Post-Bone Marrow Transplant Patient Management

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Increasingly, bone marrow transplant (BMT) is the treatment of choice for certain hematologic diseases. BMT is, however, a risky procedure with many potentially serious complications. Some complications are the result of the conditioning regimen, a stage of transplantation that includes large doses of chemotherapy and/or radiation therapy. Conditioning-induced neutropenia and thrombocytopenia often result in infection, bleeding, and mucositis. Veno-occlusive disease (VOD), a chemotherapy-induced hepatotoxicity, can cause a mild to severe form of liver disease. Other complications are directly attributable to the engrafted new marrow. Graft-versus-host disease, a rejection process initiated by immunocompetent donor T lymphocytes, is a complication frequently observed in allogeneic BMT.

Approximately 14–28 days after the day of transplant, signs of engraftment begin to appear. When specific discharge criteria are met, the BMT patient is discharged from the hospital. Specific follow-up medical care is ongoing for about one year after BMT.

INTRODUCTION

Bone marrow transplant (BMT) has evolved over the past two decades from an experimental treatment modality to the treatment of choice for certain malignant and non-malignant hematological disorders. BMT is, however, a risky procedure, with attendant side effects and complications. Many of these are serious; some can be life-threatening.

In this review, the author will identify the major acute complications associated with transplantation and provide an overview of the medical and nursing management of the patient during the immediate phase post-BMT. Indications of engraftment and discharge criteria will be addressed.

BONE MARROW INFUSION

When the preparative chemo-radiotherapy has been completed, the bone marrow is transplanted into the recipient. The bone marrow is infused through the right atrial catheter in a manner similar to a blood transfusion. (The day of the transplant is referred to as day 0.) Often, in an autologous bone marrow transplant, the thawed bone marrow is drawn up through a large syringe and pushed directly into the central catheter by the physician. The volume of bone marrow administered varies, depending on the type of transplant. The infusion time depends on the volume administered and can range from 20 minutes to four to six hours.

Side effects of the bone marrow infusion are similar to those observed in blood product administration. Most frequently seen are allergic responses such as fever, chills, urticaria, or shortness of breath. Occasionally, mild dyspnea or tachycardia can occur, due to the formation of micro-pulmonary emboli caused by the clumping of bone

Abbreviations: BMT: bone marrow transplant  CMV: cytomegalovirus  DPH: gancyclovir  GVHD: graft-versus-host disease  IP: interstitial pneumonia  VOD: veno-occlusive disease

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TABLE 1
Acute Complications of Bone Marrow Transplantation

| Complications Associated with Immunosuppressive Conditioning Regimen | Complications Associated with Engraftment |
|---|---|
| Pancytopenia: Infection | Graft-versus-host disease |
| Bleeding | |
| Anemia | Graft rejection |
| Fatigue | |
| GI Toxicities: Mucositis | Graft failure |
| Esophagitis | |
| Nausea and vomiting | Disease relapse |
| Diarrhea | |
| Urotoxicities: Hemorrhagic cystitis | |
| Renal dysfunction | |
| Hepatotoxicities: Veno-occlusive disease | |
| Fluid and Electrolyte Imbalances | |
| Cutaneous Manifestations | |
| Neurotoxicities | |
| Cardiac Toxicities | |
| Interstitial Pneumonia | |

Information from [2]

marrow cells or microscopic fat particles. Volume overload or bacterial contamination of the marrow are rare, though possible, side effects of the bone marrow infusion. Usually an antihistamine, an anti-pyretic, and, possibly, a corticosteroid are administered prior to the bone marrow infusion in order to prevent or attenuate these reactions [1]. Blood group incompatibilities mandate stricter precautions, a description of which is beyond the scope of this review. As a precaution, an oral airway, oxygen, and suction equipment are readily available at the patient’s bedside.

Nursing implications during the bone marrow infusion include monitoring vital signs every hour and observing for dyspnea, shortness of breath, chest pain, chills, hives, and fever. The physician should be notified if any of these reactions develop. The infusion may be slowed or stopped while the patient is assessed and intervention is initiated.

It take two to four weeks for the transplanted bone marrow to begin the process of hematopoiesis. During this time, the patient is at high risk for infection, bleeding, and other attendant complications associated with bone marrow transplantation.

