RadioGraphics

Imaging Evaluation of Pulmonary and Abdominal Complications Following Hematopoietic Stem Cell Transplantation[1]

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CME FEATURE

See accompanying test at http://www.rsna.org/education/rg_cme.html

LEARNING OBJECTIVES FOR TEST 1

After reading this article and taking the test, the reader will be able to:

- Describe the differences between conventional myeloablative and nonmyeloablative hematopoietic stem cell transplantation.
- Identify typical radiologic manifestations of specific pulmonary and abdominal complications of stem cell transplantation.
- Discuss the time course and risk factors for specific posttransplantation complications.

Hematopoietic stem cell transplantation is used to treat hematologic disorders and as an adjunct treatment for solid organ malignancies. After undergoing transplantation, patients are at risk for opportunistic infections and other complications caused by dysfunction of the immune system. Pulmonary complications include cryptogenic organizing pneumonia, opportunistic pneumonias caused by *Aspergillus* and *Zygomycetes* species and cytomegalovirus, alveolar hemorrhage, and constrictive bronchiolitis. Abdominal complications include hepatic veno-occlusive disease, graft-versus-host disease (GVHD), colitis, and hemorrhagic cystitis. Allogeneic transplant recipients are at risk for developing GVHD. Autologous and syngeneic transplant recipients are less likely to have chronic or late posttransplantation complications. Nonmyeloablative transplant recipients are less likely to develop opportunistic infections and other complications in the period immediately following transplantation, but are at risk for developing chronic GVHD and other chronic complications. Radiologic evaluation serves as the cornerstone for timely diagnosis of these complications, which is essential to reduce patient morbidity and mortality. Combining clinical factors—including the type of transplant and the point of time during the posttransplantation course—with characteristic imaging features yields the most specific and accurate differential diagnosis for radiologic findings in stem cell transplant recipients.

Abbreviations: BAL = bronchoalveolar lavage, CMV = cytomegalovirus, DAH = diffuse alveolar hemorrhage, GVHD = graft-versus-host disease, PTLD = posttransplant lymphoproliferative disorder, VOD = veno-occlusive disease

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See the commentary by Sivit following this article.

Introduction

The indications for hematopoietic stem cell transplantation have expanded from treatment of hematologic malignancies to include treatment of solid organ malignancies such as renal cell carcinoma and ovarian cancer, as well as treatment of severe hematologic disorders such as sickle cell anemia and other hemoglobinopathies. As stem cell transplantation becomes more widespread, radiologists encounter transplant recipients with increasing frequency.

Conventional hematopoietic stem cell transplantations are performed after high-dose chemotherapy or radiation therapy has ablated the bone marrow. Pluripotent stem cells that were previously harvested from the marrow or circulating blood of the patient or of a donor are transfused to repopulate the bone marrow and restore hematopoiesis. Autologous stem cells are harvested from the same patient into whom they are later transplanted. Syngeneic stem cells originate from a genetically identical donor (ie, a monozygotic twin). Allogeneic stem cells are harvested from an individual who is genetically different from the recipient but closely matched in terms of histocompatibility.

After undergoing stem cell transplantation, patients are at risk for opportunistic infections and other complications. Familiarity with the recovery sequence of various immune system functions over the posttransplantation course is useful because it provides a framework for understanding and predicting which transplantation-related complications are most likely to occur at a given time. The course after hematopoietic stem cell transplantation is divided into three phases. The preengraftment phase typically lasts 15–30 days and spans the period between stem cell transfusion and restoration of hematopoiesis. During this period, the immune system is severely compromised by pancytopenia. Host defense barriers may be further weakened by mucositis and other chemotherapy-related complications. Broad-spectrum antimicrobial agents as well as erythrocyte and platelet transfusions support the patient through this phase. The early posttransplantation phase begins after successful engraftment of the donor stem cells and resumption of hematopoiesis and typically spans the period from 30 to 100 days after transplantation. Although profound neutropenia has resolved by this time, lymphocyte recovery lags behind, resulting in continued deficiency of cellular and humoral immunity. The late posttransplantation phase begins 100 days after transplantation. Lymphocyte levels return to normal, but recovery of humoral immunity lags behind, gradually improving throughout the 1st year.

In older patients or in patients with significant comorbidities, nonmyeloablative ("mini") allogeneic transplants with less intense conditioning regimens are used. The conditioning chemotherapy suppresses the recipient's immunity sufficiently to allow allogeneic stem cells to engraft. Unlike in conventional transplantation, the bone marrow is only partially ablated with a "mini" transplant. Hematopoiesis from the residual bone marrow prevents pancytopenia. As a result, recipients of nonmyeloablative transplants tend to have fewer complications during the early posttransplantation phase than do recipients of conventional myeloablative transplants. However, because allogeneic stem cells are used for nonmyeloablative transplants, recipients are at risk for graft-versus-host disease (GVHD) and other related late-onset complications.

All recipients of stem cell transplants are at risk for a multitude of complications. Imaging is essential to screen symptomatic patients and assist in the diagnosis of complications, which presents a challenge to the radiologist because, in many instances, common posttransplantation conditions share similar radiologic characteristics. The differential diagnosis can be narrowed when imaging findings are combined with clinical information such as transplant type and time elapsed since transplantation. Imaging also aids in procuring or at least identifying the most easily obtained tissue for pathologic analysis, determining disease extent, and monitoring the patient's response to treatment. In this article, we review the imaging characteristics, risk factors, and typical time course of common pulmonary and abdominal complications of hematopoietic stem cell transplantation.

