The Bone Marrow Transplantation Procedure

Bone marrow transplantation (BMT) is a technique used in the treatment of leukemia, lymphoma, aplastic anemia, multiple myeloma, immune deficiency disorders, and certain solid tumors such as breast and ovarian carcinoma. It is a salvage technique that permits high-dose, myelosuppressive chemotherapy to be given, achieving greater response rates to therapy. After giving high-dose therapy, treating the disease, and ablating the marrow, BMT salvage is accomplished by infusing the patient with new marrow. New marrow obtained from HLA-matched relatives or unrelated donors is an allogeneic transplant; marrow from an identical twin is a syngeneic transplant. If the marrow is successfully incorporated into the patient, the transplant is termed engrafted. If the genetic match of an allogeneic transplant is less than ideal, the infused marrow may produce an immune response against the tissue of the host, the so-called graft-vs-host reaction. Alternatively, the patient’s immune system may destroy the new marrow, a process termed graft rejection.

If the disease does not involve the marrow, as in lymphoma or solid tumors, or if the disease involving the marrow is in remission, patients may donate their own marrow, providing autologous transplants. In such cases, marrow is extracted and stored prior to chemotherapy. Autologous transplants are more common than allogeneic transplants.

In both allogeneic and autologous BMT, cells are harvested by aspiration through a needle inserted into the marrow of the iliac crest. Recently, peripheral stem-cell harvesting and transplantation have been used increasingly instead of or in addition to autologous BMT. Peripheral stem-cell transplantation differs from autologous BMT in the method of collecting stem cells for reinfusion. In peripheral stem-cell transplant, stem cells are extracted from the peripheral blood by apheresis, which is similar to the process used to collect platelets from donors. Several donation sessions are usually necessary to collect sufficient material for transplantation.

Imaging in BMT patients relates to complications of the procedure, complications of high-dose therapy, proliferative disorders following BMT, or infections occurring in the immunocompromised patient. The primary complication of BMT is graft-vs-host disease (GVHD). The main complications of high-dose therapy include hepatic veno-occlusive disease (HVOD), hemorrhagic cystitis, and pulmonary fibrosis. The most critical time period is two to four weeks after BMT, when acute GVHD may occur or when severe infections may develop.

Graft-vs-Host Disease

GVHD is a significant posttransplantation complication that occurs in about 50% of allogeneic transplants. While most cases are mild, GVHD may be associated with a mortality rate of up to 15%. GVHD may be acute or chronic. For both the acute and chronic forms, older patients are more likely than younger patients to develop this complication of BMT; chronic GVHD is more likely in patients who have had the acute type of the complication.

Acute GVHD usually occurs during the first three months following allogeneic BMT. T cells from the donor marrow produce an immune response against host tissue in the patient’s skin, liver, stomach, or intestine. Symptoms include skin rash, abdominal cramping, nausea, diarrhea, and jaundice. GVHD is treated with immunosuppression -- using drugs such as cyclosporine, steroids, and methotrexate -- or with T-cell depletion; such immunosuppression may increase the risk of infection after BMT.

Chronic GVHD usually develops after the third month posttransplant. New T cells produced after the donor’s marrow has engrafted in the patient may be the cause of chronic GVHD. Chronic GVHD may involve the skin, liver, esophagus, and lungs.

Imaging in GVHD is relevant only in the most severe cases and usually is limited to the small bowel. Acute GVHD produces mucosal and mural inflammation in the gastrointestinal tract, resulting in fold thickening and effacement in the small bowel (Fig 1). In the most severe cases, diffuse narrowing of the intestine, with a featureless ribbon-like appearance, may occur. It has been suggested that prolonged barium coating of the bowel may be suggestive of GVHD, reflecting formation of pseudomembranes and the trapping of barium on the mucosa.
Complications of High-Dose Therapy

Hepatic Veno-occlusive Disease

HVOD is caused by high-dose chemotherapy prior to BMT salvage. Toxicity to the liver results in hepatic edema, venous compression, and stagnation, and finally occlusion of hepatic veins. Venous occlusion leads to further hepatic edema and dysfunction. Symptoms include abdominal tenderness, hepatomegaly, jaundice, edema, and ascites. The symptoms of acute HVOD may be similar to those of acute hepatic GVHD; in such instances, liver biopsy may be necessary to confirm the diagnosis. Most HVOD is mild and reversible, but severe cases may be fatal.

The small veins are occluded with HVOD, while larger veins become involved only late in the course of the disorder. Imaging of the liver in HVOD with duplex color Doppler sonography may show heterogeneous echogenicity of the liver, ascites, hepatomegaly, and thickening of the gallbladder wall. Diminished flow in the hepatic veins or reversed flow in the portal vein may occur. Direct visualization of venous thrombus is uncommon.

Hemorrhagic Cystitis

High-dose chemotherapy is toxic to the urothelium. Severe cystitis, hemorrhage, and bladder necrosis may ensue. Treatment involves hydration, transfusions of blood products, cessation of therapy, or -- in extreme cases -- cystectomy. Urography, cystography, sonography, or computed tomography (CT) may demonstrate bladder wall thickening or blood clots in the bladder as intracystic masses. Sonography is useful to assess effectiveness of therapy.

Pulmonary Fibrosis or Vasculitis

Pulmonary drug toxicity may occur following high-dose chemotherapy in up to 30% of patients. Symptoms include dyspnea, nonproductive cough, and fever. The underlying etiology is vascular and tissue injury leading to interstitial edema and fibrosis. Chest films may demonstrate bilateral air-space opacifications, patchy ground-glass pulmonary opacities, reticulonodular opacities, or interstitial honeycombing. CT scans often define the type and extent of disease more accurately. Bronchiolitis obliterans, organizing pneumonia, or nonspecific vasculitis may occur, manifesting similarly as patchy bilateral opacities.

