Hematopoietic Stem Cell Transplantation

Margaret Bevans, RN, MS, AOCN®, and Nonniekaye Shelburne, RN, MS, AOCN®

1. Which of the following newly diagnosed patients is most likely to be considered for an allogeneic hematopoietic stem cell transplant (HSCT)?
   a. Mr. Williams, a 23-year-old with acute leukemia
   b. Mrs. Smith, a 45-year-old with breast cancer
   c. Mr. Henderson, a 54-year-old with multiple myeloma
   d. Ms. Elliott, a 36-year-old with Hodgkin lymphoma

2. Mrs. Johnston is being evaluated for HSCT. Mr. Johnston states that he has done quite a bit of Internet-based research about stem cell transplants and asks you what the main disadvantage of an autologous HSCT is over an allogeneic HSCT. Your response is based on the fact that autologous HSCTs have a higher treatment-related mortality. Which of the following is also a disadvantage of autologous HSCTs?
   a. Higher incidence of graft-versus-host disease (GVHD)
   b. Higher incidence of graft-versus-host disease (GVHD)
   c. Delayed return of normal bone marrow function
   d. Higher incidence of mortality from recurrent disease

3. Which of the following antigens is consistently present on all hematopoietic stem cells?
   a. CD3
   b. CD4
   c. CD8
   d. CD34

4. To enhance the reconstitution of the immune system following an allogeneic HSCT, the recipient and donor primarily are matched for:
   a. Gender
   b. ABO compatibility
   c. Cytomegalovirus (CMV) antigen
   d. Human leukocyte antigens (HLAs)

5. A nonmyeloablative as compared to a myeloablative HSCT would involve administration of chemotherapy and/or radiotherapy resulting in:
   a. Severe myelosuppression
   b. Lower incidence of GVHD
   c. A longer inpatient hospitalization
   d. Fewer conditioning-related complications

6. The risk of GVHD increases:
   a. With an autologous HSCT
   b. When a donor is not related to the recipient
   c. When a donor and recipient are siblings
   d. When a donor and recipient are identical twins

7. Mrs. Johnston has received an HSCT and is experiencing significant pancytopenia from the conditioning regimen. Which of the following cell lines would you expect to be the last to return after engraftment?
   a. Platelets
   b. Monocytes
   c. Neutrophils
   d. Red blood cells

8. A patient is experiencing right upper quadrant pain, increased abdominal girth, and weight gain during the first 30 days after an autologous HSCT. The nurse suspects which of the following as the cause of these signs and symptoms?
   a. Hepatitis
   b. Constipation
   c. Renal failure
   d. Veno-occlusive disease (VOD)

9. Mr. Harris is three weeks postallogeneic HSCT and is being treated prophylactically for GVHD. Which of the following medications might the nurse question if ordered for GVHD prophylaxis?
   a. Methotrexate (MTX)
   b. Tacrolimus (Prograf®, Fujisawa Healthcare Inc., Deerfield, IL.)
   c. Daclizumab (Zenapax®, Roche Pharmaceuticals, Nutley, NJ)
   d. Cyclosporine A (Neoral®, Novartis Pharmaceutical Corporation, East Hanover, NJ)

10. Mr. Harris has developed a maculopapular rash with pruritus on day 55 postallogeneic HSCT. The nurse would expect the primary differential diagnosis to be:
    a. Infection
    b. Drug reaction
    c. Acute GVHD
    d. Radiation dermatitis

11. Mr. Harris has biopsy-proven grade IIB acute GVHD of the gut and skin. The initial nursing care plan would include teaching the patient about side effects associated with:
    a. Steroid therapy
    b. Monoclonal antibodies
    c. Metronidazole (Flagyl®, Pharmacia Corporation, Chicago, IL.)
    d. Loperamide (Imodium®, McNeil Pharmaceuticals, Ft. Washington, PA)

12. The nurse caring for a patient with acute liver GVHD notices that the patient has received six days of methylprednisolone at a dose of 2 mg/kg. The most important parameter for the nurse to monitor when a patient is receiving long-term, steroid treatment is:
    a. Vital signs
    b. Fluid status
    c. Platelet count
    d. Abdominal girth

Answers

Question 1: The correct answer is choice a. Mr. Williams, a 23-year-old with acute leukemia. Patients with acute leukemia usually expect the primary differential diagnosis to be infection.