Pulmonary Complications

Pulmonary complications occur in 40%–60% of stem cell transplant recipients and considerably influence morbidity and mortality (1). Risk factors for the development of pulmonary complications following transplantation include *(a)* pretransplantation chemotherapy, *(b)* duration of immune system dysfunction, *(c)* type of transplant, and *(d)* presence of GVHD. Specific conditions are categorized on the basis of cause (infectious vs noninfectious) and can be further classified according to the posttransplantation period in which they are most likely to occur.

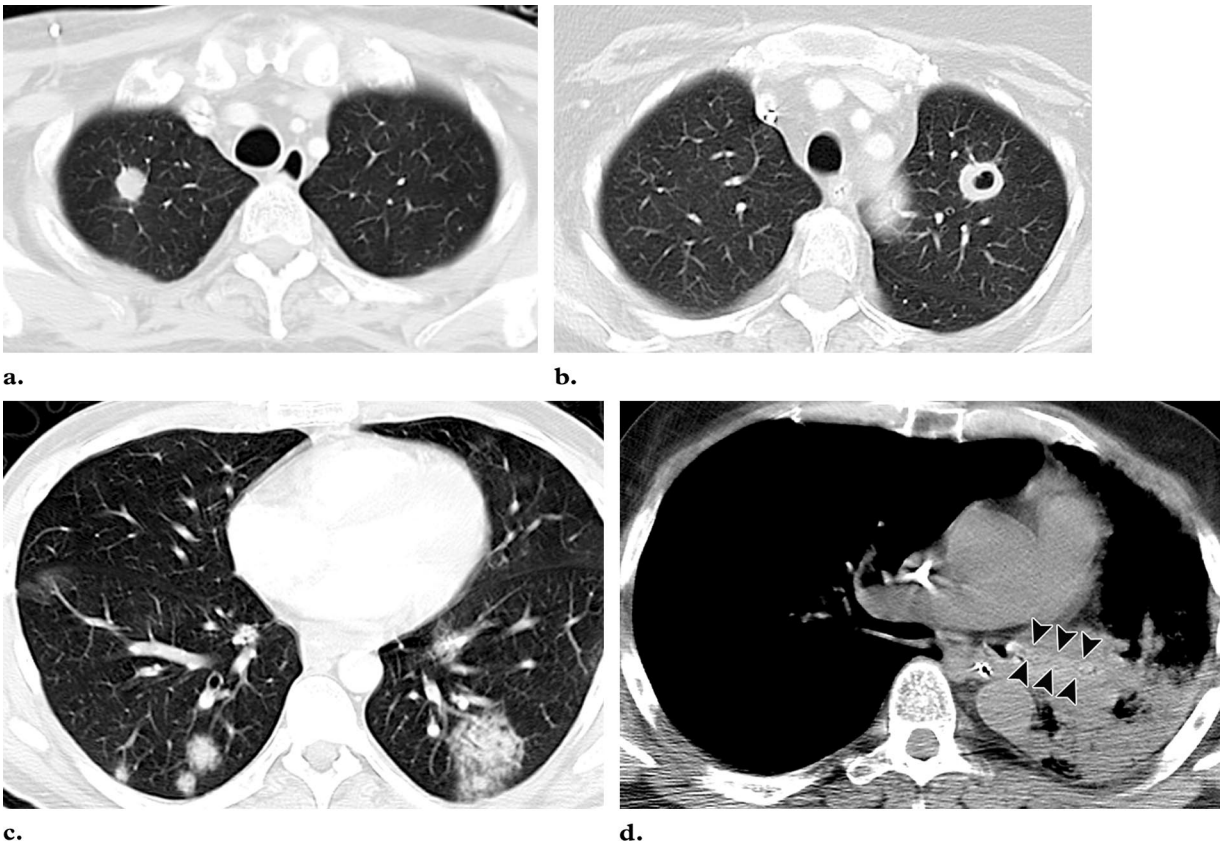


Figure 1. Pulmonary aspergillosis following hematopoietic stem cell transplantation. **(a, b)** CT scans obtained in two different patients show solitary nodules, with the nodule in **b** demonstrating cavitation. **(c)** CT scan obtained in a third patient shows multiple nodules surrounded by a halo of ground-glass attenuation, a finding that indicates hemorrhage resulting from pulmonary infarction. **(d)** CT scan obtained in a fourth patient shows tracheobronchial aspergillosis with debris filling the left lower lobe bronchus (arrowheads) and consolidation in the left lower lobe.

