case report

Successful stem-cell mobilization and transplantation using plerixafor in a patient with a germ cell tumor

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High-dose chemotherapy followed by autologous hematopoietic stem-cell transplantation is an important treatment option for a variety of malignancies. Peripheral blood stem cells (PBSCs) have replaced bone marrow-derived cells as source of stem cells in transplants, and the success of a transplant depends highly on the number of PBSCs mobilized, collected and eventually infused. Nevertheless, a good percentage of patients fail to mobilize stem cells when growth factors alone or in combination with chemotherapy are used. Recently, plerixafor has been approved as a novel agent to mobilize stem cells in multiple myeloma and lymphoma patients. Data on the efficacy and safety of plerixafor in solid tumors is lacking. We report the successful stem cell mobilization and transplantation for a patient with a germ cell tumor using plerixafor.

High-dose chemotherapy and/or radiation therapy followed by autologous hematopoietic stem-cell transplantation (HSCT) has evolved as a treatment option for a variety of malignancies.[1-4] This form of transplantation entails the infusion of a patient's own hematopoietic stem cells, after being harvested and preserved, to reestablish hematopoiesis and rescue the patient from the otherwise lethal toxicity of chemotherapy and/or radiation therapy. Peripheral blood stem cells (PBSCs) have replaced bone marrow (BM)-derived cells in transplants as the source of stem cells due to many advantages, including less invasive methods of cell collection, reduced tumor contamination, a higher number of harvested stem cells and more rapid recovery of neutrophils and platelets and thus engraftment.[5] Because PBSCs exist in the circulation in very small numbers, they must be mobilized from the BM into the circulation by a mobilizing agent(s) prior to being collected by apheresis.[5,6] The adequacy of the number of PBSCs mobilized is assessed by determining the number of cells that have the CD34 antigen marker and the CD34+ cell dose/kg has proven to be a useful value. In general, patients who receive more than 2×10^6 CD34+ cells/kg have rapid and sustained hematopoietic recovery.[6] Nevertheless, approximately 10% to 30% of patients are unable to collect this number to support HSCT when mobilized with hematopoietic growth factors alone or in combination with chemotherapy.[7,8]

Recently, plerixafor (AMD3100, Mozobil; Genzyme, USA) has emerged as a novel mobilizing agent and showed efficacy in two phase III studies in mobilizing patients with non-Hodgkin lymphoma (NHL) and multiple myeloma (MM).[8,9] Accordingly, plerixafor has been approved by the United States Food and Drug Administration (FDA) and the European Medicines Agency to enhance mobilization of stem cells to the bloodstream, in combination with granulocyte colony stimulating factor (G-CSF), for collection and subsequent autologous transplantation in patients with NHL and MM. Unfortunately, information on the safety and efficacy of plerixafor in patients with solid tumors is lacking. We report our experience at the King Hussein Cancer Center (KHCC) with using plerixafor to mobilize PBSCs in a patient with germ cell tumor who failed mobilization with G-CSF.

CASE

A 47-year-old male was diagnosed with a mixed germ cell tumor in 2006 for which he underwent orchiecto-

my followed by four courses of bleomycin plus etoposide plus cisplatin (BEP). The patient did well until February 2008, when he had relapse, so he received four cycles of vinblastin plus ifosfamide plus cisplatin (VeIP). One year later, his disease progressed and he was given four cycles of paclitaxel plus ifosfamide plus cisplatin (TIP) and referred for HSCT.