Margaret Bevans, RN, MS, AOCN®, and Nonniekaye Shelburne, RN, MS, AOCN®, are clinical nurse specialists at the National Institutes of Health Clinical Center in Bethesda, MD. ( Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing or the Oncology Nursing Society.)

Key Words: stem cell transplantation, graft-versus-host disease
respond favorably to conventional induction chemotherapy. However, most patients relapse and eventually die from their disease (Rodriguez & Stiff, 2003). An allogeneic HSCT offers Mr. Williams the best chance at long-term survival. In addition to the diagnosis, other factors must be considered prior to establishing whether allogeneic transplant is the best treatment option. These include availability of a healthy donor (related or unrelated), stem cell source, stage of disease, risk category, and age. Choice b, Mrs. Smith, a 45-year-old with breast cancer, is incorrect. Breast cancer, along with other solid tumors, is not an indication for either autologous or allogeneic transplant unless performed under the conditions of a clinical trial (Urbano-Ispizua et al., 2002). Choices c, Mr. Henderson, a 54-year-old with multiple myeloma, and d, Ms. Elliott, a 36-year-old with Hodgkin lymphoma, are incorrect. Multiple myeloma and Hodgkin lymphoma are indications for autologous HSCT. Factors such as disease stage, age, and overall health of the patient must be considered for this treatment option as well.

Question 2: The correct answer is d, higher incidence of mortality from recurrent disease. This primarily results from adoptive immunotherapy, or graft-versus-tumor effect, that is present with a “new” immune system from a donor and absent when the stem cell source is from the affected patient (autologous). Choices a, higher treatment-related mortality, and b, higher incidence of GVHD, are incorrect. Autologous patients rarely have GVHD, which is a major contributor to the treatment-related mortality with allogeneic transplant. Choice c, delayed return of normal bone marrow function, is incorrect. This is dependent more on the stem cell source, bone marrow, or peripheral stem cells, rather than the type of HSCT. Recovery time for peripheral stem cells is more rapid than stem cells of bone marrow origin.

Question 3: The correct answer is d, CD34. Even though a stem cell product can originate from a variety of sources, the CD34 antigen is expressed in all hematopoietic progenitor cells. An important factor in determining transplant success is the stem cell dose (Schmitz & Barrett, 2002). Traditionally, stem cells are harvested directly from the bone marrow. This procedure requires the donor to receive general or spinal anesthesia while the product is obtained from the iliac crest. Limitations include older age and comorbid conditions of the donor. More recently, human granulocyte colony-stimulating factor has been used to mobilize stem cells into the peripheral blood of the donor to be collected through apheresis. Another source, although less common, is umbilical cord blood. This product is used most commonly in the unrelated pediatric setting because the stem cell dose yield is too low for most adults (Gluckman, Rocha, & Chevret, 2001). Choices a, CD3, b, CD4, and c, CD8, are incorrect. These antigens are expressed on a variety of T cells. CD3 is a “total” T-lymphocyte count, whereas CD4 is primarily expressed on helper T cells and CD8 on the suppressor T cells (Naeim, 1997).

Question 4: The correct answer is d, HLAs. The major histocompatibility molecules are found on the leukocytes and, when matched, lower the risk of graft rejection and GVHD in the transplant recipient. The “best” match for a related transplant is when HLA-A, -B, and -DR antigens are identical. This is called a six of six match. The American Society of Blood and Marrow Transplantation recommended that, in the unrelated transplant setting, additional DNA-based testing be performed (Hurley et al., 2003). Choices a, gender, b, ABO compatibility, and c, CMV antigen, are incorrect because they may affect transplant outcome but not reconstitution of the marrow itself. Gender becomes an issue when more than one donor is available because female to male transplants have a higher incidence of treatment-related mortality and relapse (Gratwohl et al., 2001). The CMV status of the recipient and donor is determined prior to transplant, but it is not a factor that determines whether a transplant occurs. Rather, it provides information that will influence the use of antiviral agents during the marrow recovery phase of the transplant. ABO antigens are on red blood cells, and when incompatibilities exist, various degrees of hemolysis may result, thus increasing the associated morbidity and mortality in HSCT. Specific stem cell processing measures are put into place when ABO incompatibility is present. Therefore, ABO incompatibility is not a factor that determines whether a transplant occurs.