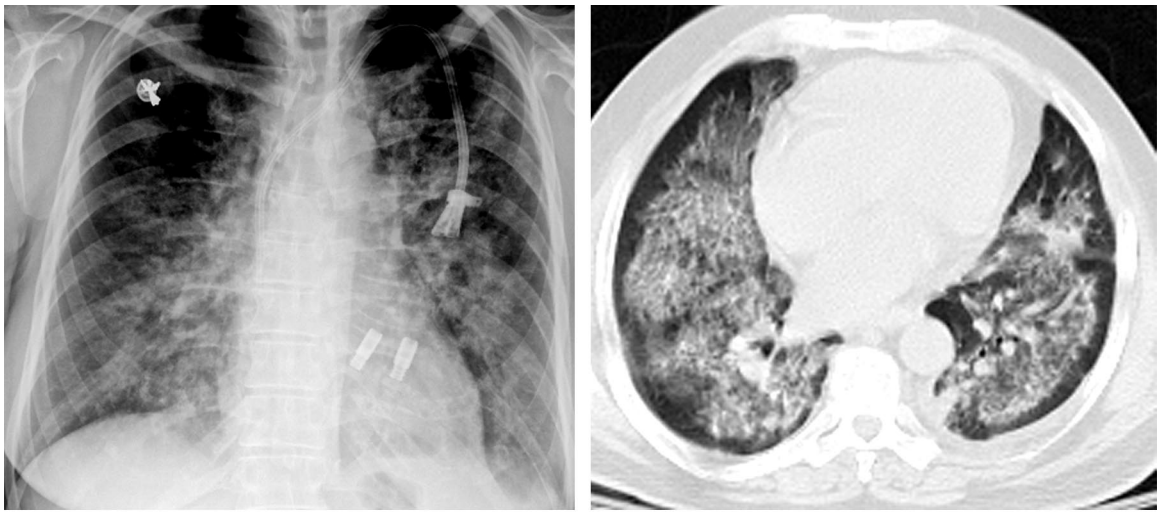
Preengraftment Period (Days 0–30)

The period immediately following myeloablative transplantation is marked by profound neutropenia. However, despite the fact that bacteremia is common, bacterial pneumonias are unusual in this phase (2). It is likely that empiric use of broad-spectrum antimicrobial agents at the earliest clinical sign of infection prevents or aborts pneumonia before it becomes radiologically apparent.

Fungal infections account for 25%–50% of all pneumonias in allogeneic transplant recipients, with *Aspergillus* species being the most frequent pathogens. The prevalence of *Aspergillus* pneumonia following allogeneic transplantation is 10%; it rarely occurs in recipients of autologous transplants (3,4). Unlike with other pulmonary pathogens, there is no specific period following stem cell transplantation during which *Aspergillus* pneumonia is most likely to occur; it can occur at any time following transplantation. Only one-third of *Aspergillus* pneumonias arise during the preengraftment period (3). Risk factors for infection with *Aspergillus* species vary depending on the point of time during the posttransplantation course. Neutropenia is the principal risk factor prior to engraftment and reestablishment of hematopoiesis. Later in the posttransplantation course, steroid treatment for GVHD is a strong risk factor (3).

At conventional radiography, angioinvasive aspergillosis usually manifests with peripheral pulmonary nodules. At computed tomography (CT), the pulmonary nodules may be surrounded by hazy ground-glass attenuation, which represents hemorrhage around the central infarction caused by angioinvasion (Fig 1) (5). Cavitation of a nodule tends to coincide with recovery of the neutrophil count (4,5). Pleural effusions and lymphadenopathy are uncommon findings.

Fungal invasion of central and peripheral airways is characteristic of tracheobronchial aspergillosis, and symptoms include cough, wheeze, and stridor. CT demonstrates thickened airway walls, debris-filled airway lumina, and small (<5-mm) centrilobular nodules or patchy peribronchial consolidation (Fig 1).



a. **b.**

Figure 2. DAH following hematopoietic stem cell transplantation. **(a)** Chest radiograph shows diffuse bilateral consolidation. **(b)** CT scan obtained in a different patient shows diffuse bilateral ground-glass attenuation with a superimposed reticular pattern representing thickened inter- and intralobular septa.

Pulmonary edema is common during the first weeks following stem cell transplantation and may be due to *(a)* increased pulmonary hydrostatic pressure from intravenous fluids (eg, parenteral nutrition, antibiotics), *(b)* chemotherapy-induced renal insufficiency, or *(c)* abnormal capillary permeability resulting from drug and transfusion reactions (1). Typically, edema has a rapid onset, with conventional radiography demonstrating Kerley B lines, indistinctness of pulmonary vessels, and pleural effusions. Diffuse ground-glass attenuation and interlobular septal thickening are seen at CT (5).

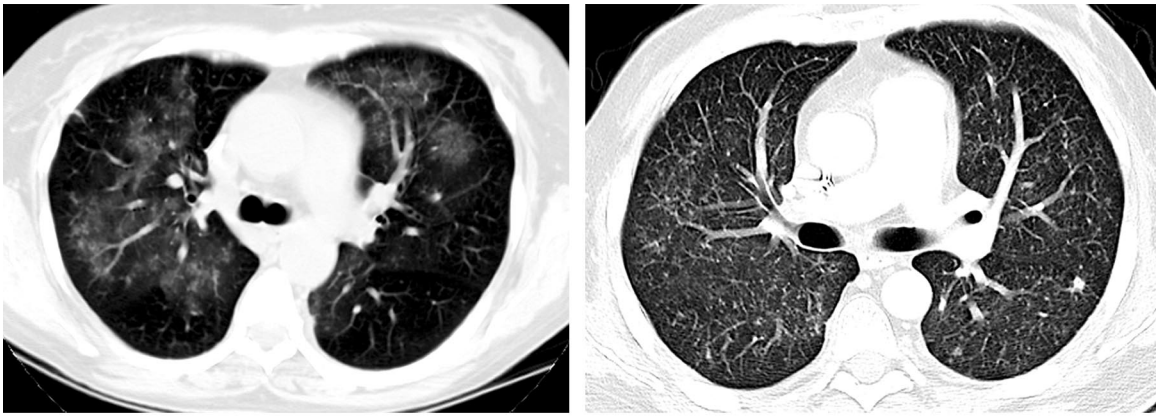
Diffuse alveolar hemorrhage (DAH) is diagnosed in 2%–20% of stem cell transplant recipients and usually occurs during the 2nd or 3rd week following transplantation (6,7). The diagnosis can be made definitively when bronchoalveolar lavage (BAL) demonstrates either progressively bloodier return with each successive lavage aliquot or the presence of hemosiderin-laden macrophages. Presenting symptoms include dyspnea, cough, hypoxemia, and, rarely, hemoptysis. The mortality rate is 22%–77% (6,7). At radiography, DAH manifests as rapidly progressive diffuse lung disease resembling pulmonary edema. CT characteristically demonstrates ground-glass attenuation with a superimposed reticular pattern representing thickened interlobular and intralobular septa (Fig 2). Because conventional radiographic and CT findings are very similar to those in pulmonary edema, BAL is necessary for diagnosis.

