Radiologic manifestations of bone marrow transplantation complications in children: A comprehensive review

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Learning objectives

The aims of this educational poster are to describe the main bone marrow transplantation complications in children, to review the most important radiologic findings of those complications and to highlight the contributions of radiology in the management of these patients.
**Background**

The bone marrow transplant is performed to restore hematologic and immunologic competence after chemotherapy and radiotherapy in some pediatric cancers, as well as to treat congenital diseases in which these functions are depressed or absent.

According to the relationship between the donor and recipient BMT can be: **syngeneic** (if the individuals are genetically identical), **allogeneic** (if they are genetically different, usually have been matched for HLA type) or **autologous** (if they are the same person, the patient's own stem cells are harvested to be reinfused later).

To prepare the recipient for the graft, malignant cells must be eradicated and immunological resistance must be reduced. These objectives are achieved with high dose chemotherapy, often used in combination with total body irradiation. Such regimens increase the risk of morbidity and mortality in both the short and long term.

Depending on when complications occur, they can be classified in: **pretransplant period** (which usually lasts 15-30 days), **early post-transplant period** (the first 100 days after grafting) and **late posttransplant period**.
Findings and procedure details

PULMONARY COMPLICATIONS:

1. Acute complications:

1.1. Interstitial pneumonitis.

It is an important cause of morbidity and mortality after bone marrow transplantation (BMT).

Cases of interstitial pneumonitis can be divided into infectious and noninfectious categories, being the virus the main causal agent of the first group.

Both radiographic and tomographic features are nonspecific, not allowing imaging to differentiate between infectious and noninfectious interstitial pneumonia. The features are: areas of ground-glass opacity, multilobar infiltrates and pulmonary nodules. The biopsy is often performed to identify the cause.

a. Infectious cause.

Cytomegalovirus is the most important viral pathogen that causes pneumonia in transplant recipients. Respiratory syncytial virus, adenovirus and human herpesvirus 6 all have been detected in patients with diffuse pneumonitis.

The fungus Pneumocystis jiroveci is another potential cause of interstitial pneumonia, however, because of the standard antimicrobial prophylaxis regimens used in patients undergoing bone marrow transplantation, it is seen less frequently.

b. Non infectious cause.

Idiopathic interstitial pneumonitis is the presence of generalized alveolar lesions without evidence of an infectious cause. It usually occurs in the early posttransplant period.

It is believed to result from a variety of pulmonary lesions including secondary to chemotherapy and radiotherapy and acute graft-versus-host disease, that appears to be a significant risk factor for developing this disease risk. Fig. 1 on page 15

1.2. Pulmonary infections.
Prolonged neutropenia is a major risk factor for **fungal infections** as those caused by species of the genus Aspergillus, Candida, Chrysosporium and Mucor. Initial **CT** findings of aspergillosis include ill-defined **nodules or parenchymal consolidations**, 80% of which have the "**halo sign**" (are surrounded by a ground glass halo). Another important aspergillosis consolidations sign is the "**hypodense sign**": infarction and necrosis occurs, showing a hypodense central area prior to cavitation. During healing of the lesions, nodules and consolidations often **cavitate** due to pulmonary necrosis. The bronchoalveolar lavage or lung biopsy may be necessary for diagnosis. **Fig. 2** on page 15

**Bacterial pneumonia** can occur, but is less common due to widespread use of antibiotic prophylaxis. Infections by Gram - organisms, such as Klebsiella pneumoniae, predominate in the post-transplant period, while those due to Gram + bacterias, such as Streptococcus pneumoniae, tend to occur later. **Fig. 3** on page 16

1.3. **Pulmonary edema.**

Pulmonary edema may occur as an early complication of bone marrow transplantation, usually within the first 2-3 weeks after the procedure.

Edema may be due to a multitude of causes, including pulmonary vascular damage, renal impairment, cardiotoxic effects of chemotherapy, radiation therapy, and iatrogenic fluid overload.

The **radiographic** signs of pulmonary edema are: interstitial pattern (septal lines, bronchial wall thickening and subpleural pulmonary edema) and alveolar pattern (patchy confluent opacities with perihilar predominance).

