CD19. Chromosomal analysis showed normal karyotypes, and no bone lytic lesions were shown by the skeletal X-ray images. In bone scintigraphy, hot spots were detected at the bilateral limbs, sternum, spine, and left sacroiliac joint. Based on these findings, we diagnosed him as PCL (6) and defined the clinical staging as stage I of ISS (7). He was treated with two cycles of VAD (vincristine 0.4 mg/day, days 1-4; doxorubicin 15 mg/day, days 1-4; and dexamethasone 40 mg/day, days 1-4, 9-12, and 17-20) and one cycle of ROAD (vincristine 1.9 mg/day, day 1; ranimustine 65 mg/day, day
Figure 1. Clinical course. The clinical course focusing on syngeneic SCT is shown. Atypical cells before SCT correspond with plasma cells, whereas atypical lymphocytes after SCT may be reactive lymphocytes resulting from a viral infection.

1; dexamethasone 40 mg/day, days 1-4; and melphalan 12 mg/day, days 1-6), but these treatments were ineffective. He was then transferred to our hospital for a syngeneic peripheral blood SCT. He received syngeneic peripheral blood stem cells containing 3.6x10^6/kg of CD34-positive cells from his HLA-identical twin with a conditioning regimen of melphalan 200 mg/m^2. He transiently had a mild skin rash and fever when the white blood cell count started to increase. Atypical lymphocytes concomitantly appeared in his peripheral blood with the rash and fever. We judged that they were reactive lymphocytes resulting from a viral infection; however, these atypical cells were not completely distinguished from malignant plasma cells because immunophenotyping was not performed. After SCT, the plasma cells rapidly disappeared from both the peripheral blood and the bone marrow (Fig. 1). M protein in serum and urine was unmeasurable, the response was defined as PR based on the reduction of plasma cells (8). Low-dose thalidomide (100 mg per day) continues to be given as a maintenance therapy after SCT without cessation. M protein in urine became undetectable soon after thalidomide was started, though it is unclear whether this disappearance of urine M protein was achieved by thalidomide or SCT. As of March 2009, Bence-Jones protein was not detectable by immunofixation, and he has maintained CR for 39 months posttransplant.

Discussion

The effectiveness of autologous peripheral blood SCT for PCL has not been established. Saccaro et al reviewed 22 cases of PCL treated with stem-cell transplantation, including 5 allogeneic SCT cases (5). In their report, the mean survival of patients was 28 months. Since there was no significant difference of outcomes between allogeneic SCT and autologous SCT, the efficacy of allogeneic stem cell transplantation for PCL appeared to be limited. In this report, 5 out of 9 cases that underwent auto-SCT relapsed, suggesting that the PCL relapse rate after auto-SCT exceeds 50% (5). Therefore the most possible reason why the present case has maintained CR for more than three years is that the patient received SCT using a syngeneic graft that was free of myeloma, though it is possible that malignant cells were sensitive to melphalan. Gahrton et al reported the efficacy of a syngeneic peripheral blood SCT in multiple myeloma compared to autologous or allogeneic SCT (9). They showed a better overall survival (OS) in a syngeneic SCT (median 73 months) than in an autologous SCT (median 44 months) or an allogeneic SCT (median 16 months). Also, progression-free survival in the syngeneic SCT (median 72 months) was longer than that in an autologous SCT (median 25 months) or an allogeneic SCT (median 9 months). An-
other study, which compared the outcomes between syngeneic and autologous SCT for multiple myeloma, has recently been reported (10). In that report, the cumulative incidence of relapse/progression was significantly lower, and progression-free survival (PFS) was significantly higher in the syngeneic SCT group, consistent with the previous report. Furthermore, Kopp et al studied the correlation between the outcome of auto-SCT and the number of malignant cells in the graft, reporting that overall survival in the low-contamination group is better than in the high-contamination group (53 months vs. 114 months) (11). These results suggest that a decrease of the number of malignant cells in the graft results in an improved outcome of autologous SCT for multiple myeloma.

Another reason for the patient’s good clinical course may be the maintenance therapy of low-dose thalidomide administered after transplantation. Recently, the effectiveness of thalidomide maintenance therapy for multiple myeloma has been reported (12). In that study, patients were randomly assigned to prednisolone maintenance therapy with or without low-dose thalidomide. Both 3-year PFS and OS rates were better in the thalidomide group than in the control group, suggesting the efficacy of thalidomide maintenance therapy after SCT. In the present case, low-dose thalidomide was given after transplantation, and it is possible that this additional maintenance therapy contributes to maintaining CR.

In conclusion, we report a case with primary PCL successfully treated with a combination therapy of syngeneic SCT with low-dose thalidomide. Our results reveal that syngeneic stem cell transplantation or autologous stem cell transplantation using a graft with reduced contamination of malignant cells followed by low-dose thalidomide maintenance therapy may improve the treatment outcome of PCL.

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References

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