Transmission of Chronic Myeloid Leukemia through Peripheral-Blood Stem-Cell Transplantation

TO THE EDITOR: Although secondary cancer is a well-established long-term complication of hematopoietic stem-cell transplantation,[1] the transmission of hematologic cancers through marrow or solid-organ transplantation is exceptional.[2] Moreover, to our knowledge, it has not been reported after peripheral-blood stem-cell transplantation.

A nine-year-old African child received a diagnosis of sickle cell disease (hemoglobin SC) in 1991. Between 1991 and 2001, he had multiple vaso-occlusive crises, despite hydroxyurea therapy. He was referred to us at the age of 19 years for transplantation of peripheral-blood stem-cells from an HLA-identical brother who was heterozygous for sickle cell disease.[3,4] Before peripheral-blood stem-cell mobilization with a six-day regimen of granulocyte colony-stimulating factor at a dose of 10 μg per kilogram of body weight, the donor's physical examination and hematologic studies were unremarkable, except for a slight inversion of the neutrophil:lymphocyte ratio, as is frequently observed in African persons (Table 1).

After conditioning with oral busulfan (16 mg per kilogram), intravenous cyclophosphamide (200 mg per kilogram), and antithymocyte globulin (90 mg per kilogram), the patient received a CD34-selected peripheral-blood stem-cell graft containing 4×10^6 CD34+ cells per kilogram and 0.01×10^6 CD3+ cells per kilogram. Prophylaxis against graft-versus-host disease was carried out with cyclosporine alone. The immediate post-transplantation course was complicated by cyclosporine-associated pancreatitis that resolved after the withdrawal of cyclosporine on day 21, and the patient was discharged on day 35. Neither acute nor chronic graft-versus-host disease developed.

The results of bone marrow evaluation on day 100 were normal, with more than 95 percent chimerism, but the karyotype showed a Philadelphia chromosome in 9 of 31 metaphases. Fluorescence in situ hybridization analysis confirmed the BCR-ABL rearrangement in 14 percent of marrow cells. Bone marrow evaluation in the donor showed chronic-phase chronic myeloid leukemia with the Philadelphia chromosome in 95 percent of the cells. The recipient was treated with STI571, and a complete cytogenetic and molecular remission was achieved three and six months later, respectively. Now, more than one year after the transplantation, the patient is well, without any sign of chronic graft-versus-host disease, and is heterozygous for sickle cell disease (the status of the donor). The donor initially received interferon alfa but did not tolerate it and then received STI571; a complete cytogenetic response was achieved, but a complete molecular response has not yet occurred.

Transmission of acute myeloid leukemia as well as T-cell lymphoma through bone marrow transplantation has been reported previously.[2,5] However, this case shows that chronic myeloid leukemia can also be transmitted through transplantation of peripheral-blood stem cells from a donor with no sign of chronic myeloid leukemia in the peripheral blood. This raises the issue of routine bone marrow and karyotype examination in donors of peripheral-blood stem cells.[4] However dramatic such cases are, it would be costly and ineffective, as well

Table 1. Hematologic Values in the Donor before and after Peripheral-Blood Stem-Cell Donation.*

Variable	Before Donation	1 Mo after Donation	5 Mo after Donation
Hemoglobin (g/dl)	14.0	14.4	15.4
White cells ($\times10^{-9}$/liter)	7.09	5.16	16.47
Differential count (%)			
Neutrophils	34	34	37
Lymphocytes	50	47	48
Monocytes	9	10	8
Eosinophils	3	4	2
Basophils	1	1	3
Peroxidase-negative white cells	3	4	ND
Myelocytes	ND	ND	2
Platelets ($\times10^{-9}$/liter)	298	234	245
Lactate dehydrogenase†	279	ND	492

* ND denotes not done.
† The normal range is 200 to 440 U per liter.

as uncomfortable for the donor, to carry out these investigations systematically in all donors.

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