The **CT** findings include bilateral septal thickening, prominent pulmonary vessels, widespread increase in parenchymal density (ground-glass opacity or consolidation) with predominantly perihilar involvement and density gradient gravity dependent, and pleural effusion. **Fig. 4** on page 17

1.4. **Pulmonary hemorrhage.**

Platelet production is usually the last function that is recovered after marrow grafting. Therefore, pulmonary hemorrhage represents another significant early complication, occurring within the first week after transplantation.

**Radiographic** findings include patchy airspace opacities and may even lead to confluent consolidations with air bronchogram.
The most common CT findings are bilateral areas of ground-glass attenuation or consolidation, which may be predominantly perihilar and in mid / low areas, or manifest diffusely. Fig. 5 on page 18

1.5. Bronchiolitis obliterans with organizing pneumonia.

It is a rare complication that usually occurs within 2-3 months after transplantation. It is believed to be predominantly a reaction to graft-versus host-disease, however other causes have been postulated, such as infection and drug toxicity.

Radiographic findings include bilateral patchy airspace opacities with a density ranging from consolidation to ground-glass opacity. The consolidation tends to be migratory and appear and disappear even without treatment.

CT shows foci of airspace consolidation and ground-glass opacities of subpleural or peribronchial distribution, and predominantly in lower lobes.

1.6. Pulmonary calcification.

It may result both of abnormal calcium metabolism (metastatic) and calcium deposition in the lung tissue damaged (dystrophic).

Calcifications occur in areas of preliminary consolidation parenchyma and appear radiographically as persistent pulmonary opacities that may be misinterpreted as unresponsive to treatment pulmonary disease. CT is more sensitive for the detection of calcifications than radiographs. Fig. 6 on page 19

2. Late pulmonary complications (complications that occur more than 100 days after engraftment):

2.1. Bronchiolitis obliterans.

The chronic graft versus host disease is a major multisystem complication for patients surviving 6 or more months after BMT. These individuals are predisposed to chronic obstructive lung disease called bronchiolitis obliterans.

The chest radiograph may be normal or may show hyperinflation, while in CT is often visualised pattern mosaic attenuation and expiratory air trapping. Bronchial dilation is usually evident in advanced cases. Fig. 7 on page 20
ABDOMINOPELVIC COMPLICATIONS

1. Gastrointestinal complications.


Is the recognition of the histocompatibility antigens (HLA) of the recipient tissues as foreign by the immune system from the donor. The result is the aggression of various target organs of the patient by effector stimulated cells graft. Appears in 50-70% of allogeneic transplantation with a fatal outcome in more than 15%.

The disease can occur acutely during three to five weeks post-BMT. The target organs in the acute form are the skin, liver and gastrointestinal tract, manifesting with skin rash, jaundice, severe mucosal inflammation and profuse secretory diarrhea. The chronic form may develop following the acute or may appear again at 45-50 days post-BMT. The skin and gastrointestinal tract are also affected in the chronic form, but in different ways: skin rash resembling scleroderma, and digestive organ most frequently affected is the esophagus.

In ultrasound is characterized by a thickening of the bowel walls, with increased echogenicity of the mesentery and intraabdominal free fluid. CT findings include abnormal bowel wall enhancement that affects both the small bowel and the colon, with or without bowel wall thickening, and mesenteric fat infiltration. However, current imaging techniques are not useful for differentiating GVH disease from infective enteritis, and a biopsy is often required. Fig. 8 on page 21

1.2. Neutropenic colitis.

Consists of acute inflammation of the ileocecal region typical of cancer patients, especially in children with acute myeloid leukemia, that suffer neutropenia secondary to chemotherapy. Represents a situation of high lifetime risk (mortality can reach 70%).

Clinically manifested by the triad of abdominal pain or tenderness, fever, and neutropenia.

Pathologically, the process of mucosal edema and ulceration may involve the whole thickness of the bowel wall and may include secondary necrosis and perforation. Bacterial, fungal, or viral infection may be present and may lead to secondary septicemia.

