Graft-Versus-Host Disease Following Autologous Transplantation

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K.T., a 76-year-old woman, was diagnosed with stage IIA multiple myeloma in 2007 when she presented with severe back pain. K.T. underwent kyphoplasty, a minimally invasive surgery to relieve compression fractures, followed by eight cycles of lenalidomide with a good response. Peripheral blood stem cells were collected after mobilization with filgrastim and plerixafor. She was admitted to the hospital and conditioned for an autologous hematopoietic cell transplantation (HCT) with melphalan followed by reinfusion of peripheral blood stem cells, receiving a cell dose of 4.26 x 10⁶ CD₃₄ cells/kg. K.T. developed neutropenic fever on day 8 that responded to broad spectrum antimicrobials. She achieved a prompt hematologic recovery, reaching an absolute neutrophil count greater than 500 mm³ by day 11 after transplantation. On day 9, however, K.T. developed diarrhea, negative for Clostridium difficile, which was managed with antiinfectious agents. She was discharged 17 days following transplantation with blood counts within normal limits, except for mild anemia.

On day 19, K.T. presented for follow-up with a pruritic, erythematous skin rash covering 45% of her body surface area, involving her upper extremities, anterior, and posterior torso. She also experienced gastrointestinal (GI) symptoms of nausea, abdominal cramping, weight loss, and anorexia. Tapered methylprednisolone dosing was prescribed for a suspected diagnosis of autologous graft-versus-host disease (GVHD). Skin rash resolved in response to corticosteroids and pruritis was managed with topical triamcinolone. GI symptoms initially improved, but recurred following completion of the methylprednisolone taper.

On day 32, K.T. presented with progressive diarrhea and diffuse skin rash involving 100% of her body surface area. Medication review did not reveal a likely source for drug reaction. A skin biopsy was taken and showed foci of basal cell vacuolization with apoptosis consistent with acute GVHD. K.T. received a dose of IV methylprednisolone followed by prednisone 2 mg/kg per day in divided doses. With initiation of corticosteroids, skin rash and pruritis abated, but K.T. continued to have diarrhea and anorexia. Her stool tested positive for C. difficile, and metronidazole was prescribed. With a maturing skin rash, confirmed C. difficile, and the development of steroid myopathy, a rapid prednisone taper was initiated.

On day 44, K.T. was readmitted after presenting with a pruritic, erythematous rash, 8–10 liquid bowel movements per day, abdominal cramping, pain with defecation, and maroon-colored stool (hematochezia). Symptom onset coincided with a taper of prednisone. Her stool tested positive for C. difficile, despite the completion of a two-week course of oral vancomycin and metronidazole. A clinical diagnosis of autologous GVHD was suspected, given the presence of GVHD identified on skin biopsy and symptoms that persisted despite receiving metronidazole and vancomycin. Resistant C. difficile infection or an opportunistic infection could not be excluded without histologic confirmation. Upper endoscopy and flexible sigmoidoscopy at day 58 revealed severe pseudomembranous colitis with severe gastritis in the antrum and body of the stomach. K.T.’s duodenal biopsy appeared normal and no apoptosis was identified. At that time, findings did not support a diagnosis of GVHD. No viral inclusions were seen and immunohistochemical stain for cytomegalovirus was negative. With an excess of 10 loose bowel movements daily, K.T. required a short course of total parenteral nutrition for adequate caloric intake. GI symptoms failed to respond to treatment with vancomycin and metronidazole; therefore, prednisone was restarted for a two-week period followed by a successful taper. Total parenteral nutrition was discontinued and K.T. was discharged on day 77 receiving prednisone 10 mg every other day, antimi- crobial prophylaxis, and vancomycin.

On day 103 (three days after discontinuation of steroids), K.T. was readmitted with complaints of progressive diarrhea while receiving vancomycin. Subsequent colonoscopy showed thick mucus covering the colonic mucosa and a severely inflamed colon. Pathology showed acute pseudomembranous colitis with foci of acute cryptitis and crypt dropout. Biopsies did not reveal apoptosis, but detachment of fibrinopurulent exudates was noted, consistent with a diagnosis of acute GVHD. Laboratory examination revealed mild anemia, thrombocytopenia, mild elevation in leukocyte count, normal liver function tests, and a negative cytomegalovirus test by polymerase chain reaction analysis. Stool assay tested positive for C. difficile on multiple occasions. High-dose prednisone was reinstituted and vancomycin was increased to 500 mg four times daily for 10 days. This was followed by a rapid steroid taper given the marked improvement in symptoms. On completion of taper, intestinal symptoms recurred, prompting readmission for correction of fluid loss. At the time of this writing, K.T. was being considered for alternative therapy in the treatment of recurrent acute GVHD and complicated C. difficile following autologous transplantation for multiple myeloma.

Autologous Graft-Versus-Host Disease

Historically, GVHD has been a complication of allogeneic HCT and a major cause of morbidity and mortality (Drobyski, Hari, Keeve-Taylor, Komoroski, & Grossman, 2009; Holmberg et al., 2006). An estimated 50%–70% of patients develop acute GVHD following allogeneic HCT (Kline, Van Besien, Nathanson, Noffsinger, & Artz, 2006). Holmberg et al. (2006) reported a similar syndrome that exists in the autologous setting after HCT, one that arises as a result of immunologic manipulation (immunosuppression administration and withdrawal to stimulate a graft-versus-tumor effect) or spontaneously without immunosuppressant stimulation. Spontaneous-onset autologous GVHD...