Question 5: The correct answer is d, fewer conditioning-related complications. In general, conditioning-related complications such as mucositis, VOD, and sepsis from prolonged neutropenia appear to be lower with most nonmyeloablative stem cell transplantation approaches compared to historical controls who received a myeloablative transplant (Barrett & Childs, 2000). The primary objective of a nonmyeloablative transplant is to decrease the toxicity and mortality associated with allogeneic HSCT by using a reduced-intensity conditioning regimen. These regimens allow for the expansion of allogeneic HSCT to patients precluded from a myeloablative transplant resulting from the risk of transplant-related mortality and may be appropriate for patients with advanced age or other medically debilitative conditions (Barrett & Childs). Choices a, severe myelosuppression, b, lower incidence of GVHD, and c, a longer inpatient hospitalization, are incorrect. Myelosuppression and inpatient hospitalization are more likely to occur when a myeloablative HSCT is performed. GVHD can occur in either setting and is more dependent on the HLA matching of donor-recipient pairs.

Question 6: The correct answer is b, when a donor is not related to the recipient. Unrelated donor-recipient pairs, although less common, have a greater DNA disparity when compared to a related donor resulting in an increased risk for the recipient to develop GVHD. Choices a, with an autologous HSCT, and d, when a donor and the recipient are identical twins, are incorrect. A “perfect” match occurs when identical twins are the donor-recipient pair, resulting in what is called a syngeneic transplant. The major disadvantage with a syngeneic transplant, as with an autologous transplant, is the lack of immune differences, which would decrease the beneficial effect of the graft-versus-tumor effect. Choice c, when a donor and the recipient are siblings, is also incorrect. Although a risk of GVHD exists with any type of HSCT, it is most likely to occur when a donor and recipient are unrelated.

Question 7: The correct answer is a, platelets. Megakaryocytes, platelet precursors, are the last cell line to return during the engraftment process, taking one to three months to return to normal levels. The cause of this delay is usually multifactorial, including GVHD, immunosuppressive therapy, viral infections, and host-versus-graft antibodies. Choices b, monocytes, c, neutrophils, and d, red blood cells, are incorrect. Monocyte and neutrophil recovery are the first indications of engraftment. Neutrophil counts greater than 0.5 x 10^9/L occur approximately 12–17 days following transplant from peripheral stem cells and 15–23 days from stem cells of bone marrow origin (Schmitz & Barrett, 2002). Circulating reticulocytes, red blood cell precursors, begin increasing in number about two weeks after stem cell infusion, slowly followed by a slow increase in the red blood cell count.

Question 8: The correct answer is d, VOD. Cytoreductive therapy produces endothelial injury, releasing fluid and cellular debris that occlude the hepatic venous outflow. Risk of VOD is heightened in patients with prior liver radiation, treatment with busulfan, second stem cell transplant, active hepatitis, liver malignancy, and residual fibrosis or cirrhosis from prior liver disease. Diagnosis of VOD is based on the clinical presence of painful hepatomegaly, jaundice, as well as weight gain, and ruling out other causes. Direct bi-
lirubin levels rapidly rise a few days after the onset of VOD. Monitoring for VOD includes daily physical examinations, serum liver function studies, fluid balance, and daily abdominal girth measurements. Treatment includes diuretic administration to prevent or decrease extravascular fluid accumulation while maintaining intravascular volume and renal perfusion (Carreras, 2000; Kumar, DeLeve, Kamath, & Tefferi, 2003). Choices a, hepatitis, b, constipation, and c, renal failure, are incorrect. Although a patient can have subclinical (chemotherapy) induced hepatitis, a degree of renal insufficiency, or constipation post HSCT, the symptoms described in the question are more typical of VOD.