**ACUTE COMPLICATIONS OF BMT**

The side effects and complications of transplantation are caused by the toxicities of the conditioning regimen of chemo-radiotherapy and other immunosuppressant therapies or by the engrafted new marrow itself. Table 1[2] identifies the side effects and complications of BMT.

The particular constellation and severity of toxicities depend on the underlying disease, past treatments, conditioning regimen, type of transplant, and the overall medical status of the recipient. Often, the complications encountered by the patient during the immediate phase following BMT are multi-factorial and may have several etiologies. Effectively managing these treatment-related toxicities requires the interdisciplinary efforts of many specialties. Physicians, nurses, the dental and psychiatric services, infectious disease, nutritional support, physical/occupational therapies, and
social service work collaboratively to provide the comprehensive care required by a BMT patient.

INFECTION

The period following BMT can be divided into three stages, as indicated in Table 2, with certain types of infection often observed during specific stages.

Because infection is a source of significant morbidity and mortality in the BMT patient, infection prevention is crucial during the immediate phase post-transplant. All efforts by health care providers are directed toward prevention, vigilant assessment for signs and symptoms of infection, and prompt intervention at the first sign of an infectious process.

The patient is placed in protective isolation. The degree of protective isolation varies, depending on the transplant center and the type of transplant. The patient may be placed in a laminar air flow room, which provides a sterile environment. Or the patient might be placed in a reverse isolation room (some may be HEPA-filtered), requiring thorough handwashing, and the wearing of mask, gown, and gloves by everyone who enters the room.

Since the skin is the first line of defense against infection, maintaining clean, intact skin and mucous membranes is an integral part of the care of a BMT patient. The patient bathes with sterile water and anti-bacterial soap. In the laminar air flow room, the patient uses sterile linen and applies anti-bacterial ointments to particular skin sites that tend to harbor microorganisms [3].

Because patients undergoing transplantation are profoundly immunosuppressed, even normal GI tract flora and bacteria commonly found in food (particularly fresh fruits and vegetables) can be a source of infection. Therefore, some BMT protocols require GI tract decontamination with oral non-absorbable antibiotics and place the patient on a sterile or low microbial diet to minimize the risk of infection [3,4]. Meeting the nutritional requirements of a BMT patient is, however, a challenge. Mucositis, nausea and vomiting, infection, graft-versus-host disease, and depression are some factors that decrease the patient’s desire and/or ability to eat and drink sufficiently. It is not uncommon for the patient to receive hyperalimentation during the hospitalization in order to maintain an adequate intake of calories and other essential nutrients.
TABLE 3
Etiologies of Interstitial Pneumonia

| Infection          | Viruses:                        |
|--------------------|---------------------------------|
|                    | Cytomegalovirus (CMV)           |
|                    | Herpes simplex virus (HSV)      |
|                    | Varicella-zoster virus (VZV)    |
|                    | Adenovirus                      |
|                    | Respiratory syncytial virus     |
|                    | Measles virus                   |
| Pneumocystis carinii|
| Legionella         |
| Chlamydia trachomatis|

| Irradiation        |
|--------------------|
| Chemical Causes    |
| Carmustine (BCNU)  |
| Cyclophosphamide   |
| Busulfan           |
| Methotrexate       |

| Idiopathic         |

Visitors are allowed to visit the patient, but only healthy immediate family members or significant friends are permitted to enter the patient’s room. Visiting restrictions decrease the BMT patient’s exposure to others, therefore decreasing the risk of a visitor-acquired infection.

For the neutropenic BMT patient, the nurse must monitor vital signs every four hours as well as the daily leukocyte count. (S)he must inspect the skin, mucous membranes, and central catheter site for pain, swelling, or redness every shift. Often, however, during this time of profound neutropenia, the patient cannot generate inflammation or pus, classic signs of an infectious process. There is an ongoing assessment for signs and symptoms of infection in any system or organ. If fever, chills, or other indications of infection appear, the patient is pan-cultured, and antibiotic therapy is initiated.

