J Clin Exp Hematop
Vol. 53, No. 3, Dec. 2013

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. 〔*J Clin Exp Hematop 53(3)：235-239, 2013*〕

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 concomitant 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 (PBSCT).

Received : September 19, 2013
Revised : October 2, 2013
Accepted : October 9, 2013

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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

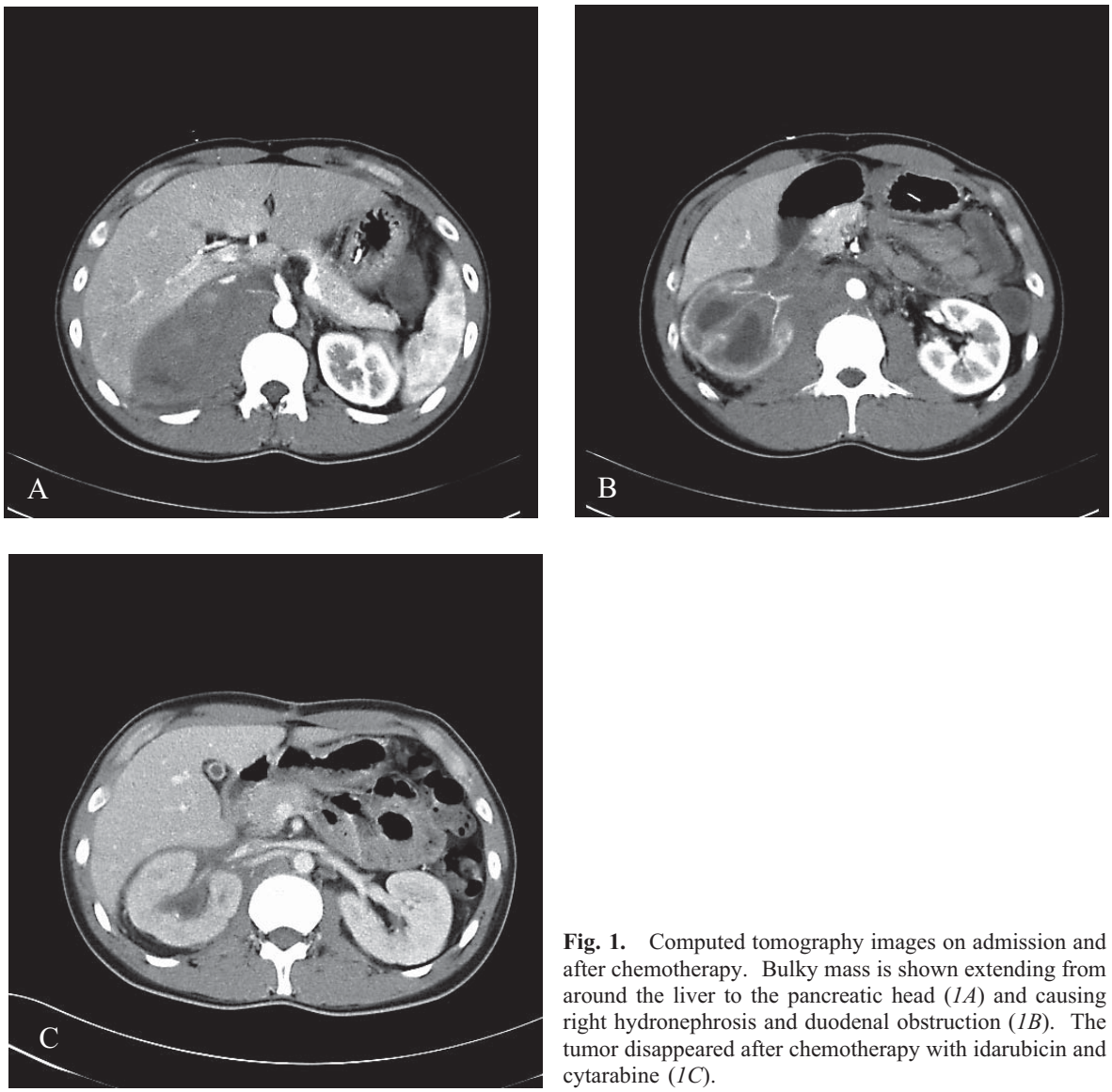

Fig. 1. Computed tomography images on admission and after chemotherapy. Bulky mass is shown extending from around the liver to the pancreatic head (*1A*) and causing right hydronephrosis and duodenal obstruction (*1B*). The tumor disappeared after chemotherapy with idarubicin and cytarabine (*1C*).