**Question 9:** The correct answer is c, dacлизumab (Zenapax). Dacлизumab is a monoclonal antibody that is being studied in the treatment of steroid-refractory GVHD and currently is not recommended for standard GVHD prophylaxis. The goal of prophylactic immunosuppressive therapy is to achieve partial suppression of the donor's immunity to avoid GVHD while gaining benefit from the graft-versus-tumor effect (Simpson, 2000). Choice a, MTX, is incorrect. Low-dose MTX frequently is given on transplant days 1, 3, 6, and 11 to inhibit the stimulation of T lymphocytes. The activation of T lymphocytes after an allogenic HSCT causes the tissue damage associated with GVHD. Side effects of MTX include mucositis, delayed engraftment, and liver toxicity. MTX is commonly given in conjunction with other immunosuppressive agents (Simpson). Choices b, tacrolimus (Prograf), and d, cyclosporine A (Gengraf, Neoral), are incorrect. Patients receiving prophylactic medications for GVHD, such as cyclosporine A and tacrolimus, can be prescribed these medications during the workup for GVHD. If a patient presents or develops an anaerobic infection, the nurse should anticipate teaching the patient about the side-effect profile and possible drug interactions associated with steroids. The dosage prescribed will vary depending on the severity of the GVHD (Flowers et al., 1999). Choice b, monoclonal antibodies, is incorrect. The use of monoclonal antibodies is being investigated in research settings to treat acute GVHD that does not respond to high-dose steroid treatment. This would not be included in an initial care plan for a patient with steroid-resistant GVHD. Choice c, metronidazole (Flagyl), is incorrect. Metronidazole is used to treat anaerobic bacterial infections such as clostridium difficile. Diarrhea secondary to a gastrointestinal infection should be ruled out during the workup for GVHD. If a patient presents or develops an anaerobic infection, the nurse should anticipate the use of metronidazole. Choice d, loperamide (Imodium), is incorrect. Loperamide is an anti-diarrheal and should be avoided with GVHD of the gut. It may slow bowel motility but will not affect the lymphocytic infiltration from GVHD.

**Question 10:** The correct answer is c, acute GVHD. Acute GVHD occurs during the first 100 days after stem cell transplantation. GVHD of the skin presents as a maculopapular, pruritic rash, most commonly involving the palms and soles of the feet, and can progress to involve the cheeks, ears, neck, and trunk (Flowers, Kansu, & Sullivan, 1999). Staging of skin GVHD is based on the percentage of the body affected by the rash. Choice a, infection, is incorrect. Based on the information given, the patient is not experiencing any signs of infection. Choice b, drug reaction, is incorrect. Although this may be a common side effect or allergic reaction to many medications, in this setting, the patient’s rash and pruritus are more typical of acute GVHD. Choice d, radiation dermatitis, is incorrect. Acute radiation dermatitis typically resolves within approximately one month after the completion of therapy. Late skin reactions can occur six months or longer after radiation; however, late radiation skin changes are not typically manifested in the form of a maculopapular rash (Bruner, Bucholtz, Iwamoto, & Strohl, 1998).

**Question 11:** The correct answer is a, steroid therapy. Steroids commonly are used to treat the initial onset of acute GVHD of the gut, skin, and liver. Therefore, the nurse should anticipate teaching the patient about the side-effect profile and possible drug interactions associated with steroids. The dosage prescribed will vary depending on the severity of the GVHD (Flowers et al., 1999). Choice b, monoclonal antibodies, is incorrect. The use of monoclonal antibodies is being investigated in research settings to treat acute GVHD that does not respond to high-dose steroid treatment. This would not be included in an initial care plan for a patient with steroid-resistant GVHD. Choice c, metronidazole (Flagyl), is incorrect. Metronidazole is used to treat anaerobic bacterial infections such as clostridium difficile. Diarrhea secondary to a gastrointestinal infection should be ruled out during the workup for GVHD. If a patient presents or develops an anaerobic infection, the nurse should anticipate the use of metronidazole. Choice d, loperamide (Imodium), is incorrect. Loperamide is an anti-diarrheal and should be avoided with GVHD of the gut. It may slow bowel motility but will not affect the lymphocytic infiltration from GVHD.

**Question 12:** The correct answer is a, vital signs. Steroids are immunosuppressive agents, making patients more susceptible to infections. Patients receiving a dose of more than 1 mg/kg per day of methylprednisolone or equivalent are at high risk for viral, bacterial, and fungal infections from immunosuppression. Patients also are less likely to mount an inflammatory response; therefore, a change in vital signs may be the first indicator that an infection is present. At this point, assessing patients’ vital signs is the highest priority in terms of assessment parameters. Choices b, fluid status, c, platelet count, and d, abdominal girth, are incorrect. Although the nurse should assess these parameters in all patients, this particular patient is most at risk for developing an acute septic reaction secondary to immune deficiency from high-dose steroid therapy, requiring immediate intervention.

**Author Contact:** Margaret Bevans, RN, MS, AOCN®, can be reached at mbevans@cc.nih.gov, with copy to editor at CJONeditor@jsobel.com.

**References**