Early Posttransplantation Period (Days 31–100)

Between 1 and 3 months following stem cell transplantation, the most common infectious pulmonary complications are angioinvasive aspergillosis and cytomegalovirus (CMV) pneumonia. *Pneumocystis carinii* pneumonia is rare in transplant recipients because of effective prophylaxis.

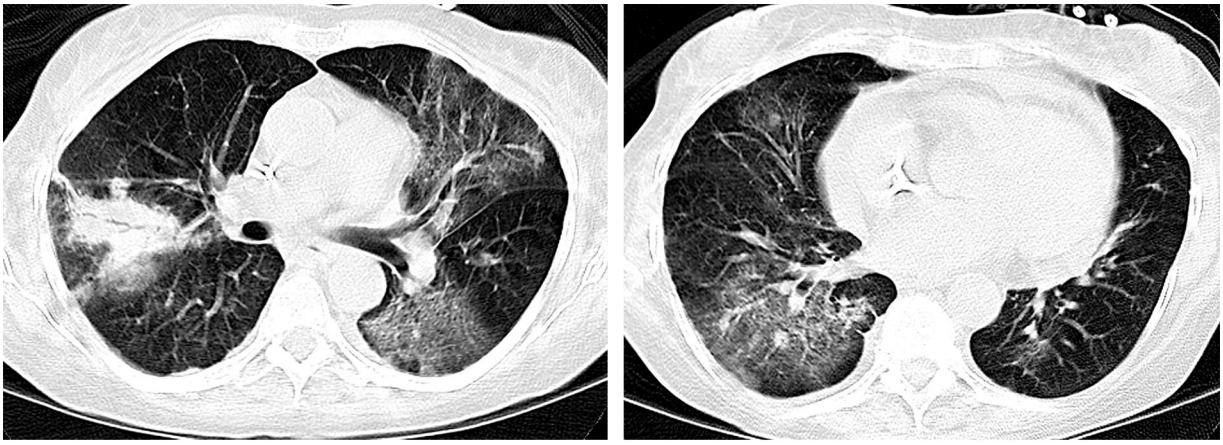
CMV pneumonia occurs in 10%–40% of allogeneic transplant recipients but less frequently following autologous transplantation (2%) (8,9). In the majority of cases, CMV is reactivated from a latent virus in seropositive patients. The diagnosis of CMV pneumonia requires radiographic evidence of pneumonia and isolation of the virus in either BAL or lung tissue samples. Typical findings at chest CT are small (1—5-mm) or poorly defined nodules, ground-glass attenuation, and sometimes dense consolidation or a reticular attenuation pattern (Fig 3). CMV pneumonia is usually bilateral and its distribution variable (5,10). Pleural effusions and lymphadenopathy are unusual.

Idiopathic pneumonia syndrome has a prevalence of 10% and is a diagnosis of exclusion, being defined as the presence of widespread alveolar damage in the absence of lower respiratory tract infection (7). Although its pathogenesis is not clearly understood, idiopathic pneumonia syndrome may be the result of toxicity from chemotherapy, undiagnosed infection, or GVHD. The radiographic pattern of idiopathic pneumonia syndrome consists of nonspecific bilateral pulmonary consolidation. There is no effective treatment for this disease, and the 1-year survival rate is only 15% (7).



a. b.

Figure 3. CMV pneumonia following hematopoietic stem cell transplantation. CT scans obtained in two different patients show small nodules, along with patchy **(a)** and diffuse **(b)** ground-glass attenuation.



a. b.

Figure 4. *Zygomycetes* pneumonia following stem cell transplantation. CT scans obtained in two different patients show patchy consolidation **(a)** and ground-glass attenuation and nodules **(b)**.