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/m^2 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 (1.6×10^6 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 PBSCT. The patient was treated with conditioning chemotherapy using a G-CSF-combined BEA (busulfan, eto-

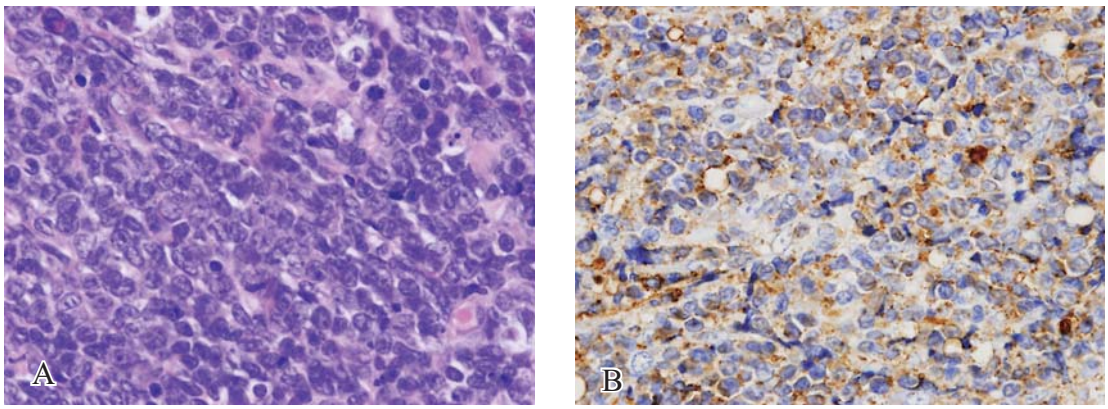

Fig. 2. Pathological images of the granulocytic sarcoma from the retroperitoneum. Cancer cells are small, have scanty cytoplasm on hematoxylin-eosin staining (*2A*) and are myeloperoxidase-positive on immunohistochemical staining (*2B*).

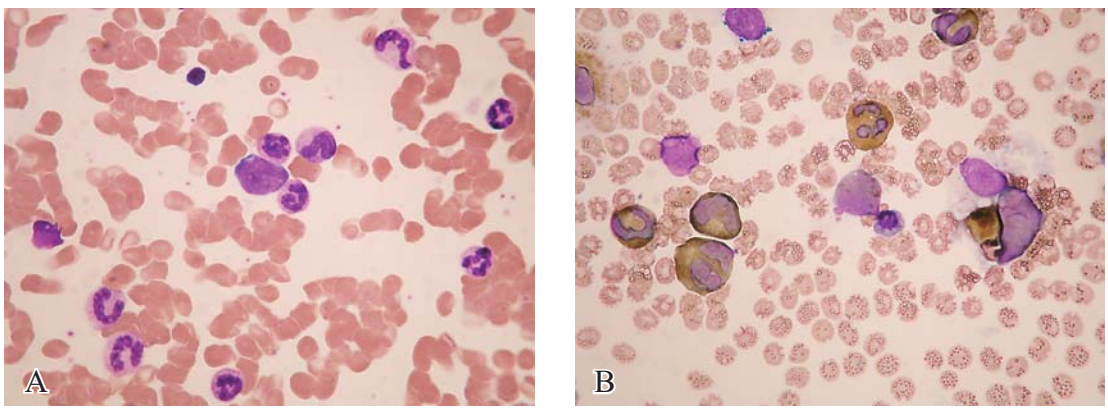

Fig. 3. Photomicrographs of the bone marrow smears. Blast cells have scanty cytoplasm and fine nucleoreticulum on May-Giemsa staining (*3A*), and are myeloperoxidase-positive (*3B*).

poside, cytarabine) regimen. The safety and efficacy of this regimen for the treatment of AML were evaluated previously,[5,6] and the administration of G-CSF enhanced the efficacy of chemotherapy in patients with AML.[7] After the conditioning chemotherapy, peripheral blood stem cells were reinfused. Neutrophil engraftment was achieved on day 24 after transplantation without G-CSF administration. Magnetic resonance imaging, ^{18}F-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.[1,2] 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.[8] Previous studies reported that there were many chromosomal aberrations relevant to granulocytic sarcoma, such as AML1/ETO fusion, CBF−b splitting and trisomy.[8] 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.[3,4] However, intensive chemotherapy is not sufficient to prevent the development of leukemia completely.[8,9] Previous studies reported that the leukemia-free rate after intensive chemotherapy was approxi-

mately 30% to 40%.[3,4] In addition, leukemia cells acquired resistance to chemotherapy in most cases once leukemic relapse occurred in patients with granulocytic sarcoma. These findings suggest that intensive chemotherapy alone is not sufficient for curative purposes, and additional treatment strategies must be considered.

