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Granulocytic Sarcoma as Isolated Extramedullary Relapse after Donor Lymphocyte Infusion in a Patient with CML Who Relapsed after Allogeneic Bone Marrow Transplantation
: A Case Report

Isolated granulocytic sarcoma (GS) has rarely been reported in a patient who underwent allogeneic bone marrow transplantation (BMT) for chronic myelogenous leukemia (CML). We report here a patient who developed an isolated GS after achieving hematologic and cytogenetic remission by donor lymphocyte infusion for the relapse of CML following BMT. The size of GS was slightly decreased after local irradiation of 1,500 cGy without further systemic chemotherapy or immunotherapy. He remained in hematologic and cytogenetic remission without systemic relapse of CML for 8 months. Thereafter, he died of sepsis. The appropriate treatment of GS and impact of its occurrence on prognosis following allogeneic BMT has yet to be determined.

Key Words : *Sarcoma, Granulocytic; Transplantation, homologous; Bone marrow Transplantation; Leukemia, myeloid, chronic; Lymphocyte transfusion*

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INTRODUCTION

Granulocytic sarcoma (GS), or chloroma, is a rare extramedullary tumorous aggregates of malignant myeloid precursor cells in patients with any form of acute nonlymphoblastic leukemia, myeloproliferative disorders or myelodysplastic syndrome (1, 2). In CML, GS has been reported to occur in 4.5% of cases heralding an impending blastic crisis (2, 3). GS has rarely been reported to occur following allogeneic BMT. In a recent report from the European BMT Registry (EBMTR), GS was found in 0.22% of allografted CML patients (4). Conventionally, CML patients with GS require an intensive combination chemoradiotherapy with or without stem cell transplantation to achieve long-term survival, as a blastic crisis usually ensues with the median duration of 4 months (5). However, a treatment option for GS developing after BMT has not been established (4).

We report a patient who developed an isolated GS in the right clavicular area without the evidence of overt systemic disease 7 months after donor lymphocyte infusion (DLI) to treat relapsed CML following BMT. He remained in hematologic and cytogenetic remission for 8 months after the partial response of GS with local irradiation alone. However, he died of sepsis.

CASE REPORT

A 50-year-old male patient, who was first diagnosed as having CML in September 1994, underwent an allogeneic BMT using busulfan plus cyclophosphamide as the conditioning regimen in August 1995. The posttransplant course was uneventful without evidence of graft-versus-host disease (GVHD) on the standard methotrexate/cyclosporin A prophylaxis until ten months later when he became Philadelphia chromosome positive and developed a subsequent hematological relapse of CML. Leukocytes were collected from the original donor using a Fenwal CS-3000 plus cell separator. He received a total T-cell dose of 2.1×10^8/kg of donor lymphocytes and interferon-α (6×10^6 U/day) with abrupt discontinuation of previous GVHD prophylaxis. BM examination done 110 days after the DLI showed hypocellular marrow with

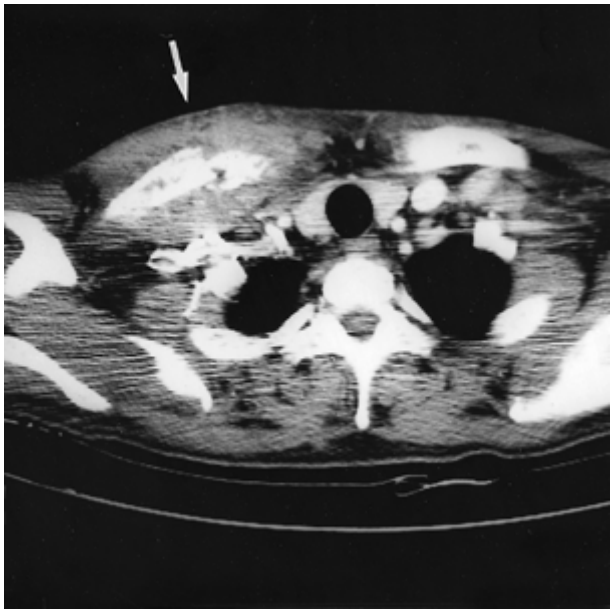

Fig. 1. Chest CT scan shows relatively well-marginated 5×8 cm sized soft tissue mass (arrow) in right clavicular area with pathologic fractrure of clavicle.