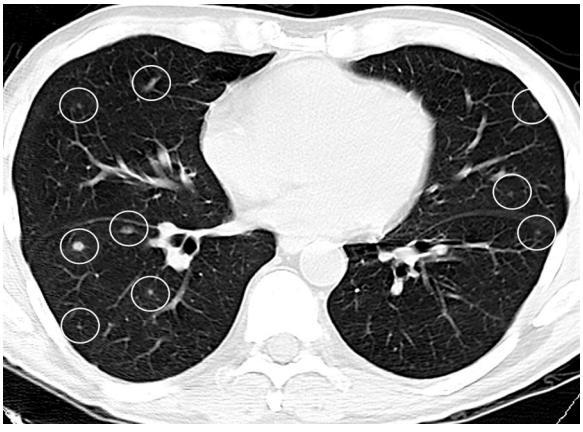
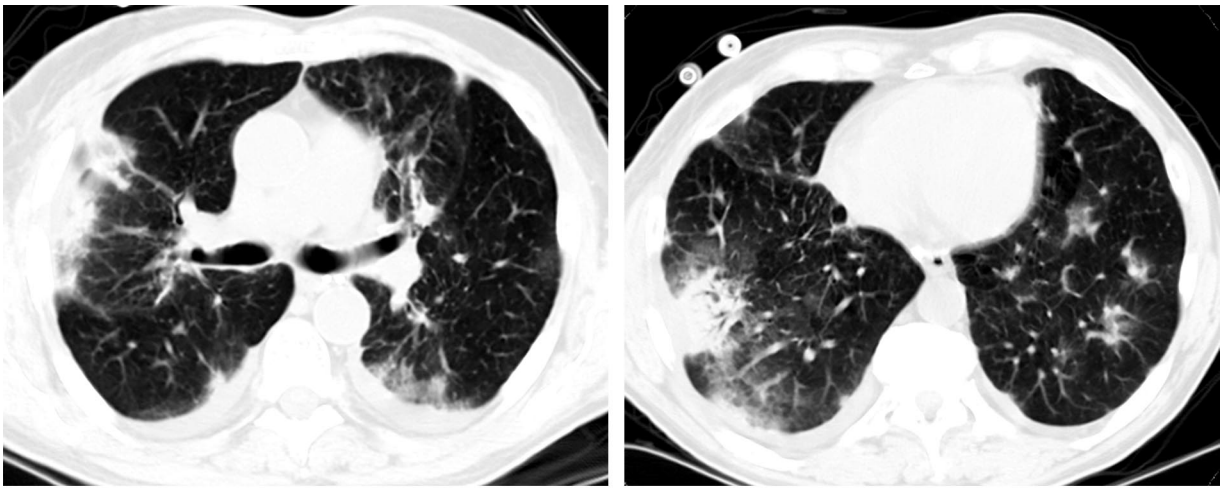


Figure 5. Varicella zoster pneumonia following stem cell transplantation. CT scan shows scattered small nodules (circles).

Late Posttransplantation Period (Beyond Day 100)

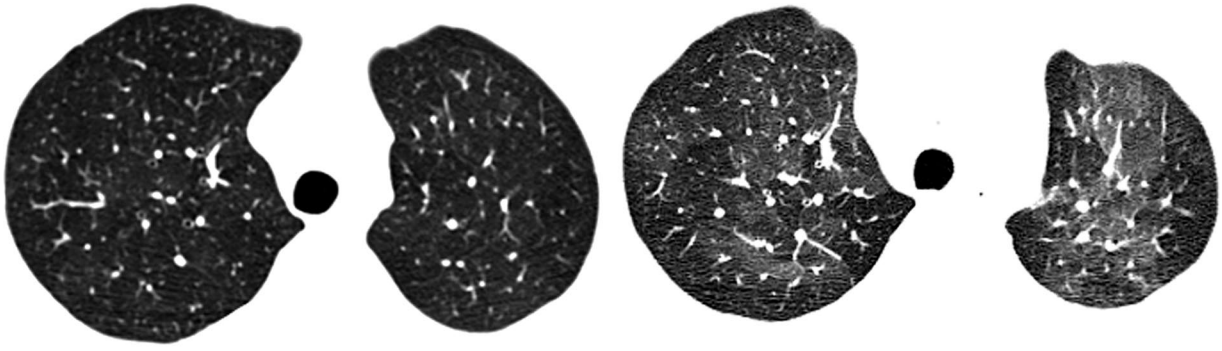
After day 100, and for the remainder of the year following stem cell transplantation, humoral and cell-mediated immunity continue to recover, reducing the pulmonary complications among recipients of autologous and syngeneic transplants. In contrast, allogeneic transplant recipients often develop GVHD, which renders them susceptible to late complications. The end result of GVHD is dysfunctional immunity, whether from a direct inhibition of immune function or from the corticosteroids that are used to treat GVHD. Affected patients are at risk for bacterial, viral, and fungal pneumonias. *Aspergillus* and *Zygomycetes* species (Figs 1, 4) are the most common fungal pathogens, and adenovirus, respiratory syncytial virus, varicella zoster, and parainfluenza are the most common viral pathogens (Fig 5) (11).

Late posttransplantation noninfectious pulmonary complications include cryptogenic organizing pneumonia (also known as bronchiolitis



a. b.

Figure 6. Cryptogenic organizing pneumonia in the late posttransplantation period. CT scans show peripheral consolidation **(a)** and increased centrilobular attenuation **(b)**.



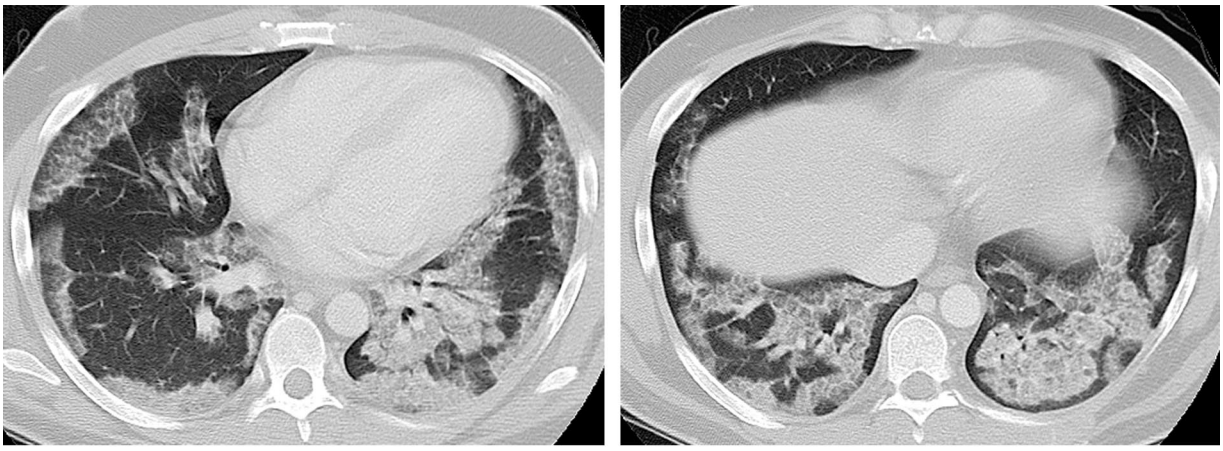
a. b.

