

CLINICAL CHALLENGES

Lori A. Williams, RN, DSN, OCN®, AOCN®
Associate Editor

Chronic Graft-Versus-Host Disease

Ellaine Galbizo, RN, BSN, and Lori A. Williams, RN, DSN, OCN®, AOCN®

Case Study

Mr. F is a 62-year-old Caucasian man who was diagnosed with acute myelogenous leukemia (AML) 15 months prior. Following two cycles of induction chemotherapy, his AML was in remission. Four months ago, after a reduced-intensity conditioning regimen, Mr. F received an allogeneic peripheral blood stem cell transplant from his human leukocyte antigen-identical 56-year-old sister. Mr. F received a regimen of the calcineurin inhibitor tacrolimus and antimetabolite methotrexate for graft-versus-host disease (GVHD) prophylaxis. Mr. F was diagnosed with biopsy-proven stage 1 acute GVHD of the skin on his arms and the palms of his hands 43 days following his transplant. At the time, he was receiving tacrolimus 8 mg per day for GVHD prophylaxis, and that was continued. In addition, the GVHD was treated with topical steroid cream and resolved promptly. Mr. F had no other signs of acute GVHD.

Mr. F arrives at the blood and marrow transplantation (BMT) outpatient clinic for a routine follow-up visit. He complains of pain and dryness in the mouth, with occasional bleeding after brushing his teeth, and skin redness and irritation on his arms. He states that he has an increased visual sensitivity to sunlight with frequent feelings of dryness and irritation in his eyes. Mr. F denies nausea, vomiting, and diarrhea but has lost eight pounds since his last visit to the clinic one month prior. He reports pain in his wrists and elbows that slightly limits his movements and interferes with his daily strength-training regimen. He is being tapered off of his immunosuppressive prophylaxis and currently is taking tacrolimus 2 mg per day.

Physical examination reveals small, patchy, firm, erythematous maculopapular eruptions on his neck, shoulders, and arms, with dry desquamation and mild pigmentation changes. Mr. F states that he has a pain level of 2 (on a scale of 1–10) in the skin on his arms. Evaluation of his oral cavity reveals ulcers in the oral mucosa and inflammation of the gums.

Mr. F's temperature is 97.9°F, blood pressure is 145/95 mmHg, pulse is 80 beats per minute, and respirations are 18 breaths per minute. His oxygen saturation, measured by pulse oximeter at rest, is 98%. He has a white blood cell count of 3.5 K/UL with 42% neutrophils, 40% lymphocytes, and 12% eosinophils. His hemoglobin is 11.1 G/dl, hematocrit is 31%, and his platelet count is 85,000 K/UL. Serum liver function tests show a total bilirubin of 0.9 mg/dl, alanine aminotransferase of 17 IU/L, aspartate aminotransferase of 21 IU/L, and alkaline phosphatase of 94 IU/L. The advanced nurse practitioner who initially evaluates Mr. F suspects that he has developed chronic GVHD.

Clinical Problem Solving

What is chronic GVHD?

Chronic GVHD is an autoimmune-like reaction, occurring months to years following allogeneic BMT, that damages tissues and organs and causes pronounced immunodeficiency. It can affect almost any organ of the body, but common sites are the skin, liver, mouth, and eyes (Bhushan & Collins, 2003). Chronic GVHD also is associated with constitutional symptoms of fatigue, weight loss, and muscle wasting. Approximately 38%–77% of patients receiving allogeneic BMTs are reported to develop chronic GVHD, depending on patient, donor, and cell product characteristics (Akpek, 2002). The effects of chronic GVHD can be extremely debilitating and devastating to patients who often have been cured of underlying malignancies.

What are the risk factors for the development of chronic GVHD?

Risk factors that are consistently associated with the development of chronic GVHD include patient factors of older age, a diagnosis of chronic myeloid leukemia or aplastic anemia, and a history of acute GVHD (Bhushan & Collins, 2003; Lee, Vogelsang, & Flowers, 2003; Socie, 2004). Donor factors consistently associated with the development of chronic GVHD include

a female donor for a male patient and a mismatched or unrelated donor (Bhushan & Collins; Lee et al.). Cell product characteristics consistently associated with chronic GVHD include a cell source of peripheral blood stem cells versus bone marrow (Cutler et al., 2001) and a cell product that is not T-cell depleted (Bhushan & Collins; Cutler et al.; Lee et al.; Socie). In addition, use of donor lymphocyte infusions following BMT is associated consistently with the development of chronic GVHD (Lee et al.; Socie). Risk factors that are more controversial or less established include patients who are seropositive for cytomegalovirus (CMV) or have a reactivation of CMV infection, patients who have had a splenectomy, ethnic disparity between donors and patients, use of corticosteroids or not using methotrexate for acute GVHD prophylaxis, and a high number of CD34+ cells in the cell product (Bhushan & Collins; Lee et al.; Socie). Mr. F's risk factors for the development of chronic GVHD included his age and receiving a BMT from a female donor. His most significant risk factor was a prior episode of acute GVHD (Bhushan & Collins; Cutler et al.; Socie).

What treatments might be prescribed for Mr. F to treat his chronic GVHD, and what would be the expected side effects?

Mr. F's current dosage of tacrolimus 2 mg per day most likely would be increased, and his physician also may prescribe a topical corticosteroid to treat the skin and oral manifestations (Bhushan & Collins, 2003). The side effects of tacrolimus include tremor, headache, nausea, constipation, nausea, vomiting, renal

Ellaine Galbizo, RN, BSN, is a clinical nurse in the Blood and Marrow Transplant Unit and Lori A. Williams, RN, DSN, OCN®, AOCN®, is an instructor in the Department of Symptom Research, both at the University of Texas M.D. Anderson Cancer Center in Houston.

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