Abdominal radiographs may show a paucity of right lower quadrant bowel gas with thickening of the cecal wall. US and CT images may demonstrate cecal wall thickening with hyperemia. Additional findings at CT may include inflammatory stranding in the
pericecal fat, as well as free intraabdominal gas and fluid collections in cases complicated by perforation.

1.3. Pneumatosis intestinalis.

Pneumatosis intestinalis radiological sign is defined as the presence of gas within the wall of the small or large intestine. This finding may be incidental or indicate the presence of severe abdominal pathology, and this distinction is made based on clinical history, physical examination and laboratory tests.

NI benign seems to be related to the use of high doses of corticosteroids, which produce defects in the mucosa through which intraluminal gas can be introduced. Unless these findings are accompanied by signs of serious illness, do not justify surgery, disappearing radiological findings after a period of conservative treatment.

2. Hepatosplenic complications.


This disease is a potentially disastrous complication that usually occurs in the first 2 weeks after the transplant and produces painful hepatomegaly, jaundice and fluid retention. Histopathologically, this condition reflects concentric narrowing of the terminal hepatic venules and necrosis of the adjacent hepatocytes, secondary to hepatotoxicity induced by immunosuppressive therapy pre and post-transplant regimen.

The Doppler US findings are: hepatofugal flow, an increased hepatic arterial resistive index, hepatosplenomegaly, periportal areas of low attenuation, small-caliber hepatic veins, gallbladder wall thickening, and ascites. These findings are suggestive but not specific, so the final diagnosis must be histologically. Fig. 9 on page 22

2.2. Liver infections.

The liver is vulnerable to the formation of bacterial or fungal infective abscesses in the post-transplantation setting.

On US images these generally appear as hypoechoic foci. Fungal lesions, in particular, commonly measure only 1-3 mm in diameter, and are often better appreciated with the use of a high-frequency linear-array transducer. Contrast-enhanced CT can be superior to US for fungal lesion detection and it is important to use both arterial phase and portal venous phase acquisitions. The most common lesional appearance on arterial phase
images consist of either a uniformly hyperattenuating focus or a hypoattenuating center with a hyperattenuating rim. Fig. 10 on page 23 Fig. 11 on page 24

2.3. Regenerative hepatic nodules.

Their development may be related to hepatotoxic effects of pretransplantation chemotherapy.

The lesions usually have a lobulated contour and often a hypervascular center on US, CT, and MR images. Typically showing hypervascularity during the arterial phase of dynamic CT and MR imaging, the lesions usually appear isoattenuated or isointense during the delayed phase.

2.4. Focal nodular hyperplasia.

It is rare in children, but there is evidence that it may arise as a consequence of tissue reperfusion following an episode of local hepatic arterial or portal venous thrombosis secondary to chemotherapy or radiation therapy.

At US, appears as an isoor hypoechoic mass, and, at unenhanced CT, as an iso or hypoattenuating mass, compared with the normal liver parenchyma. After the administration of contrast material, both CT and MR images show homogeneous arterial phase enhancement of focal nodular hyperplasia, which has attenuation or signal intensity similar to the normal liver during the portal venous phase and the delayed phase. The most characteristic finding is a central scar that exhibits delayed enhancement and may be seen in up to 50% of cases.

2.5. Iron deposition.

Increased hepatic, splenic, and bone marrow iron deposition exhibited as relative hypointensity on T1- and T2-weighted MR images.

The MR findings were thought to be related to multiple blood transfusions that were required over a relatively short period of time before and during engraftment. Fig. 12 on page 25

2.6. Splenomegaly.
It is a very common finding after BMT and may reflect the underlying condition that required treatment with the transplant, as well as infection, infarction, or posttransplantation lymphoproliferative disorder. Fig. 13 on page 26

3. Renal and urinary tract complications.

Fungal and bacterial renal abscesses are relatively common complications after BMT. In US initially appear as areas of distortion of the normal renal parenchyma then forming hypoechoic collections with thick walls. CT shows intra or perirenal collections of low attenuation and peripheral ring enhancement.

Hemorrhagic cystitis secondary to the use of cyclophosphamide may be seen. CT and US images show focal or diffuse bladder wall thickening, and intraluminal hematoma also may be present.

