Case Report

A Case of Mycosis Fungoides Transmitted From Donor to Recipient, and Review of Literature of T-Cell Malignancies After Transplantation

John C. Loh,[1] David S. Cassarino,[2] Wayne W. Grody,[1,3] Melvin W. Chiu,[1,4] Lauren C. Pinter-Brown[1,5]

Clinical Practice Points

- Transmission of hematologic malignancy during bone marrow transplantation has been previously reported for acute myeloid leukemia, chronic myeloid leukemia, and subcutaneous panniculitis-like T-cell lymphoma.
- We present a case of mycosis fungoides appearing after bone marrow transplantation, which was clinically manifested in the donor at the time of bone marrow donation.
- To our knowledge, this case represents the first clearly documented case of likely transmission of mycosis fungoides described in the english-language literature.
- In this case report, we review the literature on T-cell malignancies after transplantation, and discuss the implications of our unusual case on ensuring the safety of bone marrow transplantation.

Clinical Lymphoma, Myeloma & Leukemia, Vol. ■, No. ■, ■-■
Keywords: Allogeneic bone marrow transplantation, Cutaneous T-cell lymphoma, Exposure to Agent Orange, Screening of bone marrow donors, transmission of donor malignancy

Introduction

Disease transmission is a rare, but well documented complication of bone marrow transplantation (BMT).[1] Transmissible donor diseases include infections, congenital disorders, autoimmune diseases, and hematological and nonhematological malignancies.[2] We present a case of mycosis fungoides developing after BMT, which was clinically manifested in the donor at the time of bone marrow donation. To our knowledge, this report represents the first case of likely transmission of mycosis fungoides described in the english-language literature. We also review the literature on T-cell malignancies arising after transplantation.

Case

A 52-year-old man with Philadelphia chromosome-positive chronic myelogenous leukemia (CML) refractory to alpha interferon underwent allogeneic peripheral stem cell transplantation using a matched-related donor in 1998. He was a Vietnam veteran, who was otherwise healthy at the time of transplantation. The patient's histocompatible sister served as his stem cell donor. She was noted to be in relatively good health at the time of donation with a history of arthritis, hypertension, and fibromyalgia. However, photographs taken from that time show that she also had a skin rash (Fig. 1A).

The patient was conditioned with busulfan and cyclophosphamide, and his course after transplantation was largely uneventful. There was no evidence of acute graft versus host disease (GvHD). GvHD prophylaxis consisted of cyclosporine and 4 doses of methotrexate. Immunosuppression was discontinued in 2000. Subsequently, the patient developed asymptomatic liver enzyme increases that were deemed to be chronic GvHD, which was successfully managed with prednisone.

The patient was first seen for an erythematous plaque arising on his left axilla in 2006. The differential diagnosis at the time included granuloma annulare, ringworm infection, or contact dermatitis. On learning that his donor sister had recently been diagnosed with mycosis fungoides, the patient was sent for a skin biopsy, which was diagnosed as consistent with mycosis fungoides. Further staging evaluation was negative, resulting in a diagnosis of mycosis fungoides, stage IA.

The patient's disease initially responded well to clobetasol and narrow band UVB phototherapy 2 to 3 times per week. In 2012,

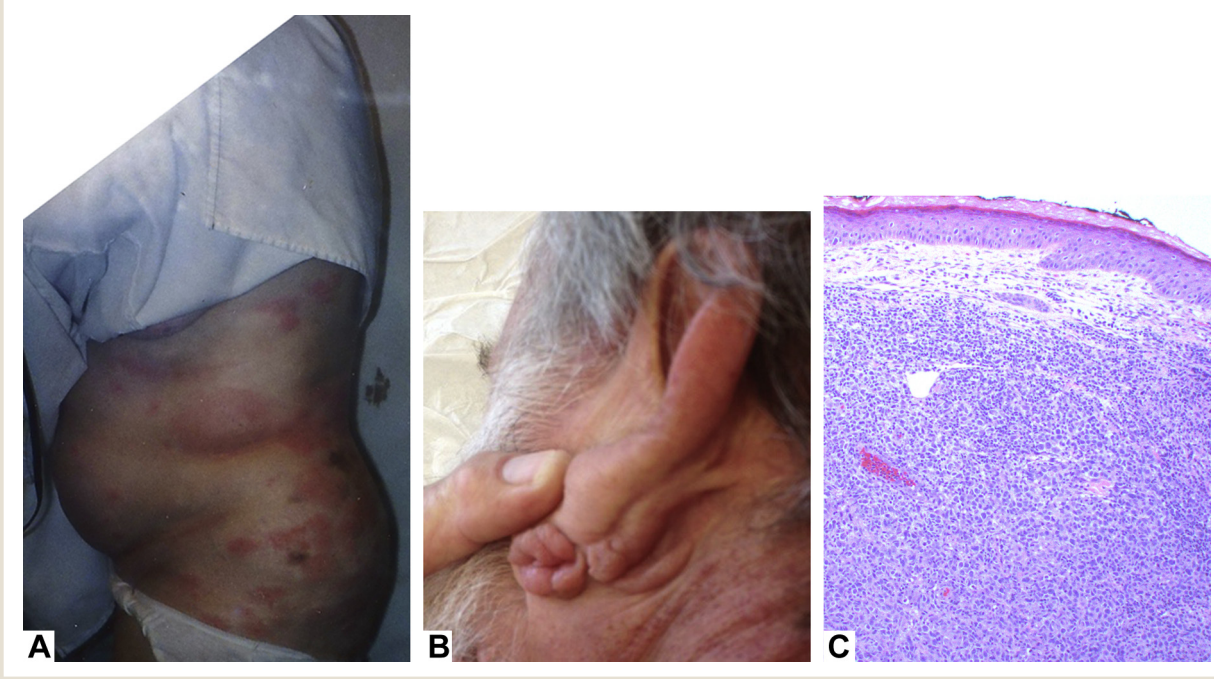
[1]David Geffen School of Medicine at University of California, Los Angeles, CA
[2]Department of Pathology, Kaiser Permanente, Southern California, Los Angeles, CA
[3]Departments of Pathology and Laboratory Medicine, Pediatrics and Human Genetics, University of California, Los Angeles, CA
[4]Division of Dermatology, University of California, Los Angeles, CA
[5]Division of Hematology-Oncology, University of California, Los Angeles, CA