Hematopoietic stem cell transplantation is potentially curative for granulocytic sarcoma, and superior outcomes are achieved with the use of allogeneic or autologous transplantation when compared with chemotherapy alone.[2] Several reports have stated that long-term relapse-free survival was achieved in response to allogeneic transplantation.[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.[12] Several studies have reported that extramedullary relapse occurred after allogeneic transplantation,[13] and extramedullary relapse appeared to be more common after allogeneic transplantation when compared with that after chemotherapy alone.[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,[15] and previous reports indicated that autologous transplantation could also be a definitive treatment for granulocytic sarcoma.[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.

DISCLOSURE STATEMENT

The authors declare that they have no conflicts of interest.

ACKNOWLEDGEMENTS

The authors wish to thank the nursing staff of National Hospital Organization Kumamoto Medical Center and all of the participants evaluated in this report.

REFERENCES

1 Liu PI, Ishimaru T, McGregor DH, Okada H, Steer A: Autopsy study of granulocytic sarcoma (chloroma) in patients with myelogenous leukemia, Hiroshima-Nagasaki 1949-1969. Cancer 31:948-955, 1973

2 Bakst RL, Tallman MS, Douer D, Yahalom J: How I treat extramedullary acute myeloid leukemia. Blood 118:3785-3793, 2011

3 Byrd JC, Edenfield WJ, Shields DJ, Dawson NA: Extramedullary myeloid cell tumors in acute nonlymphocytic leukemia: a clinical review. J Clin Oncol 13:1800-1816, 1995

4 Yamauchi K, Yasuda M: Comparison in treatments of nonleukemic granulocytic sarcoma: report of two cases and a review of 72 cases in the literature. Cancer 94:1739-1746, 2002

5 Gondo H, Harada M, Miyamoto T, Takenaka K, Tanimoto K, *et al*.: Autologous peripheral blood stem cell transplantation for acute myelogenous leukemia. Bone Marrow Transplant 20:821-826, 1997

6 Harada M, Akashi K, Hayashi S, Eto T, Takamatsu Y, *et al*.: Granulocyte colony-stimulating factor-combined marrow-ablative chemotherapy and autologous blood cell transplantation for the treatment of patients with acute myelogenous leukemia in first remission. The Fukouka Bone Marrow Transplant Group. Int J Hematol 66:297-301, 1997

7 Löwenberg B, van Putten W, Theobald M, Gmür J, Verdonck L, *et al*.: Effect of priming with granulocyte colony-stimulating factor on the outcome of chemotherapy for acute myeloid leukemia. N Engl J Med 349:743-752, 2003

8 Pileri SA, Ascani S, Cox MC, Campidelli C, Bacci F, *et al*.: Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients. Leukemia 21:340-350, 2007

9 Breccia M, Mandelli F, Petti MC, D'Andrea M, Pescarmona E, *et al*.: Clinico-pathological characteristics of myeloid sarcoma at diagnosis and during follow-up: report of 12 cases from a single institution. Leuk Res 28:1165-1169, 2004

10 Kitagawa Y, Sameshima Y, Shiozaki H, Ogawa S, Masuda A, *et al*.: Isolated granulocytic sarcoma of the small intestine successfully treated with chemotherapy and bone marrow transplantation. Int J Hematol 87:410-413, 2008

11 Tan D, Wong GC, Koh LP, Hwang W, Loh Y, *et al*.: Successful treatment of primary granulocytic sarcoma by non-myeloablative stem cell transplant. Leuk Lymphoma 47:159-162, 2006

12 Lee KH, Lee JH, Kim S, Lee JS, Kim SH, *et al*.: High frequency of extramedullary relapse of acute leukemia after allogeneic bone marrow transplantation. Bone Marrow Transplant 26:147-152, 2000

13 Park J, Park SY, Cho HI, Lee D: Isolated extramedullary relapse

in the pleural fluid of a patient with acute myeloid leukemia following allogeneic BMT. Bone Marrow Transplant 30:57-59, 2002

14 Au WY, Kwong YL, Lie AK, Ma SK, Liang R: Extra-medullary relapse of leukemia following allogeneic bone marrow transplantation. Hematol Oncol 17:45-52, 1999

15 Fernandez HF, Sun Z, Litzow MR, Luger SM, Paietta EM, *et al*.: Autologous transplantation gives encouraging results for young adults with favorable-risk acute myeloid leukemia, but is not improved with gemtuzumab ozogamicin. Blood 117:5306-5313, 2011

16 Tresoldi M, Onida P, Ponzoni M, Rugarli C: Primary granulocytic sarcoma presenting with bone pain and hypergammaglobulinemia. Leuk Lymphoma 41:689-692, 2001

17 Binder C, Tiemann M, Haase D, Humpe A, Kneba M: Isolated meningeal chloroma (granulocytic sarcoma)- -a case report and review of the literature. Ann Hematol 79:459-462, 2000