In addition, hemolytic uremic syndrome, papillary necrosis, renal vein thrombosis, nephrolithiasis, and spontaneous subcapsular hematoma have been reported as rarer complications. Fig. 14 on page 27 Fig. 15 on page 28

4. Posttransplantation lymphoproliferative disorder.

When an Epstein-Barr viral infection occurs in an immunodeficient host, uncontrolled proliferation of B lymphocytes may result in a spectrum of abnormalities, including mononucleosis sepsis, polyclonal B cell hyperplasia, and monoclonal B cell malignancies. In the setting of organ transplantation, however, this process is termed posttransplantation lymphoproliferative disorder and usually occurs within a year of transplantation. The imaging appearances comprise lymphadenopathy, focal parenchymal masses and nodules, and diffuse organ infiltration without a focal mass.

MUSCULOSKELETAL COMPLICATIONS

1. Bone infarction and avascular necrosis.

Both bone infarction and avascular necrosis may be related to total body irradiation in preparation for transplantation as well as to either GVH disease or the steroids used to treat GVH disease.

RM findings consist of heterogeneous changes in signal intensity with or without collapse of the articular surface. T1-weighted MR images show a peripheral hypointense band surrounding a central roughly hypointense marrow looks, while T2-weighted MR images show the double line sign (hypointense peripheral edge surrounding an inner margin...
hyperintense). The administration of contrast is useful in assessing the viable areas. Fig. 16 on page 29

2. Septic arthritis.

The typical clinical presentation of bacterial arthritis is the acute monoarthritis form. Monoarthritis infectious is classified in septic or pyogenic (of which produced by the S. aureus is the most common) and non-pyogenic (as produced by the M. tuberculosis).

The MR findings are: enhancement of the synovial membrane, joint effusion, bone reactive edema, synovial thickening, destruction of articular cartilage and / or bone erosions and periarticular abscesses. Fig. 17 on page 30

3. Osteomyelitis.

It is the infection of bone with bone marrow involvement, distinguishing between acute, subacute and chronic osteomyelitis.

It is defined as chronic osteomyelitis when it persists longer than one month, usually as a result of inadequate treatment or a state of immunosuppression. It is characterized by necrosis with trabecular bone destruction and formation of intraosseous abscess that may contain sequestrum (necrotic bone fragments separated from the healthy bone by granulation tissue). It is usual subperiosteal bone neoformation around the sequestrum, called involucrum. Fig. 18 on page 31

4. Intramuscular hematomas.

In these patients increases the incidence of bleeding because the conditioning treatment destroys most of the platelet supply and the immunosuppressive medication can cause thrombocytopenia.

MR imaging shows a pattern of a signal change with interruption of the fibers, and generally increased muscle size. The signal depends on the time evolution of the hematoma. If the evolution time is <48 hours is isointense in T1-weighted MR images and if subacute lesion is characteristically hyperintense, similar to fat. The sequences with fat suppression help us distinguish fat (deleted) and blood (not deleted). Fig. 19 on page 32
1. Infections.

Infection is the most common complication of bone marrow transplantation, although the frequency of its occurrence may be decreasing.

The immune impairment seen at various stages after bone marrow transplantation dictates the types of infections that may occur. In the **pre-engraftment period** (the first 15-30 days after transplantation), there is a high risk of sepsis due to Gram-negative bacterial infection as well as various fungal and viral infections. During the **early postengraftment period** (the first 100 days after engraftment), CMV, fungal, and Gram-positive bacterial infections predominate at this time. During the **late postengraftment period** (the months and years after transplantation), infections due to encapsulated bacteria and herpes zoster virus are most commonly seen at this time.

**Aspergillus** infection is the most common infectious cause of focal lesions after a bone marrow transplant. These lesions usually appear on CT images as multiple foci of low attenuation with minimal mass effect and with little contrast enhancement. The T2-weighted MR images represent foci of intermediate signal intensity with a peripheral ring of hyperintensity.

**Abscesses** and **bacterial meningitis** are relatively rare due to routine antibiotic prophylaxis. **Toxoplasmosis** and **viral infections of the central nervous system** such as herpes encephalitis, are also often rare.

