

HOSPITAL PHYSICIAN®

PULMONARY DISEASE BOARD REVIEW MANUAL

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The *Hospital Physician Pulmonary Disease Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in pulmonary disease. Each quarterly manual reviews a topic essential to current practice in the subspecialty of pulmonary disease.

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Pulmonary Complications of Bone Marrow Transplantation

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Cover Illustration by mb cunney

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Pulmonary Complications of Bone Marrow Transplantation

Rodolfo M. Pascual, MD

INTRODUCTION

Bone marrow transplantation (BMT) is a rapidly evolving technology that offers the possibility of cure to many patients diagnosed with diseases that formerly had a very poor prognosis. When cells are collected from the peripheral blood rather than the marrow, the terms *hematopoietic cell transplant* and *stem cell transplant* are used. Although BMT is most often used to treat hematologic malignancies and diseases with a poor prognosis (eg, acute leukemia, chronic myelogenous leukemia, and aplastic anemia), it also has been used as salvage treatment after intensive chemotherapy for lymphoma, breast cancer, and a variety of other tumors.

Patients with malignancy who undergo transplantation with a graft of their own cells (autologous) or a donor's cells (allogeneic) receive pretreatment conditioning that subjects all organs, particularly the lungs, to a heavy dose of cytotoxic chemotherapeutic agents and sometimes radiation therapy. In addition, most patients approach transplantation immunocompromised to some degree because of underlying disease and prior chemotherapy. Allogeneic transplantation requires post-transplant immunosuppressive regimens to prevent graft rejection and hence predisposes these patients to infectious disease caused by typical and atypical bacteria, molds, yeasts, *Pneumocystis carinii* (PCP), and viruses.

Graft-versus-host disease (GVHD) causes substantial morbidity and mortality following BMT. GVHD frequently occurs in patients who undergo allogeneic transplantation even when the donor is a well-matched sibling and prophylactic immunosuppressive therapy is initiated. Acute GVHD presents as a rash, usually maculopapular, that can progress to a blistering form similar to toxic epidermal necrolysis. Acute GVHD typically involves the liver and gastrointestinal tract and sometimes leads to life-threatening complications. Therapy for acute GVHD includes steroids and other immunosuppressive agents, particularly those that suppress T-lymphocyte function. Although this complication usually is not associated with direct lung toxicity, it often leads to chronic GVHD, which

is an important risk factor in several posttransplant pulmonary complications, including cytomegalovirus (CMV) pneumonitis, idiopathic pneumonia syndrome (IPS), bronchiolitis obliterans organizing pneumonia (BOOP), and chronic airflow obstruction, often due to bronchiolitis obliterans. Pulmonary complications affect 40% to 60% of allogeneic BMT recipients¹ and present considerable diagnostic and therapeutic challenges.

LATE NONINFECTIOUS PULMONARY COMPLICATIONS

CASE PATIENT

Initial Presentation and History

A 50-year-old man diagnosed with acute myelogenous leukemia undergoes allogeneic BMT with bone marrow donated by his HLA-matched sister. The transplantation is completed following a standard conditioning regimen consisting of high-dose cyclophosphamide, total body irradiation, and busulfan. Pretreatment with antithymocyte globulin and cyclosporine was used as prophylaxis for GVHD.

Bone marrow biopsy results demonstrate successful engraftment. At the same time, the patient develops a maculopapular rash on the neck, hands, and feet as well as mild diarrhea. A skin biopsy sample is consistent with acute GVHD. High-dose steroids are administered, and the rash and diarrhea resolve; the patient remains on maintenance prednisone. He has been taking trimethoprim-sulfamethoxazole (TMP-SMZ) since engraftment occurred. He does well for 4 months but then presents with a nonproductive cough, dyspnea with exertion, and low-grade fever (100°F).

Physical Examination

The patient appears to become short of breath with movement. The temperature is 100.3°F, pulse is 100 bpm, respiratory rate is 22 breaths/min, blood pressure is 122/88 mm Hg, and pulse oximetry shows an oxygen saturation of 91% on room air. Scattered crackles are