INTERSTITIAL PNEUMONIA

Interstitial pneumonia (IP) is a conspicuous infection that often occurs during the first 100 days after BMT and is the greatest cause of death during this phase of transplantation. IP has several etiologies (refer to Table 3) [2]. Cytomegalovirus (CMV) is the causative agent in approximately 50 percent of the IP cases in BMT patients [5]. The mortality rate for CMV pneumonia is 85–90 percent [2].

Some risk factors for developing IP are allogeneic BMT, conditioning total body irradiation, prior radiotherapy to the chest, graft-versus-host disease, seropositivity for CMV, transfusion of CMV-positive blood products, female bone marrow donor, and age greater than 30 [2,5]. Clearly, a BMT patient can have several risk factors for IP.

Signs and symptoms of IP are dry cough, tachypnea, dyspnea, chest pain, and fever. The BMT patient with IP can clinically deteriorate very quickly. Therefore, prompt and aggressive measures to elicit the causative agent are required so that treatment can be initiated without delay; however, establishing the diagnosis of IP can be difficult. Auscultation of breath sounds is often nonspecific and not particularly reliable in establishing a diagnosis. A chest X-ray frequently shows diffuse interstitial infiltrates. Arterial blood gases indicate hypoxia. The patient rarely can produce sputum for examination, which seldom is accurate in determining a causative agent. Broncho-
alveolar lavage with immunocytochemistries and cultures or open lung biopsy are the most effective diagnostic methods. In the neutropenic, thrombocytopenic, respiratory-compromised BMT patient, however, an open lung biopsy is an especially risky invasive diagnostic procedure.

Gancyclovir (DHPG), vidarabine, trimethoprim-sulfamethoxazole, and interferon are drugs currently used to treat IP.

The nurse must assess the respiratory status, exercise tolerance, and fatigue levels of the patient with IP. (S)he must monitor vital signs frequently, provide oxygen support as indicated, and assist with diagnostic procedures. Providing emotional support to the patient and family is essential during this critical time.

**MUCOSITIS**

Mucositis is a frequent complication of the conditioning phase. In the setting of neutropenia and thrombocytopenia, mucositis can lead to infection and bleeding in the oral cavity. Herpes simplex, candida, or local infection may worsen the clinical picture. Meticulous mouth care that includes thorough, careful cleaning of the lips, teeth, gums, and tongue is imperative in the care of a transplant patient. The mouth is inspected daily for ulcerations, redness, lesions, leukoplakia, bleeding, and pain. It is not uncommon for a transplant patient to require a continuous morphine sulfate infusion for the pain associated with moderate to severe mucositis. Generally, as the leukocyte count rises, the mucositis gradually improves.

**THROMBOCYTOPENIA**

The BMT patient is severely thrombocytopenic due to the effects of the disease process and the conditioning regimen. Skin and mucous membrane breakdown, persistent vomiting and diarrhea, infection, and veno-occlusive disease can exacerbate the patient's risk for bleeding.

The BMT nurse must observe the patient for signs of bleeding—bruising, petechiae, hemoptysis, hematemesis, hematuria, melanotic or bloody stools, changes in vital signs or neurological status. irritability, and restlessness. Invasive procedures such as peripheral venopunctures, intramuscular injections, urinary catheterizations, and lumbar punctures are avoided as much as possible. Rectal examinations, temperatures, and suppositories are avoided to prevent accidental tearing of the mucosa lining the rectum, which could become a source of infection and bleeding. Certain exercises, such as stationary bicycle riding or muscle strengthening, are restricted when the platelet count falls below 20,000. This restriction is imposed to minimize the risk of bleeding into joints or muscles or intracranial bleeding due to increased blood pressure while exercising.

**BLOOD PRODUCT SUPPORT**

Blood product support is a key component in the care of a BMT patient. Improved availability of blood products, especially platelets, has contributed to increased survival during the intra-transplant phase. All blood products are irradiated before administration in order to inactivate lymphocytes which can initiate graft-versus-host disease or graft rejection. Pre-medications for transfusions should only be given to patients with a history of transfusion reactions. Usually, red blood cells are transfused to maintain a hematocrit of 25 percent or greater, or when the patient becomes symptomatic. Platelets are transfused when the platelet count drops below 20,000 or the patient is
actively bleeding. Initially, random donor platelets are infused. HLA-matched platelets are infused if the patient becomes refractory to random donor platelets. Generally, granulocyte transfusions are given only under extraordinary circumstances.