2. Cerebrovascular complications.

The most common reported cerebrovascular complications are **subdural hematoma**, which may reflect thrombocytopenia, and **cerebral infarction**, which is most commonly attributable to either nonbacterial or infective endocarditis, or to the cumulative deleterious effects of the pretransplantation regimen. Fig. 20 on page 33 Fig. 21 on page 34

3. Therapy-induced complications.

Among the complications induced by the therapy will include those related to pre-transplant regimen and the prophylaxis of graft-versus-host disease.

Radiation therapy can cause **white matter lesions** or multiple foci of necrosis in the brain stem. The induced **cavernous hemangiomas** are well documented in the pediatric population.
Cyclosporine is used, often in combination with methotrexate, as prophylaxis for graft-versus-host disease. This treatment carries a risk of potentially reversible neurotoxic effects that are collectively called posterior reversible encephalopathy syndrome. This complication occurs typically within the first month of initiation of prophylaxis and is manifested by severe visual impairment, cerebellar ataxia, confusion, and seizures. MR imaging may reveal focal abnormalities wedge showing hyperintensity predominantly in the occipital lobes. After reduction in the level of serum cyclosporine, these abnormalities tend to show almost complete resolution.

Other complications to consider are the venous sinus thrombosis, generalized brain atrophy and secondary malignancies induced by radiation. Fig. 22 on page 35 Fig. 23 on page 36

4. Malignant recurrences.

Patients who have undergone a bone marrow transplantation for the treatment of primary brain tumors, neuroblastoma, and leukemia appear to have an increased risk for recurrent malignancy.

Abnormal foci of contrast enhancement are typically seen at CT and MR imaging.

PARANASAL SINUS COMPLICATIONS

1. Paranasal sinusitis.

More than a third of patients develop paranasal sinusitis within the first 2 years after transplantation of bone marrow, beeing this type of infection a little known source of fever in the transplant population. A fungal origin, usually Aspergillus, is identified in a little less than one quarter of patients.

The CT findings of paranasal sinusitis include fluid levels, which often occur in association with thickening of the soft tissues. Fig. 24 on page 37 Fig. 25 on page 38

2. Angioinvasive paranasal sinusitis.

This condition implies mucosal, submucosal, bone or vascular invasion; and is usually due to Aspergillus species. The initial symptoms of invasive sinusitis are common in the posttransplantation population and overlap with the symptoms of bacterial sinusitis. Consequently, the diagnosis may be delayed. Since rapid progression is the norm and the condition is frequently fatal, such a delay may be catastrophic.
Some CT findings like mucosal thickening, paranasal sinus opacification and facial soft-tissue swelling, are common in both invasive and bacterial sinusitis. The classic signs, such as periantral soft-tissue invasion, bone erosion and orbital invasion are not pathognomonic and are rarely seen.

A definitive diagnosis can be made only on the basis of histopathologic evidence of tissue invasion by fungal hyphae.
Fig. 1: Idiopathic interstitial pneumonitis in a 2-year-old boy with Thalassemia major treated with allogeneic bone marrow transplantation. He presented also intestinal and skin GVH Disease. CT image shows extensive bilateral perihilar ground-glass opacities.

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**Fig. 2:** A, B and C: Angioinvasive aspergillosis with multiple nodules with peripheral ground glass halus and one of them with central necrosis (white arrow) in a 3-year-old girl after allogeneic bone marrow transplantation for acute myeloid leukemia. D: Angioinvasive aspergillosis with a cavitated nodule (black arrow) in a 2-year-old girl after allogeneic bone marrow transplantation for acute lymphoblastic leukemia.

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Fig. 3: A and B: Bilateral bacterial pneumonia in a 3-year-old girl after autologous bone marrow transplantation for neuroblastoma. CT images shows bilateral areas of consolidation with air bronchogram sign. C: Bacterial pneumonia in a 3-year-old girl after allogeneic bone marrow transplantation for mucopolysaccharidosis type I. CT image shows consolidation in the lower lobe of the right lung.

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Fig. 4: Pulmonary edema in a 3-year-old girl after autologous bone marrow transplantation for neuroblastoma. CT image shows diffuse areas of ground glass atenuation and dilatation of pulmonary trunk.