Initially, PBSC mobilization was tried with G-CSF at 5 mcg/kg every 12 hrs for five days. On day five of mobilization, the white blood cell (WBC) count was 23.3×10^6/mL and the absolute circulating CD34+ cells count was 9.3 per μL, so the collection was not performed. Another attempt was made after five weeks using G-CSF at a dose of 10 mcg/kg every 12 hours for five days. On day five, the WBC count was 36.2×10^6/mL and the absolute circulating CD34+ was 7.2 cells per μL, so the collection was aborted again. Three months later plerixafor had become available at our center for compassionate use and the patient consented to receive the medication so G-CSF was started at 10 μg/kg in the morning for four days followed on day four by plerixafor at 0.24 mg/kg subcutaneously in the evening, approximately 11 hours prior to initiation of apheresis. Following plerixafor administration, the WBC count was 34.5×10^{86}/mL, and CD34 reached 17.3 cells per μL, so we collected 4.22×10^6/kg CD34+ cells in the first session. Following to this, we decided to give our patient another dose of plerixafor and the yield of CD34+ cells this time was 1.52×10^6/kg, so the total collected cells were 5.74×10^6/kg. The collection procedure went smoothly and the patient complained only of mild nausea and gastrointestinal discomfort. For the HSCT part, the plan was to give our patient two consecutive courses of high-dose chemotherapy, each followed by an infusion of autologous PBSCs so he received high-dose chemotherapy of carboplatin 750 mg/m^2 plus etoposide 700 mg/m^2 for three days followed by stem cell infusion. The patient engrafted on day +11 with complete platelet recovery on day +28. Upon follow up around day +60, the patient was found to have disease progression. Consequently, he was referred to his primary oncologist for palliative chemotherapy.

DISCUSSION

High-dose chemotherapy with HSCT is an accepted second- or third-line salvage approach to treat patients with metastatic germ cell tumors. Two consecutive courses of high-dose chemotherapy consisting of carboplatin and etoposide, each followed by an infusion of autologous PBSCs can achieve 70% disease-free survival.[4] The success of this approach depends on the collection of adequate number of PBSCs. To achieve this, transplantation teams have attempted several strategies, including the use of colony stimulating factors alone or in combination with chemotherapy. Adding chemotherapy to growth factor enhances mobilization but at the expense of increased cost and toxicity.[10,11] Nevertheless, a significant proportion of patients fail to collect the desired number of CD34+ cells due to factors such as age, sex, diagnosis, prior radiotherapy or chemotherapy regimens, cumulative alkylator dose, pre-collection infections, and time from last chemotherapy.[10,11] Our patient was heavily pretreated with several courses of chemotherapy and failed to mobilize despite continued and escalated dosing of G-CSF.

Plerixafor is the first in a new class of agents that reversibly inhibits the binding of stromal cell-derived factor 1 (SDF-1) to its receptor CXC chemokine receptor 4 (CXCR4) resulting in the mobilization of highly functional PBSCs into the circulation.[5] In clinical trials, plerixafor, in combination with G-CSF, increased the number of patients achieving both the minimum and target stem cell levels in fewer apheresis sessions.[8,9] In addition, this agent demonstrated an excellent safety profile with mild-to-moderate side effects reported from the clinical studies, mainly gastrointestinal disorders and injection site reactions.[8,9] Adding plerixafor to G-CSF resulted in a significant increase in the collected cells from our patient and with only two sessions of apheresis, the collected cells were adequate to conduct two transplants. Furthermore, our patient reported only mild gastrointestinal disorders and did not complain of any severe adverse event while taking plerixafor. We have used plerixafor to mobilize our lymphoma and MM patients under the compassionate use program and after its approval by the FDA. The application of plerixafor in patients with solid tumors is an off-label use of this medication. Nevertheless, we chose to offer plerixafor to our patient under the compassionate use program since we had no alternatives. To the best of our our knowledge this is the first published report of plerixafor use in mobilizing patients with solid tumors.

Finally, it is worth mentioning that one major concern with the use of plerixafor is its high cost (approximately $7000 for a single-use vial). However, taking into consideration that the high failure rates of mobilization can adversely affect patient outcomes and negatively impact resource utilization in terms of higher doses of G-CSF and repeated apheresis sessions, it seems essential to develop guidelines and tools to help institutions make the most cost-effective use of this novel medication.[12]

Author Contributions

Dr. Abdel-Rahman wrote the manuscript. Dr. Tuffaha edited and reviewed the manuscript.

Conflict of Interest

None declared.

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