The immunosuppressed BMT patient is at risk for acquiring a CMV infection through a blood product transfusion. The best way to prevent the transmission of a CMV infection is to administer only CMV-negative blood products to specific BMT patients (particularly CMV-negative recipients with CMV-negative marrow donors) [5]. Using leukocyte removal filtration when administering blood products is effective in minimizing the risk of CMV transmission and the risk of alloimmunization via blood products.

VENO-OCCCLUSIVE DISEASE

Veno-occlusive disease (VOD) is a form of liver disease that occurs in 20–30 percent of BMT patients one to three weeks after the conditioning chemotherapy; VOD is caused by the cytotoxic effects of the chemotherapy. The endothelial cells lining the blood vessels are damaged, and the blood clots in the venules of the liver; blood flow through the liver is diminished or obstructed. This process causes liver damage with subsequent hepatic dysfunction. Occlusion of hepatic circulation often leads to decreased renal flow. Renal insufficiency is frequently associated with VOD [2,6].

Signs and symptoms include insidious weight gain, right upper quadrant pain, jaundice, hepatomegaly, ascites, elevated serum enzymes, and, in severe cases, hepatic encephalopathy.

VOD can be mild to severe and is fatal in 30–50 percent of BMT patients who develop this hepatotoxicity [2].

Treatment is primarily symptomatic and includes fluid and sodium restrictions, diuretic administration, electrolyte replacement, red blood cell transfusions to maintain a hematocrit of 30 percent or greater, analgesic administration, and support to the patient and family. Currently, there is no prophylactic treatment for VOD.

The nursing responsibilities for the BMT patient with VOD include:
- Careful assessment for signs and symptoms of VOD
- Maintaining a balanced fluid and electrolyte status
- Monitoring vital signs, daily weights, and abdominal girths
- Monitoring liver enzymes and hematology counts
- Blood product administration
- Analgesic administration
- Assessment for changes in neurological status

GRAFT-VERSUS-HOST DISEASE

Graft-versus-host disease (GVHD) is a syndrome unique to BMT, especially allogeneic transplants. GVHD is a rejection process whereby the immunocompetent T lymphocytes of the transplanted marrow (graft) identify cells in the recipient (host) as foreign and attack them. GVHD occurs in 30–60 percent of allogeneic bone marrow transplant patients [4,7]. There are two forms of GVHD. Acute GVHD occurs within two weeks to 100 days of an engrafted marrow transplant, while chronic GVHD occurs 100 days or beyond transplantation. GVHD is graded on a I–IV scale, depending upon the severity of the symptoms and the number of organs involved. Organs classically affected by acute GVHD are the skin, the GI tract, and the liver. Chronic GVHD may in addition involve the eyes and the lungs; it resembles a collagen vascular disease.
GVHD can be mild, causing minimal discomfort, or it can be severe enough to be life-threatening.

The skin is usually the first organ to be affected by GVHD. An erythematous skin rash may initially develop on the face, the palms of the hands, and the soles of the feet. The rash may be pruritic and cause dry, flaky skin. A fever may be present. The rash may spread the involve all the skin surfaces. In severe skin GVHD (Grade IV), there may be bullae formation with subsequent skin desquamation.

GVHD of the GI tract is characterized by vomiting, watery or bloody diarrhea (often in large amounts), and abdominal cramping. In severe GVHD of the GI tract, weight loss, malnutrition, and GI bleeding may occur.

In early liver GVHD, the patient may be asymptomatic, manifesting only an increased serum bilirubin, alkaline phosphatase, and other liver enzymes. Advanced liver GVHD is characterized by hepatomegaly, right upper quadrant pain, jaundice, ascites, and liver dysfunction.

There are several ways to prevent GVHD, all of which attempt to inactivate or eliminate T lymphocytes. One strategy is through manipulation of the donor marrow before the marrow is infused. Another strategy is to administer immunosuppressant agents after the transplant. Drugs currently used singly or in combination include methotrexate, cyclosporine, corticosteroids, and anti-thymocyte globulin. Administration of only irradiated blood products also decreases the risk of developing GVHD [2,4]. The use of a sterile laminar air flow room with skin and GI tract decontamination may also contribute to preventing or minimizing GVHD.