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Fig. 5: A: Pulmonary hemorrhage in a 5-year-old boy after allogeneic bone marrow transplantation for mevalonic aciduria. Chest radiograph shows multiple bilateral pulmonary infiltrates with right hemithorax predominance. B: Pulmonary hemorrhage in a 12-year-old boy after allogeneic bone marrow transplantation for adrenoleukodystrophy. Chest radiograph shows multiples bilateral pulmonary infiltrates.

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Fig. 6: Dystrophic pulmonary calcification secondary to multiple respiratory infections in a 9-year-old girl after allogeneic bone marrow transplantation for aplastic anemia. CT image shows a calcification of 5 mm in the left pulmonary apex (arrow).

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Fig. 7: A y B: Bronchiolitis obliterans in a 9-year-old girl after allogeneic bone marrow transplantation for aplastic anemia. Expiration CT image shows bilateral areas of air trapping. C y D: Bronchiolitis obliterans in a 15-year-old girl after allogeneic bone marrow transplantation for acute myeloid leukemia. CT images show bilateral patchy airspace consolidation and ground-glass opacities with bronchiectasis and broncholectasis.

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**Fig. 8:** Small-bowel GVH disease in a 4-year-old boy after allogeneic bone marrow transplantation for thalassemia major. A: CT image shows increased mesenteric vasculature with bowel loops wall thickening and increased wall enhancement. B: US image shows severe bowel loops wall thickening, hyperechogenicity of mesenteric fat and abundant intraabdominal free fluid.

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**Fig. 9:** Hepatic veno-occlusive disease in a 3-year-old boy after allogeneic bone marrow transplantation for acute lymphoblastic leukemia. A: Color Doppler US image shows filiform hepatic veins with loss of the normal wave on the left and slight flattening of the wave in the middle and right. B and C: Gray-scale US images show heterogeneous liver, periportal edema and gallbladder thickening.

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Fig. 10: Hepatic fungal infection in a 12-year-old boy after allogeneic bone marrow transplantation for adrenoleukodystrophy. A: Gray-scale US image shows multiple hyperechoic liver lesions. B: High-resolution US image obtained with a linear-array transducer shows the same lesions.

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Fig. 11: Hepatosplenic candidiasis in a 9-year-old boy after allogeneic bone marrow transplantation for acute lymphoblastic leukemia. A: High-resolution US image obtained with a linear-array transducer shows multiple calcificated lesions. This lesions represent the calcification of treated bacterial abscess. B: Gray-scale US image shows the same lesions.

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**Fig. 12:** Hepatic iron deposition in a 12-year-old boy after allogeneic bone marrow transplantation for adrenoleukodystrophy. The patient had elevated serum ferritin levels because of many blood transfusions. Hepatosplenic hypointensity on opposed-phase T1-weighted MR image (A) and high liver signal on phase T1-weighted MR image (B). C: Axial T2-weighted Gradient-Echo MR image shows marked hepatosplenic hypointense. A liver biopsy was performed for another reason which confirmed the secondary hemochromatosis.

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**Fig. 13:** Splenomegaly in a 12-year-old boy after allogeneic bone marrow transplantation for adrenoleukodystrophy.

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Fig. 14: Medical nephropathy in a 13-year-old boy with Non-Hodgkin Lymphoma treated with allogeneic bone marrow transplantation. Gray-scale US image shows increase in renal echogenicity.

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Fig. 15: A: Hemorrhagic cystitis due to BK virus in a 12-year-old boy after allogeneic bone marrow transplantation for acute myeloblastic leukemia. Gray-scale US image shows a large intravesical clot. B and C: Hemorrhagic cystitis after treatment with cyclophosphamide in a 12-year-old boy after allogeneic bone marrow transplantation for adrenoleukodystrophy. In the first image diffuse thickening of the bladder wall is observed, while in the second one a large intravesical clot is displayed.

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Fig. 16: Bone infarcts in a 12-year-old boy after allogeneic bone marrow transplantation for adrenoleukodystrophy. Coronal T1-weighted (A and B) and SPAIR (C) MR images show multiple geographic areas of abnormal signal intensity in the distal femoral metaphyses and epiphyses (straight arrows). C: Coronal T1-weighted MR image shows a geographic hyperintense lesion in the right femoral head (curve arrow).

