

Case 14

H.D. is a 35 year-old man who presented with weakness and bleeding of the gums. Physical examination was notable for tachycardia and splenomegaly. He had petechiae (pinpoint non-blanching hemorrhagic lesions) over his chest and neck. A CBC revealed profound anemia, thrombocytopenia (low platelet count) and a WBC of 35,000 cells/ μ l which were 30% myeloblasts. A bone marrow biopsy was consistent with acute myelogenous leukemia. His leukemia did not respond to standard induction chemotherapy and it was determined that his best chances for survival were with myeloablation followed by bone marrow transplantation (BMT). He had no living first-degree relatives. He underwent allogeneic BMT with a donor who was closely matched with respect to classical MHC class I and II molecules. Prior to transplantation, the bone marrow of the donor was purged of T-cells using magnetic bead-based separation.



Fig. 1. Rash on H.D. upon presentation two years following allogeneic BMT.

H.D. did well on immunosuppressive agents until two years after transplantation when he noted an erythematous maculopapular (both flat and raised) skin rash over his arms and trunk (Fig. 1). Over several weeks the rash worsened and he noted tenderness over the rash sites. He also complained of dyspnea (shortness of breath), crampy abdominal pain, intermittent bloody diarrhea, and malaise. Physical examination was notable for the rash as described, normal breath sounds, normal cardiac exam; his abdominal exam was notable for hepatosplenomegaly (enlarged liver and spleen). His rectal exam was normal except for heme-positive stool. Laboratory studies revealed abnormal liver function tests. Colonoscopy was performed (Fig. 2). A skin biopsy was also performed (Fig. 3).

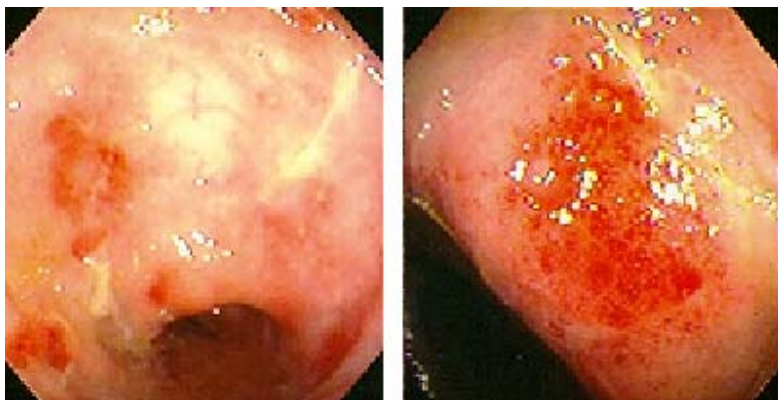


Fig. 2. Images taken during colonoscopy of H.D. Note areas of erythematous mucosa.

Case 14, cont'd

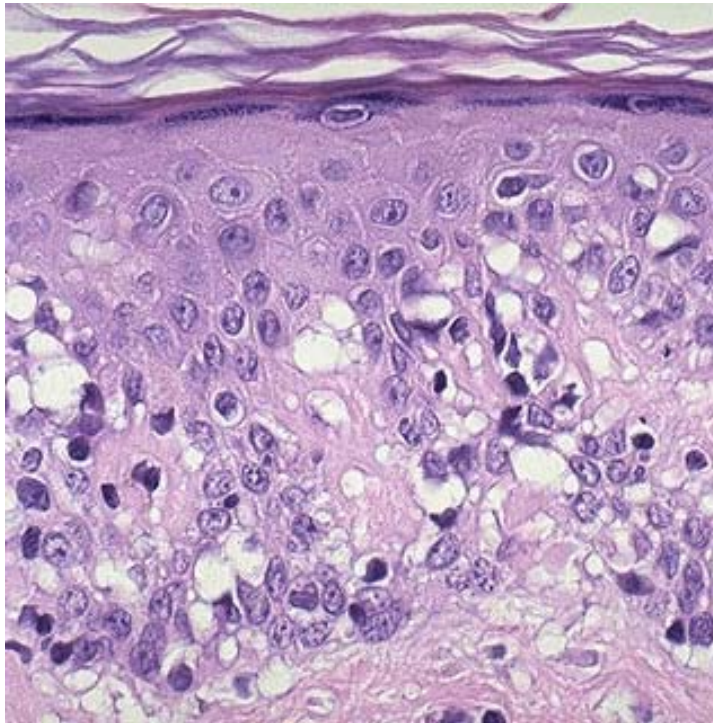


Fig. 3. Skin biopsy of H.D. There is vacuolization and dissolution of epidermal cells along the basal layer, along with lymphocytes.

Questions for Case 14

- (1) What is the current risk of developing chronic GVHD 5 years following allogeneic BMT? What type of cell is implicated in causing tissue injury in chronic GVHD? How is magnetic bead separation of donor lymphocytes performed and why is this relevant to the current case?
- (2) The pathology of GVHD is most apparent in epithelia. Can you speculate as to why this might be so?
- (3) The patient developed GVHD despite excellent matching of class I and II MHC molecules between host and donor. Why?
- (4) Recent studies have suggested that individuals with polymorphisms in the promoter region of the IL-10 gene, associated with decreased IL-10 production, are at a greater risk for the development of GVHD. Can you speculate as to why this might be so?