Case Study

Successful Treatment of Bulky Granulocytic Sarcoma of the Retroperitoneum with High-Dose Chemotherapy and Autologous Peripheral Blood Stem Cell Transplantation

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Granulocytic sarcoma is a rare disease that is rarely curable with conventional chemotherapy. This report describes a case of a patient with bulky granulocytic sarcoma of the retroperitoneum who was treated with high-dose chemotherapy and autologous peripheral blood stem cell transplantation without administering granulocyte colony-stimulating factor before stem cell collection. According to bone marrow assessment and imaging studies, the patient remained in complete remission at 5 years after transplantation. This case suggests that high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation is a therapeutic option for granulocytic sarcoma.

Keywords: granulocytic sarcoma, myeloid sarcoma, autologous peripheral blood stem cell transplantation

INTRODUCTION

Granulocytic sarcoma is a tumor that is localized outside of the bone marrow and is composed of granulocytic precursor cells. Generally, this tumor occurs concomitantly to or after the onset of myeloid leukemia or emerges at the time of relapse of the leukemia. In rare cases, the tumor occurs before the onset of myeloid leukemia. Granulocytic sarcoma is a very rare disease, comprising approximately 2% to 9% of all patients with acute myeloid leukemia (AML).1,2 The histologic morphology of granulocytic sarcoma may lead to its misdiagnosis as malignant lymphoma,3,4 and early diagnosis of this tumor is very difficult.

There are no definitive treatment strategies for this entity, and precise indications for hematopoietic stem cell transplantation after chemotherapy or local therapy (e.g., radiation, surgical resection) have not been established. The present report describes the case of a patient with bulky granulocytic sarcoma of the retroperitoneum who was successfully treated with high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation (PB SCT).

CASE REPORT

In March 2007, a 28-year-old man presented to his doctor with anorexia, nausea and vomiting. Computed tomography scan of the abdomen revealed a bulky tumor in the right retroperitoneum as well as right hydronephrosis and duodenal obstruction due to the tumor (Fig. 1A, 1B). The patient was referred to our hospital for diagnosis and management of the tumor. A tumor biopsy by diagnostic laparotomy revealed small cancer cells with scanty cytoplasm (Fig. 2A). On immunostaining, the neoplastic cells were positive for CD45, weakly and partially positive for CD3 and negative for CD20, CD79a and CD56. G-banding stain did not have a helpful result because cell division images of the tumor cells were not detected. We did not conduct fluorescent in situ hybridization analysis. A diagnosis of T-cell lymphoma was made from pathological findings and immunohistochemical staining.

The patient’s condition was thought to be medically urgent because of severe back pain due to the bulky tumor, and he was immediately treated with CHOP therapy (cyclophosphamide, doxorubicin, vincristine and prednisolone). Laboratory studies before treatment showed no cytopenia or blastoid cells, but analysis of bone marrow specimens that were obtained just before the initiation of chemotherapy ultimately revealed 12% myeloperoxidase-positive myeloblasts (Fig. 3A, 3B). Subsequent examination of the retroperitoneal
specimen revealed strongly myeloperoxidase-positive tissue (Fig. 2B). On the basis of these findings, the diagnosis was revised to granulocytic sarcoma. Although CHOP therapy was not the appropriate treatment, the patient experienced resolution of severe pain and duodenal obstruction after treatment.

After resolution of chemotherapy-induced myelosuppression, remission induction therapy was performed using idarubicin and cytarabine. Bone marrow aspiration revealed complete remission after induction therapy, and the tumor had nearly disappeared on computed tomography imaging (Fig. 1C). The patient was treated with two courses of consolidation therapy, including cytarabine and anthracyclines, followed by consolidation therapy with high-dose cytarabine (2,000 mg/m² every 12 hr on days 1 to 5).

After this chemotherapy, peripheral blood stem cell harvest was performed following recovery from myelosuppression. A sufficient quantity of peripheral blood stem cells (1.6 × 10⁹ CD34-positive cells/kg) was collected without the administration of granulocyte colony-stimulating factor (G-CSF). On serial magnetic resonance imaging studies, the tumor had disappeared, and bone marrow aspiration showed complete remission. Human leukocyte antigen studies failed to identify a matched-sibling donor, and no human leukocyte antigen-matched unrelated donor was found in the Japan Marrow Donor Program registry.