If GVHD does occur, despite prophylaxis, the treatment involves additional immunosuppressant therapy and/or increasing the drugs used for prophylaxis.

It is thought that T lymphocytes produce not only a graft-versus-host reaction, but also a graft-versus-leukemia effect. Leukemia relapse rates are lower in BMT patients who develop GVHD than in those patients who do not [2]; however, strategies to prevent GVHD, while maintaining a graft-versus-leukemia effect, have yet to be fully developed.

The goals of nursing care of the patient with GVHD of the skin are to maintain intact skin and mucous membranes, maintain mobility, maintain patient comfort, and promote strategies to cope effectively with body image changes [8].

Other nursing interventions for the patient with GVHD are:
- Maintaining a balanced fluid and electrolyte status
- Monitoring the amount, consistency, and characteristics of diarrhea
- Monitoring serum electrolytes and liver enzymes
- Monitoring vital signs, abdominal girths, and daily weights
- Administering anti-emetics and analgesics
- Providing emotional support to the patient and family

ENGRAFTMENT

About 14–28 days after the infusion of bone marrow, signs of engraftment begin to appear. Gradually, the leukocyte count rises. Platelet and red blood cell counts increase, and there is less dependence on blood products. Bone marrow aspirate and biopsy are done to verify engraftment.

Clinically, the patient shows signs of improvement. In patients without lingering complications, the mucositis improves; nausea, vomiting, and diarrhea subside; appe-
tite slowly increases; and fatigue gradually abates. In allogeneic transplant patients, this stage is the time to be especially observant for signs of GVHD.

DISCHARGE

Barring any major complications, the patient is usually discharged 40–50 days after the day of transplant. Discharge criteria include:

- Patient in stable condition
- Absolute neutrophil count of 500/mm³ or greater for three consecutive days
- Platelet count of 20,000 or greater
- Hematocrit 25 percent or greater
- Off antibiotics for at least 48 hours
- Afebrile for at least 48 hours
- Adequate oral nutritional intake
- If present, GVHD under good control
- Discharge teaching complete [7,9]

Discharge teaching is comprehensive and must involve full understanding and cooperation by the patient and the family. Since the patient’s immune system is immature for the first year following BMT, much of the teaching is focused on infection prevention. Thorough instructions regarding discharge medications are given. Follow-up medical and nursing care continues on an outpatient basis for about one year after transplantation.

REFERENCES

1. Hutchison MM, King AH: A nursing perspective on bone marrow transplantation. Nursing Clin N Amer 17:697–711, 1983
2. Deeg HJ, Klingeman H-G Phillips GL: A Guide to Bone Marrow Transplantation. New York, Springer-Verlag, 1988
3. Lindgren PS: The laminar air flow room. Nursing practices and procedures. Nursing Clin N Amer 18:553–561, 1983
4. Zaia JA, Forman SJ: Management of the bone marrow transplant recipient. In The Critically Ill Immunosuppressed Patient. Diagnosis and Management. Edited by JE Parrillo, H Masur. Rockville, MD, Aspen Publishers, Inc, 1987, pp 381–413
5. Meyers JD, Thomas ED: Infection complicating bone marrow transplantation. In Clinical Approach to Infection in the Compromised Host. Edited by RH Rubin, LS Young. New York, Plenum Medical Book Company, 1988, pp 525–556
6. Ford R, Ballard B: Acute complications after bone marrow transplantation. Semin Oncol Nurs 4:15–24, 1988
7. Hutchison MM, Itoh K: Nursing care of the patient undergoing bone marrow transplantation for acute leukemia. Nursing Clin N Amer 17:697–711, 1982
8. Brown MH, Kiss ME: Standards of care for the patient with “graft-versus-host disease” post bone marrow transplant. Cancer Nursing 4 (June):191–198, 1981
9. Corcoran-Buchsel P, Parchem C: Ambulatory care of the bone marrow transplant patient. Semin Oncol Nurs 4:41–46, 1988