Figure 7. Constrictive bronchiolitis in the late posttransplantation period. CT scans obtained during inspiration **(a)** and expiration **(b)** show hypoattenuating secondary lobules during expiration, which represent airtrapping from obstructed bronchioles.

obliterans organizing pneumonia), which has a prevalence of 1%–2% (7). Presenting symptoms include fever, dyspnea, nonproductive cough, and pulmonary function abnormalities. Because cryptogenic organizing pneumonia is found almost exclusively in recipients of allogeneic transplants and is associated with preexisting GVHD, it may, at least in some cases, represent rejection of the lung by the allogeneic transplant (12). On the microscopic level, inflammatory cells and fibrotic tissue form plugs that occlude distal bronchioles, alveolar ducts, and adjacent alveolar spaces. This obstruction leads to accumulation of foamy, lipid-laden macrophages in the alveolar airspaces, forming a postobstructive endogenous lipoid pneumonia (13). The characteristic CT findings are patchy consolidation in a peribronchial or subpleural distribution (Fig 6) (5). Corticosteroids are often an effective treatment, and radiologic findings resolve over 1–3 months (7). Despite treatment, the mortality rate is 21% (7).

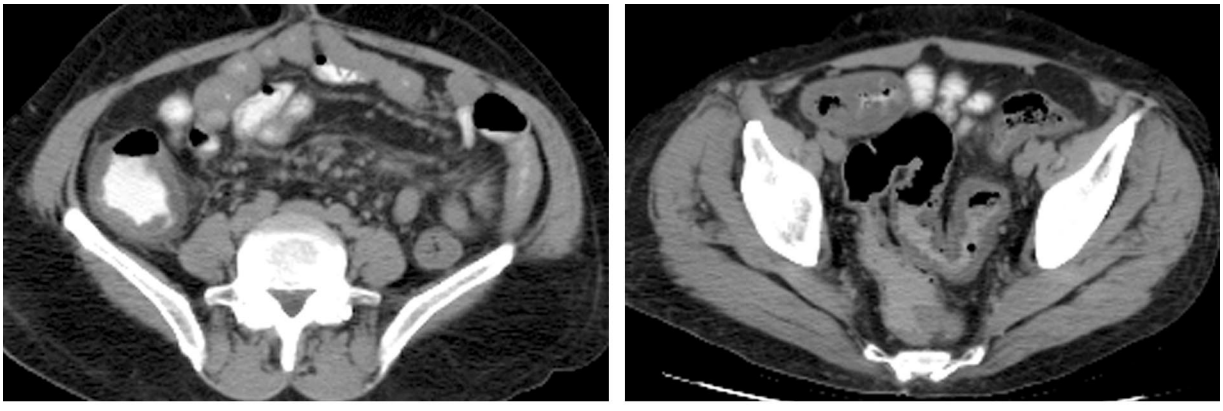
Constrictive bronchiolitis occurs in 10% of allogeneic transplant recipients. Histologic analysis reveals progressive concentric fibrosis that obstructs bronchioles. Patients present with dyspnea, nonproductive cough, and pulmonary function abnormalities; fever is unusual. As the disease progresses, airflow deteriorates and dyspnea worsens. The mortality rate is 61%, and there is no effective treatment (7). Conventional chest radiographs may be normal. CT findings that have been described include bronchial dilatation, airtrapping on expiratory scans, and a mosaic attenuation pattern (Fig 7) (5). The low attenuation of lobules affected by constrictive bronchiolitis reflects hypoxic vasoconstriction that results from impaired ventilation.

Secondary alveolar proteinosis is a rare complication occurring late in the posttransplantation



a. b.

Figure 8. Secondary alveolar proteinosis following stem cell transplantation. CT scans obtained at different levels show geographically distributed ground-glass attenuation and interlobular septal thickening.



a. b.

Figure 9. Pseudomembranous colitis following stem cell transplantation. CT scans show diffuse wall thickening and edema of adjacent fat in the cecum **(a)** and sigmoid colon **(b)**.

phase. Dyspnea is accompanied by imaging findings similar to those in DAH, with ground-glass attenuation of alveolar airspaces and thickening of interlobular septa (Fig 8) (14). In contrast to the rapid clinical course of DAH, secondary alveolar proteinosis tends to have a more indolent onset and course. BAL yielding phospholipids and proteinaceous material helps make this diagnosis.

Abdominal Complications

Common abdominal complications in the peritransplantation period include infections (bacterial, viral, or fungal), hepatic veno-occlusive disease (VOD), GVHD, neutropenic colitis (typhlitis), pneumatosis intestinalis, and hemorrhagic cystitis (15). As discussed in the preceding section, the complications that arise shortly after transplantation often result from the toxicity of the pretransplantation conditioning regimen or the resulting pancytopenia. Complications occurring later in the posttransplantation course are more chronic and usually stem from alloreactivity of the graft to the recipient.

