Dose-intensive Chemotherapy with Syngeneic Peripheral Blood Stem Cell Support for Poor Risk Germ Cell Tumor of Extragonadal Origin: a Case Report

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A variety of regimens of high-dose chemotherapy with hematopoietic stem cell support for poor risk germ cell tumors have been established. However, a series of chemotherapy steps carried out prior to the harvest sometimes leads to an insufficient number of peripheral blood stem cells. Here, we report a case of a patient who successfully underwent high-dose chemotherapy for the treatment of poor risk extragonadal germ cell tumor by receiving peripheral blood stem cell transplantation donated from his genically identical twin brother.

Key words: germ cell tumor – syngeneic peripheral blood stem cell transplantation – high-dose chemotherapy

CASE REPORT

A 35-year-old man presented elsewhere with back pain in June 1999. Physical examination and computed tomography (CT) scans demonstrated swollen left supraclavicular, paraaortic and iliac lymph nodes, while bilateral testes were normal. Serum β-subunit of human choriogenic gonadotropin (β-HCG) and lactic dehydrogenase (LDH) was elevated to 8.32 IU (normal <0.1 IU) and 2779 IU (normal <480 IU), respectively. Biopsy of the left supraclavicular node yielded a diagnosis of poorly differentiated germ cell tumor of extragonadal origin.

Although five courses of conventional chemotherapy consisting of bleomycin, etoposide and cisplatin allowed complete serological remission and relief of symptoms, retroperitoneal lymph node dissection revealed residual viable cells of embryonal cell carcinoma, leading to two courses of adjuvant chemotherapy (etoposide, ifosfamide and cisplatin). Three months later, he again suffered back pain with elevated serum levels of β-HCG (30.7 IU) and LDH (1151 IU). Abdominal CT scans demonstrated re-swollen paraaortic lymph nodes and bilateral hydronephroses. Serum creatinine was 7.2 mg/dl. A total dosage of 1215 mg of cisplatin, 5825 mg of etoposide, 2.0 g of ifosfamide and 180 mg of bleomycin had been administered until this time.

Regarded as a poor risk case, it was planned that the patient should undergo high-dose chemotherapy including paclitaxel, ifosfamide, carboplatin and etoposide, with peripheral blood stem cell (PBSC) support (1). Since a sufficient number of CD34+ stem cells (2.0 × 10⁶/kg/course) to complete three courses of a high-dose chemotherapy regimen was not obtained through two courses of induction regimen with paclitaxel and ifosfamide, his monozygotic twin brother was requested to donate PBSCs for this purpose. Informed consent was carefully obtained from both the donor and the patient.

First, we informed the donor of the necessity and risk of harvest and transplantation in the absence of the recipient. Only after the donor’s consent had been obtained was the patient informed about the possibility of syngeneic stem cell support. Ten loci (A, B, C, DR and DQ) of HLA genotyping and 10 DNA microsatellite markers (HPG, F12A1, TH01, TPOX, CSF1PO, D11S534, INT2, TCF1ID, D6S89 and ACTBP2) were proved to be completely matched between the twins (Fig. 1), limiting the probability of dizygosity to <10⁻⁴ (2). PBSCs of the donor were mobilized by 10 μg/kg of granulocyte colony-stimulating factor (G-CSF) for five consecutive days and collected by leukapheresis over 2 days, resulting in harvest of 6.28 × 10⁶/kg of CD34+ cells, which allowed completion of the second and third cycles of high-dose therapy including carboplatin and etoposide. The donor complained of very mild pain in the vertebralae and no pain in the spleen after G-CSF administration. No obvious splenomegaly was observed on physical examination and computed tomography (CT) scans.

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Abbreviations: TI, chemotherapy consisting of paclitaxel and ifosfamide; CE, chemotherapy consisting of carboplatin and etoposide, PBSCT, peripheral blood stem cell transplantation.
Syngeneic PBSCT for testicular tumor examination. Blood tests in weeks two and four revealed no abnormality including thrombocytopenia. The number of days from the transplantation until recovery of neutrophils to 500/mm³ for the cycle with autologous stem cell support and the two cycles with syngeneic stem cell support was 10, 10 and 11 days, respectively, and for platelet recovery to 50 000/mm³ 13, 15 and 13 days, respectively. Twenty units of allogeneic platelet transplantation were required in every cycle. The syngeneic transplantations were conducted as autologous settings in a conventional clean room.

The three courses of dose-intensive chemotherapy normalized serum LDH and β-HCG levels (Fig. 2) and completely shrank the paraaortic lymph nodes. No sign of graft versus host disease was observed without administration of immunosuppressive agent. The patient has been recurrence-free for 4 months after completion of the chemotherapy and the donor has been healthy without any physical problems.

DISCUSSION

The introduction of cisplatin-based combination chemotherapy has achieved high cure rates for patients with advanced Germ Cell Tumors (GCTs). Dose-intensive chemotherapy with PBSC support has recently cured even poor risk cases including bulky disease and extragonadal GCTs (1). However, repetition of chemotherapy with poor risk GCT frequently led to exhausted bone marrow without the ability to supply a sufficient amount of autologous PBSCs for transplantation in dose-intensive therapy.

In this case, the patient fortunately had a monozygotic twin brother, who accepted the donation of his PBSCs. Here, we proved that the syngeneic PBSC support by the monozygotic twin could enable a patient with poor risk GCT to undergo safely dose-intensive chemotherapy. There was no critical difference in the recovery of the cells between heavily chemotheraped autologous stem cell support and intact syngeneic stem cell support. Since there was no difference in the infused cell count of each transplantation, a possible explanation is as follows: damage to the bone marrow by multiple chemotherapy steps causes the mobilization of stem cells and the quality of the stem cells once mobilized by G-CSF administration does not differ significantly. This rare case may have very important implications in this respect.

Although both autologous and allogeneic PBSC transplantations are now common, syngeneic PBSC transplantation for germ cell tumors is extremely rare. Only one case of this was reported in the annual review of 18 923 cases, Blood and Marrow Transplantation Activity in Europe 1997 (3). To our knowledge, this is the first case of extragonadal GCT treated with high-dose chemotherapy supported by PBSC donated by a monozygotic twin.

References