Asthma as a Consequence of Bone Marrow Transplantation*

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Atopy, allergy, or asthma rarely can complicate organ transplantation. We identified two patients who developed asthma following bone marrow transplantation. Neither patient had a documented history of allergy, atopy, or asthma, but their donors were human leukocyte antigen-identical siblings who had a history of asthma. Pulmonary function testing revealed decreased airflow. Investigation of the bronchial biopsy specimens revealed eosinophilia and histologic features that were compatible with asthma. No infectious pathogens were identified. Both patients received therapy with bronchodilators and inhaled corticosteroids with symptomatic improvement. A diagnosis of asthma should be entertained in the differential diagnosis of pulmonary complications in bone marrow transplant recipients.

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Key words: asthma; bone marrow transplantation; complications

Abbreviations: BBx = bronchial biopsy; BMTx = bone marrow transplantation; HLA = human leukocyte antigen

Within the past few decades, organ transplantation has achieved great success, but with a potential for serious complications. Of the many disorders that can follow organ transplantation, the transmission of disease is a rare occurrence, as infections, malignancies, or autoimmune disorders have been transmitted from the donor to the recipient. Several case reports or series have reported atopy and related disorders following organ transplantation. Previously published cases have described the occurrence of eczema, allergies (eg, to food, drugs, or latex), or asthma. However, the pulmonary findings and pathologic features have not been reported in detail in patients who develop asthma following transplantation. In this study, we present two patients who developed asthma after bone marrow transplantation (BMTx).

Case Reports

Case 1

An 18-year-old woman, who had no history of allergy or asthma, with acute myelogenous leukemia (M3) received an allogeneic BMTx from her human leukocyte antigen (HLA)-identical sister (HLA A1, A24, B57, B60, DR3, and DR7). Seventeen months after undergoing transplantation, she was admitted to the hospital with nonproductive cough, wheezing, and dyspnea. Pulmonary function tests revealed the following: total lung capacity, 4.46 L (87% of predicted); vital capacity and FVC, 2.85 L (70% of predicted); and FEV1, 2.29 L (75% of predicted). A peripheral blood count showed a total WBC count of 10,200 cells/µL with 82 neutrophils, 8 lymphocytes, 5 basophils, 4 eosinophils, and 1 monocyte. Fiberoptic bronchoscopy with BAL and bronchial biopsy (BBx) excluded an infection or malignancy. Following a diagnosis of asthma, the patient was treated with albuterol and a corticosteroid inhaler (ie, triamcinolone acetonide). Her asthma improved, but her clinical course was subsequently complicated by several recurrent episodes of bacterial pneumonia requiring multiple hospitalizations. Approximately 16 months later, the patient developed recurrent leukemia and died of disseminated candidiasis.

Case 2

A 43-year-old woman, who had no history of allergy or asthma, with acute myelogenous leukemia (M2) received an allogeneic BMTx from her asthmatic HLA-identical sister (HLA A3, A32, B44, B97, DR 04, and DR 13). Approximately 6 weeks into her initial hospitalization she developed progressive wheezing and dyspnea. Pulmonary function testing showed the following: total lung capacity, 5.03 L (94% of predicted); vital capacity and FVC, 2.84 L (76% of predicted); and FEV1, 1.95 L (78% of predicted). A peripheral blood count showed a total WBC count of 4,500 cells/µL, with 63 neutrophils, 7 lymphocytes, 6 basophils, 14 eosinophils, and 10 monocytes. Bronchoscopy with BAL and BBx did not show an infection or malignancy. The patient also symptomatically improved following treatment with albuterol and a corticosteroid inhaler (ie, triamcinolone acetonide). Although follow-up was brief, she was alive and well at last contact.

BAL

In patient 1, the BAL fluid showed an acute inflammatory population of neutrophils (95%), lymphocytes (3%), eosinophils (1%), and histiocytes (1%). In patient 2, the BAL fluid demonstrated a mixture of degenerating neutrophils, and other inflammatory cells within a background of cellular debris and mucus. The cell count was not performed in this case. No organisms were identified in microbiological cultures or on cytospin slides stained with Papinicolaou and Gunori methenamine silver stains.
**BBx**

In both cases, the BBx demonstrated an edematous bronchial wall with marked basement membrane thickening and eosinophilia, with a lesser population of lymphocytes, plasma cells, and neutrophils (Fig 1). The infiltrate extended to the epithelial surface, which showed reserve cell hyperplasia. No lung parenchyma was present in either case to evaluate for obliterative bronchiolitis. Immunohistochemical stains for cytomegalovirus and herpes virus were negative in both cases.

**Discussion**

Among the vast differential diagnosis of pulmonary complications in BMTx recipients, we initially considered an infectious etiology, but there was no specific pathogen in the BAL fluid, the BBx specimen, or the microbiological cultures of the BAL fluid. The clinical presentation and the results of pulmonary function testing did not rule out obliterative bronchiolitis. After excluding a drug allergy, the diagnosis of asthma was made based on the clinical presentation, the results of pulmonary function testing, and the histologic findings of basement membrane thickening, intramucosal edema, and eosinophilia. This diagnosis was supported by a favorable therapeutic response to bronchodilators and an inhaled corticosteroid.

Several pathologic mechanisms could be implicated in the pathogenesis of atopy following organ transplantation. Although elevated IgE levels can follow BMTx, it is unlikely that the transfer of donor IgE occurred, given its relatively short half-life. The most likely mechanism is the transfer of allergen-specific donor lymphocytes, either as stem cells or committed hematopoietic cells, to the recipient during the BMTx. Both patients received bone marrow from HLA-identical siblings who had a history of asthma, but neither of the recipients had prior evidence of allergy, asthma, or atopy. Agosti et al reported the results of skin testing for allergy pretransplantation and post-transplantation in allogenic BMTx recipients. In their study, the skin-testing profile of the recipients was similar to that of the donors. Seven recipients experienced worsening of allergic rhinitis, and two developed asthma. This suggests that postengraftment development of allergen-specific reactivity is related to the transfer of B-cell clones with IgE-specific memory, which then is expressed clinically in the form of atopy, allergy, or asthma.

In conclusion, asthma and other related atopic disorders may rarely follow BMTx. The pathologic mechanisms are unclear but are probably related to the transmission of marrow elements from the donor to the recipient. These findings suggest that asthma should be considered in the differential diagnosis of respiratory complications following BMTx.

**References**


**Tracheobronchial Stenting for Tuberculous Airway Stenosis**

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We reviewed the results of the use of the Dumon silicone stents in patients experiencing tuberculous tracheobronchial stenosis since 1994, using a retrospective case review in a university teaching hospital with 1,450 beds serving a population of > 1.8 million. Between February 1994 and September 2001, seven patients with tuberculous tracheobronchial stenosis (mean age, 43 years) underwent a total of 11 dilatations with placement of 10 straight stents and 1 Y stent. Under general anesthesia, all patients under-