Preengraftment and Early Posttransplantation Periods (Days 0–100)

Bacterial pathogens are the predominant cause of infection during the 1st month following stem cell transplantation (16,17). The use of antimicrobial agents during this period provides effective treatment but can lead to overgrowth of normal bowel flora such as *Clostridium difficile*, resulting in the frequently encountered pseudomembranous colitis (Fig 9).

Fungal infections result from neutropenia and antimicrobial treatment. *Candida* and *Aspergillus* species usually manifest as erosive infections of the gastrointestinal tract, most frequently involving the esophagus. In severe cases, dissemination

can result in microabscesses of the liver, spleen, or kidneys. These microabscesses appear as multiple small, scattered hypoattenuating nodules at CT (Fig 10).

During the early posttransplantation period (days 31–100), CMV is the leading cause of intraabdominal infectious complications. CMV gastroenteritis and hepatitis are major causes of infection-associated mortality following transplantation (16).

Hepatic VOD is a common complication following stem cell transplantation. VOD can occur in any transplant recipient, irrespective of transplant type, stem cell source, or chemotherapeutic conditioning regimen, and most often occurs during the first 20 days following transplantation (18,19). Patients at highest risk for developing VOD are those treated with cyclophosphamide, busulfan, or whole-body irradiation. The proposed mechanism of injury is toxic metabolite–induced endothelial damage of the hepatic sinusoids that leads to obstruction of sinusoidal outflow and hepatic fibrosis (19).

The diagnosis of VOD is established with the clinical criteria of painful hepatomegaly, jaundice, and ascites or unexplained weight gain. However, formulating a diagnosis in an individual patient can be challenging because other conditions may have similar manifestations. Ultrasonographic (US) findings vary depending on the severity of disease. The most common US findings are ascites and marked gallbladder wall thickening (>6–8 mm). In the most severe cases, Doppler US of the hepatic vasculature reveals portal venous pulsatility, hepatofugal portal venous flow, elevated hepatic artery resistive indexes (>0.8), and loss of triphasic hepatic venous outflow (Figs 11, 12). Most patients (70%–85%) recover with conservative diuretic treatment designed to manage fluid balance (19). In more severe cases, defibriotide may be helpful.

Hemorrhagic cystitis following stem cell transplantation has a prevalence of 7%–76% depending on the type of transplant and the conditioning regimen (20). Patients can present with hematuria severe enough to require blood product transfusions. There are two forms of hemorrhagic cystitis, and the two differ with respect to time of onset and underlying pathogenesis. Early-onset hemorrhagic cystitis occurs within a few days following transplantation and results from urothelial injury induced by chemotherapeutic agents, most commonly cyclophosphamide. Later-onset hemorrhagic cystitis occurs 40–80 days following transplantation and is thought to result from reactivation of latent BK virus or CMV, or may be a manifestation of GVHD (17,20). US and CT findings include bladder wall thickening and, occasionally, intravesicular blood or sloughed mucosa (Fig 13) (17). Occasionally, the blood clots and debris will obstruct the bladder outlet and result in hydronephrosis.

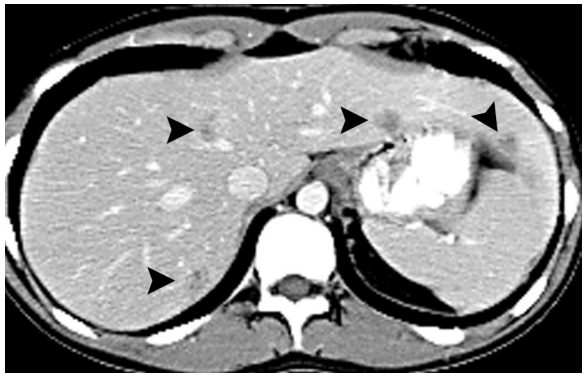
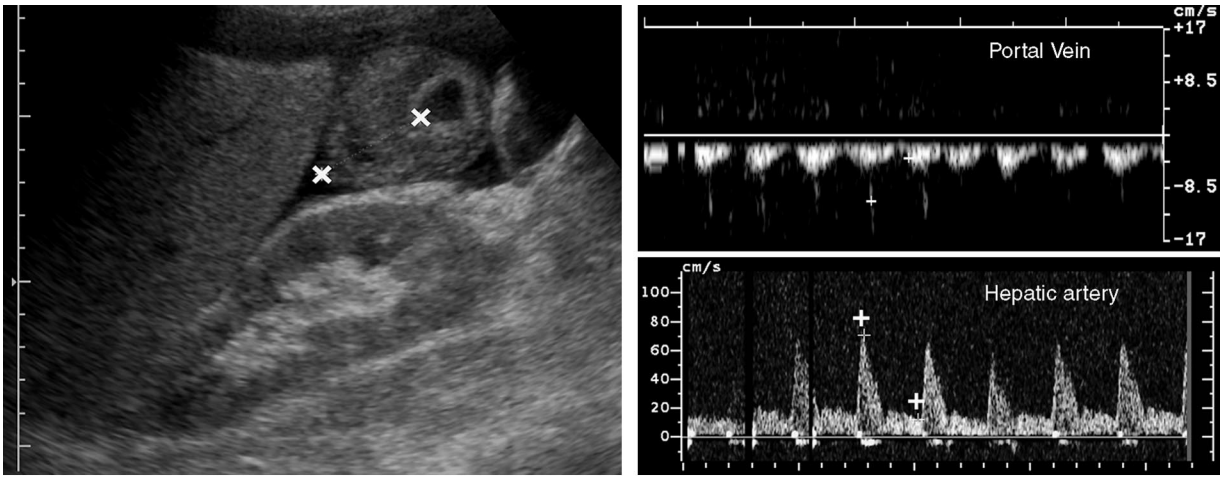


Figure 10. Candidiasis following stem cell transplantation. CT scan shows small hepatic abscesses (arrowheads) resulting from disseminated candidiasis.