Encephalopathy

High-dose chemotherapy may also affect the brain, resulting in encephalopathy. The etiology is thought to be vascular and tissue damage due to cytotoxicity. Symptoms include seizures, confusion, and lethargy. CT scans and magnetic resonance imaging (MRI) may demonstrate multifocal white matter lesions. A similar clinical radiographic appearance may develop after treatment of GVHD with cyclosporine because of the drug’s neurotoxicity.

Infections in the Compromised Host

For the first month after BMT, when marrow ablation due to chemotherapy has occurred and transplant engraftment is incomplete, the patient is severely immunocompromised. In most cases, immune status improves gradually, but the immunocompromised state persists to some degree for six to 12 months after transplant and may persist longer for those with GVHD.

Bacterial Infections

Bacterial infections are most common during the first month following BMT, occurring in 50% of patients. Bacterial infections may involve catheter sites, bowel, bladder, and lungs. The radiographic manifestations are most common in the lungs and bowel.

Bacterial pneumonias manifest in BMT patients much as they do in any other patient as segmental or lobar air-space consolidations and atelectasis. Infections with both Gram-positive and Gram-negative organisms are common in BMT patients.

Nonspecific bacterial infections occur in the small bowel in BMT patients and may mimic the gastrointestinal appearance of GVHD, with fold thickening and effacement in the small bowel. Other opportunistic infections may occur, such as giardiasis, with irregular, nodular fold patterns or thumbprinting. Neutropenic enterocolitis, typhlitis, and bacterial colitis may also occur, with bowel changes of wall thickening, thumbprinting, and mucosal ulcerations. If infection is severe, pneumatosis, accumulation of pericolonic fluid, and perforation may occur.
Fungal Infections

Fungal infections are common during the first three months after transplant, particularly among allogeneic BMT patients with GVHD. Candida and Aspergillus infections are the most common posttransplant fungal infections. Candida albicans typically infects the esophagus, stomach, liver, or spleen. Aspergillus may involve the lungs, sinuses, or brain.

Candida is a common cause of infection of the esophagus and stomach in the immunocompromised host (Fig 3). Candida and viral infections may have similar radiographic appearances. The earliest radiographic changes of Candida esophagitis are small, marginal, nodular filling defects. Irregular serrations and a cobblestone pattern may also occur, representing submucosal edema and ulceration. Mucosal plaques may be seen, representing colonization by the fungus. In severe cases, a shaggy mucosal surface may be seen, indicating ulceration and mucosal sloughing. If the infection is severe and prolonged, long strictures may ensue (Fig 4).

Candidal infection in the liver or spleen is manifest as hypoechoic focal lesions by sonography, or hypodense focal lesions by CT (Fig 5). The findings are indistinguishable from those of other fungal lesions. Percutaneous image-guided aspiration may be performed to confirm the diagnosis if necessary.
Invasive pulmonary Aspergillus infection may be seen as focal air-space consolidation, a nodular mass, a cavitary mass, or diffuse air-space consolidation. Eccentric cavitation, the "air-crescent" sign, is characteristic for aspergillosis (Figs 6A-B). CT is often better than plain chest radiographs in defining the type and extent of disease and is useful in guiding procedures for tissue diagnosis. If the infection is focal, early diagnosis and surgical resection are critical in these immunocompromised patients.

Aspergillus infection in the sinuses is best evaluated by CT; opacification, masses, fluid, calcifications, and bone expansion or erosion may be seen.

In the brain, Aspergillus infection may appear as single or multiple lesions. With CT or MRI, a lesion may be a nonenhancing mass, a diffusely enhancing mass, or a ring-enhancing mass (Fig 7).

Viral Infections

Viral infections may occur in the first 12 months after BMT. Herpes, varicella, and cytomegalovirus (CMV) are the most common agents identified. Herpes and CMV may affect the gastrointestinal tract or lungs; varicella causes "shingles" or may infect the optic nerve.

Viral pneumonias may manifest themselves as unilateral or bilateral air-space consolidation, patchy opacities, ground-glass opacities, or reticular densities.

In the esophagus, viral infections may appear as mucosal disorganization, nodularity, and ulceration and may be indistinguishable from Candida infections. Discrete ulceration in an otherwise normal esophageal mucosa may suggest herpetic esophagitis, while candidal ulceration usually occurs on a background of diffuse plaque formation and nodularity. Focal giant ulceration in the esophagus may suggest CMV infection.

In the bowel, viral infections mimic GVHD, with luminal dilation, fold thickening, and effacement.

In the brain, viral infections may demonstrate a variety of nonenhancing and enhancing lesions. In patients with normal white blood cell counts, edema and enhancement are common; in those with low white blood cell counts, edema and enhancement are negligible.
Proliferative Disorders

Day et al. reported five children who developed B-cell proliferative disorders following BMT. These disorders are similar to the lymphoproliferative disorders reported in other immunocompromised hosts in that they are associated with Epstein-Barr virus. However, these cases differ in that they do not respond to antiviral therapy, immunotherapy, or chemotherapy. The radiographic findings include diffuse or focal liver lesions, mural thickening of the bowel or gall-bladder, ascites, lung nodules, and symmetric high-attenuation lesions of the basal ganglia in the brain.

References


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