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Pregnancy after Hematopoietic Cell Transplantation: A Report from the Late Effects Working Committee of the Center for International Blood and Marrow Transplant Research (CIBMTR)

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Preservation of fertility after hematopoietic cell transplantation (HCT) can have a significant influence on the quality of life of transplant survivors. We describe 178 pregnancies in HCT recipients that were reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) between 2002 and 2007. There were 83 pregnancies in female HCT recipients and 95 pregnancies in female partners of male HCT recipients. Indications for transplantation included hematologic and other malignancies (N = 99) and nonmalignant disorders (N = 79, of which 75 patients had severe aplastic anemia). The cohort included recipients of autologous HCT (20 women, 13 men), myeloablative (MA) allogeneic HCT (12 women, 50 men), and nonmyeloablative allogeneic HCT (2 women, 2 men). Age at HCT was <20 years for 50% of women and 19% of men. Conditioning regimens included total body irradiation (TBI) in 16% of women and 19% of men; doses were MA in 10% of women and in 16% of men. Live births were reported in 86% of pregnancies in partners of male transplant patients and 85% of pregnancies in female transplant patients, with most pregnancies occurring 5 to 10 years after HCT. We conclude that some HCT recipients can retain fertility, including patients who have received TBI and/or MA conditioning. Young patients undergoing HCT should be counseled both before and after HCT about potential loss of fertility, methods for preserving fertility, and planning for future pregnancy. Fertility and outcomes of pregnancy after HCT need prospective evaluation in large transplant cohorts.

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INTRODUCTION

Long-term survivors of hematopoietic cell transplantation (HCT) are increasing in number because of improved transplant outcomes and better supportive care. In addition, the expanding indications for transplantation have led to an increase in the number of patients receiving HCT. Hence, quality of life after HCT is of greater concern. Among young patients, fertility preservation after transplantation can have a significant influence on quality of life [1,2]. Infertility is a frequently reported "loss" experienced by HCT recipients, especially by women [3]. HCT recipients may already be at high risk for gonadal damage and infertility from previous exposure to chemotherapy and irradiation during pretransplant therapies. These risks are further increased by most transplant conditioning regimens [4-9].

Successful pregnancies have been reported in female HCT recipients and in female partners of male HCT recipients [4,10-15]. The 2 largest studies are from the European Group for Blood and Marrow Transplantation (EBMT) and the Bone Marrow Transplant Survivor Study (BMTSS). Salooja et al. [12] addressed this issue in the EBMT by sending questionnaires to 199 centers relating to nearly 38,000 transplants (autologous and allogeneic) inquiring about pregnancy rates in their posttransplant patients. They included data on patients who had conceived via assisted reproductive technologies (ART) as well as those who conceived naturally. They reported 312 pregnancies from 232 patients, for an overall conception rate of 0.6%. Overall, the authors found that the frequency of pregnancy complications was much higher in female allograft recipients compared to the normal population, particularly among those receiving total body irradiation (TBI) containing conditioning regimens. These women had higher rates of cesarean section, preterm delivery, and low birth weight infants compared to the normal population. Partners of male HCT recipients had uncomplicated pregnancies. In 2006, the BMTSS reported on pregnancy outcomes of 619 HCT survivors or their partners [4]. Data was collected via a mailed questionnaire to participants in the study and their siblings. There were 54 pregnancies reported from 34 patients (26 male, 8 female), with 46 live births. Compared to their siblings, HCT survivors had a lower prevalence of conception, but if pregnancy did occur, outcome was likely to be favorable. Risk factors for reporting inability to conceive a pregnancy after transplant included female sex of the HCT recipient, age at HCT >30 years, and use of TBI in conditioning.

We report a large case series of pregnancies after autologous and allogeneic HCT that were reported to the Center for International Blood and Marrow Transplant Research (CIBMTR). Our study describes associations of conditioning regimen, age, and disease with pregnancy after HCT.

METHODS

Data for this study were obtained from the CIBMTR, which is a voluntary group of more than 500 transplant centers worldwide. Participating centers register basic information on all consecutive HCTs to a Statistical Center at the Medical College of Wisconsin. Detailed demographic and clinical data are collected on a representative sample of registered patients using a weighted randomization scheme. Patients are followed longitudinally, with yearly follow-up. Observational studies conducted by the CIBMTR during the time period of this study were done with a waiver of informed consent and are compliant with HIPAA regulations as determined by the institutional review board and the Privacy Officer of the Medical College of Wisconsin.

From 2002 to 2007, the CIBMTR requested that centers report whether a transplant recipient or the recipient's partner became pregnant during post-HCT follow-up. Patients could have received a transplant at any time prior to 2007. Our study describes disease and transplant characteristics of the HCT recipients who reported a pregnancy during this time period. Data for these analyses were limited to the representative sample of patients on whom CIBMTR requests detailed report forms and we did not contact centers for providing supplemental data about reported pregnancies. The date of conception was not collected on CIBMTR forms and was imputed as the median time point between 2 successive follow-up reports submitted before and after pregnancy. This is a descriptive case series only, and no comparative statistical analyses were planned for this study.

RESULTS

Our cohort included 178 patients for whom a pregnancy was reported to the CIBMTR during the study period. These included 83 female HCT recipients and female partners of 95 male HCT recipients (Tables 1 and 2). In this cohort, 99 patients (34 women, 65 men) were transplanted for a malignant disorder and 79 patients (49 women, 30 men) were transplanted for a nonmalignant disorder. The group transplanted for malignancy comprised 97 patients with a hematologic malignancy, primarily acute leukemia (N = 35, 10 women, 25 men), and chronic myelogenous leukemia (CML; N = 25, 3 women, 22 men), as well as 2 patients with solid cancers. The group transplanted for nonmalignant disorders included 75 patients with