Submitted: Nov 15, 2013; Revised: Jan 30, 2014; Accepted: Feb 11, 2014

Address for correspondence: Lauren C. Pinter-Brown, MD, University of California, Los Angeles, 10945 Le Conte Avenue, Suite 2333, Los Angeles, CA 90095
E-mail contact: lpinterbrown@mednet.ucla.edu

2152-2650/$ - see frontmatter
http://dx.doi.org/10.1016/j.clml.2014.02.005

Figure 1 Clinical and Histopathological Characteristics of Mycosis Fungoides in Donor and Recipient. (A) Self-Photograph of Donor Sister in 1998, Showing Multiple Lesions of Presumed Mycosis Fungoides. (B) Clinical Examination of the Patient's Left Preauricular Lesion Demonstrating Mycosis Fungoides, Stage IIB With Gross Tumors. (C) Histologic Examination of the Patient's Left Preauricular Lesion Demonstrating Mycosis Fungoides, With Dense Sheets of Atypical Lymphoid Cells in the Dermis, Consistent With Tumor Stage Mycosis Fungoides (Magnification ×10)



a left preauricular lesion of mycosis fungoides appeared that was thickened and was rebiopsied, which showed tumor stage mycosis fungoides with large cell transformation (Fig. 1B and C). The patient has since been given desatinib and oral bexarotene to treat his advanced stage of disease.

Review of the self-photographs of the patient's donor sister taken from the time of peripheral stem cell donation in 1998 show a rash that was consistent with mycosis fungoides (Fig. 1A). However, she was not diagnosed until 2006, at which time she had progressed to stage IVA mycosis fungoides with axillary lymph node involvement, and had a rapid demise thereafter.

Discussion

Exposure to dioxin-containing herbicides such as Agent Orange has multisystem effects, including an increased risk of certain malignancies.[3] This might occur by a variety of carcinogenic mechanisms including increased oxidative stress, DNA damage, chromosome rearrangement, and upregulation of anti-apoptotic mRNA. Our patient, a Vietnam veteran, developed CML 30 years after being exposed to Agent Orange. Unlike lymphomas, Agent Orange has not been strongly linked to the development of CML. A recent survey of 67 photopheresis centers identified 7 Vietnam veterans who had developed cutaneous T-cell lymphoma 27 to 35 years after their exposure.[4] However, our case demonstrates that mycosis fungoides appearing in a similar time frame after exposure to Agent Orange might not be exposure-related.

Lymphoproliferative disorders that occur after transplant (PTLD) not associated with the Epstein-Barr virus are increasingly recognized.[5] These PTLD are considered 'late' appearing (> 1 year) and are associated with a poorer prognosis. PTLD are classified as T-cell in origin (T-PTLD) when they meet the criteria for a T-cell lymphoma or leukemia.[6-8] Knowledge of these rare forms of PTLD is based predominantly on case reports and small series.[7] Like PTLD of B-cell origin, T-PTLD are thought to occur because of chronic immunosuppression resulting in dysregulation of lymphogenesis. However, most T-PTLD do not appear to be driven by the Epstein-Barr virus. T-PTLD have been reported to occur 2 to 43 months after BMT, with a median of 5 months.[7] Extranodal sites are usually involved. However, the skin is a less common site of involvement, with only 25 cases reported to have occurred after solid organ transplantation, and a single case reported after BMT.[9] Our patient developed mycosis fungoides 7 years after BMT, which does not fit within the timeline of reported T-PTLD. Furthermore, he had not been taking immunosuppressive drugs for some years before developing clinical manifestations of his mycosis fungoides.

Case reports of transmission of donor malignancy in BMT are extremely rare in the literature.[2] Malignancies reported to be transmitted include acute myeloid leukemia, chronic myeloid leukemia, and lymphoma.[10-12] Stewart et al. first raised the possibility of transmission of mycosis fungoides during BMT with a case of mycosis fungoides-associated follicular mucinosis appearing after allogeneic BMT.[13] However, they were not able to demonstrate disease manifestation in the donor, nor the origin of cells from