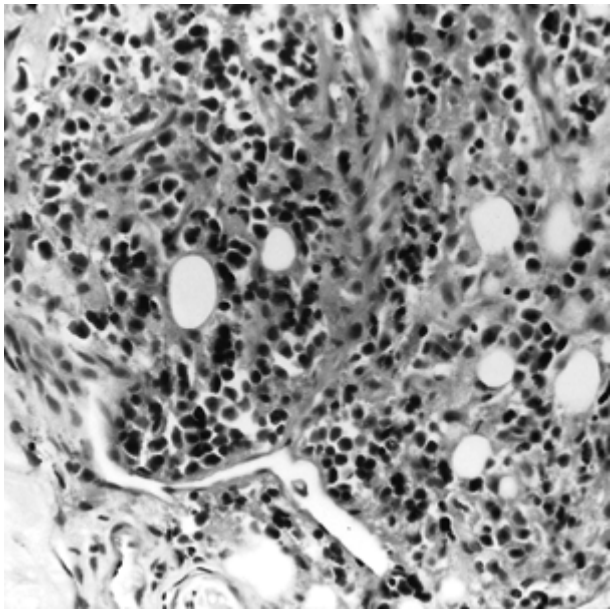

Fig. 2. Diffuse and infiltrative population of small round tumor cells show scant granular eosinophilic cytoplasm (H&E, ×200).

cytologically and cytogenetically normal cells. Further treatment with interferon-α was discontinued. A complete donor chimerism was documented by the fluorescent in situ hybridization (FISH) with X chromosome minisatellite probes; but BCR/ABL mRNA remained positive by reverse-transcriptase polymerase chain reaction. He was dependent on platelet and/or red cell transfusions. GVHD was not apparent.

Seven months after DLI, a painful hard mass developed in the right clavicular area. A computed tomographic scan of the chest outlined a relatively well-marginated 5×8 cm soft tissue mass with a pathologic fracture of clavicle and manubrium sterni (Fig. 1). The blood count showed a white cell count 2.7×10^9/L with 50% polymorphonuclear leukocytes, hemoglobin 9.1 g/dL, and platelet count 33×10^9/L. Peripheral blood smear showed pancytopenia without visible blasts. Findings on BM examination showed about 20% cellularity with less than 5% myeloblasts. The specimen obtained by a needle biopsy showed clusters of myeloid series cells (Fig. 2). Immunohistochemical staining was positive for lysozyme antibody. Cytogenetic study of BM demonstrated 46, XX cells without evidence of t(9:22)(q34:q11) [20/20 metaphases]. FISH analysis showed 97% of donor signals (XX). However, he remained in positive for BCR/ABL mRNA.

He received only local radiotherapy of 1,500 cGy to the field of GS as the initial donor declined to donate additional buffy coat cells. The size of GS was decreased. He has been in hematological and cytogenetic remission for 8 months. Thereafter, he died of sepsis.

DISCUSSION

The occurrence of GS as isolated extramedullary relapse after allogeneic BMT was 0.45%, found in 26 patients out of 5,824 transplanted patients reported in EBMTR. Among them six (0.22%) were patients grafted for CML or myelodysplasia (4). This case report is unique in that the patient developed a GS after having achieved a hematological and cytogenetic remission by DLI for relapsed CML following BMT.

DLI, an attempt to induce graft-versus-leukemia (GVL) effect, was first reported successful by Kolb et al. (6). It seemed to be quite effective for CML patients who relapse after BMT, with a 3-year survival of 67%. However, complications of DLI included severe acute GVHD (59-80%) and marrow aplasia (50%) (7). The current patient restored a hematologic and cytogenetic remission after DLI without development of GVHD, but marrow continued to show an aplasia. This case attested to the possible discrimination of GVL effect from GVHD.

As in the conventional chemotherapy group, GS after BMT usually represented the first manifestation of systemic disease, despite strict initial local involvement. However, the optimal management of isolated GS after BMT is controversial and remains to be defined (4, 8). There has been no documentation of superior results among various modalities; local radiotherapy, both alone

and in combined treatment modalities such as aggressive systemic therapy and subsequent regrafting. From the EBMTR study, only 9 patients out of 26 were alive for 15-151 months after the onset of GS, with the 5-year actuarial survival for the group of 33%. Among 4 patients who underwent high dose chemoradiotherapy and second transplant 2 were alive, while 3/6 were alive who were treated only by local radiotherapy (with or without surgery) without systemic chemotherapy (4). Buffy coat infusion was tried in only one case and it was successful to revert the isolated GS. But the contribution of buffy coat cells was not completely evaluated as the patient received 50 Gy radiation to the involved field (4).

In our study, the patient remained in hematologic and cytogenetic remission 7 months after local radiotherapy to GS. However, it is too early to draw any conclusions as he remains positive for mRNA for BCR/ABL, which might imply a high risk of developing an overt relapse (9). Long term studies are required to ascertain the appropriate treatment of GS and impact of its occurrence on prognosis following allogeneic BMT.

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