After receiving informed consent from the patient, myeloablative chemotherapy was performed with combined autologous PBSC. The patient was treated with conditioning chemotherapy using a G-CSF-combined BEA (busulfan, eto-
The safety and efficacy of this regimen for the treatment of AML were evaluated previously, and the administration of G-CSF enhanced the efficacy of chemotherapy in patients with AML. After the conditioning chemotherapy, peripheral blood stem cells were rein infused. Neutrophil engraftment was achieved on day 24 after transplantation without G-CSF administration. Magnetic resonance imaging, 18F-fluorodeoxy glucose positron emission tomography imaging, and bone marrow aspiration were performed regularly after transplantation, all of which showed complete remission. The patient remains well and asymptomatic at 5 years after transplantation.

**DISCUSSION**

Granulocytic sarcoma is a rare disease, comprising approximately 2% to 9% of all patients with AML. In many cases, granulocytic sarcoma emerges at the time of relapse of myeloid neoplasm. In the present case, however, the tumor occurred concurrent with the onset of myeloid leukemia, and such pattern of onset is relatively uncommon. Previous studies reported that there were many chromosomal aberrations relevant to granulocytic sarcoma, such as AML1/ETO fusion, CBF-b splitting and trisomy. Genetic information is useful and important for the decision on the therapeutic strategy, so genetic abnormality of granulocytic sarcoma must be examined by G-banding stain and fluorescent in situ hybridization analysis to the extent possible.

Treatment for granulocytic sarcoma involves systemic chemotherapy and localized treatment, such as surgical resection and radiation. A number of previous reports have indicated that intensive chemotherapy based on the regimen employed for patients with AML, including cytarabine, significantly reduced the risk of subsequent leukemia and contributed to long-term survival. However, intensive chemotherapy is not sufficient to prevent the development of leukemia completely. Previous studies reported that the leukemia-free rate after intensive chemotherapy was approxi-
allogeneic transplantation when compared with that after extramedullary relapse appeared to be more common after allogeneic transplantation.\textsuperscript{10,11} However, the graft-versus-leukemia effect, which is a major antitumor effect after allogeneic transplantation, may be less efficient at the extramedullary site when compared with the bone marrow.\textsuperscript{12} Several studies have reported that extramedullary relapse occurred after allogeneic transplantation,\textsuperscript{13} and extramedullary relapse appeared to be more common after allogeneic transplantation when compared with that after chemotherapy alone.\textsuperscript{14} We utilized autologous transplantation in this patient because we anticipated that autologous transplantation followed by mega-chemotherapy was comparable to allogeneic transplantation in terms of the anti-leukemic effect exerted on the extramedullary site. Moreover, autologous transplantation was associated with less treatment-related mortality than allogeneic transplantation, such as that associated with graft-versus-host disease and graft failure.

High-dose chemotherapy with autologous hematopoietic stem cell transplantation can be used for post-remission therapy in young AML patients with first complete remission,\textsuperscript{15} and previous reports indicated that autologous transplantation could also be a definitive treatment for granulocytic sarcoma.\textsuperscript{16,17} However, the collection of hematopoietic stem cells can pose a challenge when utilizing autologous transplantation for granulocytic sarcoma. When collecting stem cells from the peripheral blood, it is common to administer G-CSF after the infusion of high-dose anticancer therapy. However, G-CSF can accelerate the cell cycle of leukemia cells and increase the tumor volume if leukemia cells are still present. Thus, in the present case, peripheral blood stem cells were collected without G-CSF administration. Fortunately, we were able to harvest stem cells efficiently during the recovery period after high-dose cytarabine treatment.

In conclusion, this case suggests that autologous PBSCT is an alternative treatment strategy for patients with granulocytic sarcoma. However, further follow-up and confirmation of these observations in a larger number of patients is needed to confirm this conclusion.

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