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Fig. 17: Septic arthritis in a 12-year-old boy after allogeneic bone marrow transplantation for adrenoleukodystrophy. A, B and C: Evolution over four months on coronal T1-weighted MR images of septic arthritis of the left hip with avascular necrosis of the femoral head and secondary ipsilateral subluxation. D: Coronal T2 FAT SAT-weighted MR image showing a substantial thickening of the synovium of the left hip joint with nodular enhancement after administration of paramagnetic contrast and joint effusion. E and F: CT Volume Rendering images where a significant alteration of the morphology of the left femoral head, subluxation and neoacetabulo formation is observed.

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Fig. 18: Chronic osteomyelitis in a 12-year-old boy after allogeneic bone marrow transplantation for adrenoleukodystrophy. A: Radiograph showing rarefaction texture of the femur bone and lamellar periosteal reaction in the medial part of the distal metaphysis of the left femur with adjacent ossification (arrow), findings regarding sequestrum-involucrum. B: Coronal T1-weighted MR image shows the ossification observed in the radiograph (arrow). C: Bone scan showing a focus of tracer uptake in the medial condyle of the left femur, visible in the three phases of the study, although the vascular and tissue phases intensity is lower.

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**Fig. 19:** Intramuscular hematoma in a 12-year-old boy after allogeneic bone marrow transplantation for acute myeloblastic leukemia. A: Axial T1-weighted MR image shows hyposignal area in all sequences in the thickness of the right gluteus maximus muscle and right gluteus minimus muscle. B: Axial contrast-enhanced fat-saturated T1-weighted MR image (B) shows no enhancement after administration of paramagnetic contrast.

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**Fig. 20:** Bilateral subdural hemorrhage in a 1-year-old girl after allogeneic bone marrow transplantation for infantile malignant osteopetrosis. A: Transfontanellar ultrasound image shows bilateral extra-axial collections outside the dura (white arrow), on the left side a thin septum identified in the thickness of the collection. B: CT image shows an extensive bilateral chronic subdural hemorrhage.

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Fig. 21: Chronic extraaxial hematoma in a 2-year-old boy after allogeneic bone marrow transplantation for infantile malignant osteopetrosis. T2-weighted MR image (A) and Fluid-attenuated inversion recovery MR image (B) show a right frontal extra-axial hematoma.

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Fig. 22: White matter lesions secondary to radiation therapy in a 7-year-old boy with a medulloblastoma treated with surgery, chemotherapy, radiotherapy and an autologous bone marrow transplant. Fluid-attenuated inversion recovery MR image shows periventricular white matter hyperintensity adjacent to the occipital horns of the lateral ventricles.

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Fig. 23: Posterior reversible encephalopathy syndrome in a 9-year-old boy in treatment with cyclosporine for hemophagocytic lymphohistiocytosis. A, B and C: Fluid-attenuated inversion recovery MR images show cortical and subcortical areas of abnormal signal hyperintensity. After reduction in the serum cyclosporine level, these abnormalities showed complete resolution.

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Fig. 24: Sinonasal and pulmonary aspergillosis 3-year-old girl after allogeneic bone marrow transplantation for acute myeloid leukemia. CT image shows maxillary sinuses occupation. No bony erosions were observed.

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**Fig. 25:** Sinusopathy in an 13-year-old boy after autogenous bone marrow transplantation for Non-Hodgkin Lymphoma. A, B and C: Fluid-attenuated inversion recovery MR images show mucosal thickening of the maxillary sinuses and occupation of the sphenoid sinuses and the ethmoid cells.

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Conclusion

The increasing use of bone marrow transplantation to treat a wide variety of conditions has lead to an increased incidence of complications associated with these procedures. Imaging techniques play a key role in the diagnosis of these problems and in the assessment of response to therapy. This mandates that the radiologist be familiar with the full range of potential complications and their imaging appearances.
References


- Worthy SA, Flint JD, Muller NL. Pulmonary complications after bone marrow transplantation: high-resolution CT and pathologic findings. RadioGraphics 1997;17:1359-1371.