GVHD is a significant cause of morbidity in recipients of myeloablative and nonmyeloablative stem cell transplants. GVHD results from reactivity of allogeneic graft (donor) lymphocytes to the recipient. The most commonly affected organs are the skin, liver, and gastrointestinal tract. Moderate to severe GVHD occurs in 30%–50% of patients receiving matched allogeneic transplants (21,22). The degree of histocompatibility between the stem cell donor and recipient affects the risk for development of GVHD. Among patients receiving allogeneic transplants, those with related stem cell donors have a decreased prevalence of GVHD. Recipients of mismatched transplants are at greatest risk.

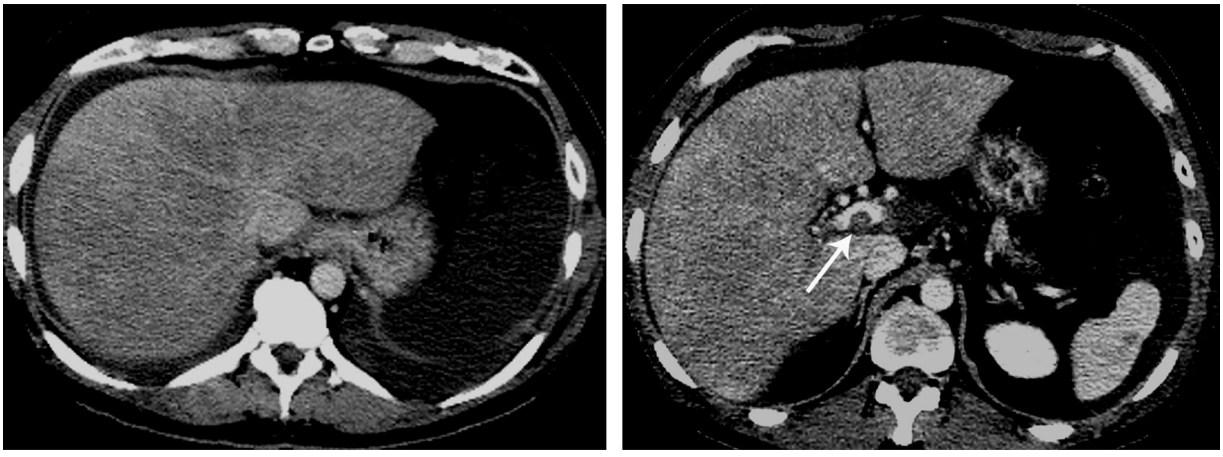
Acute GVHD develops 10–40 days after transplantation and is usually heralded by development of a maculopapular rash and pruritus. Gastrointestinal GVHD develops after the dermatologic disease is clinically evident; rarely does gastrointestinal GVHD occur in isolation. Symptoms and findings depend on the site of involvement. In the esophagus, mucositis and development of webs or strictures result in odynophagia. Gastric GVHD results in nausea and vomiting. Esophageal and gastric GVHD are best demonstrated with contrast fluoroscopic studies, although severe cases may manifest as wall thickening at CT.

The most commonly encountered imaging findings in GVHD are small bowel and colon disease. Patients present with secretory diarrhea, ileus, fever, and abdominal pain. On a microscopic level, GVHD denudes the gastrointestinal mucosa, which is replaced by granulation tissue. Close inspection of the bowel wall at CT may



a. **b.**

Figure 11. Hepatic VOD following hematopoietic stem cell transplantation. **(a)** Right upper quadrant US image demonstrates ascites and marked gallbladder wall thickening (cursors). **(b)** Doppler US images obtained in a more severely affected transplant recipient show pulsatile hepatofugal portal venous flow (top) and reduced diastolic hepatic arterial flow (bottom) indicated by an elevated resistive index (>0.8).



a. **b.**

Figure 12. Severe hepatic VOD following stem cell transplantation. Contrast material–enhanced CT scans demonstrate heterogeneous hepatic enhancement **(a)** and a nonocclusive portal vein thrombus (arrow in **b**) resulting from slow portal venous flow caused by hepatic sinusoidal obstruction.

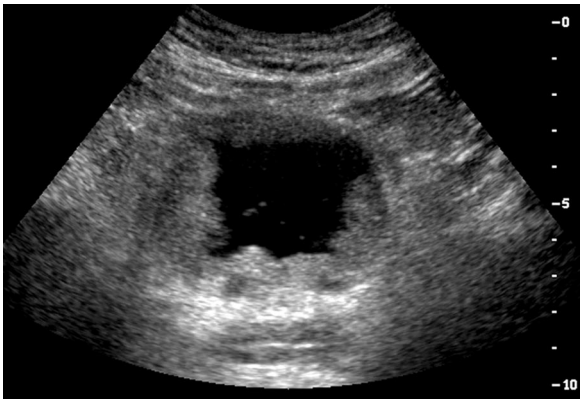
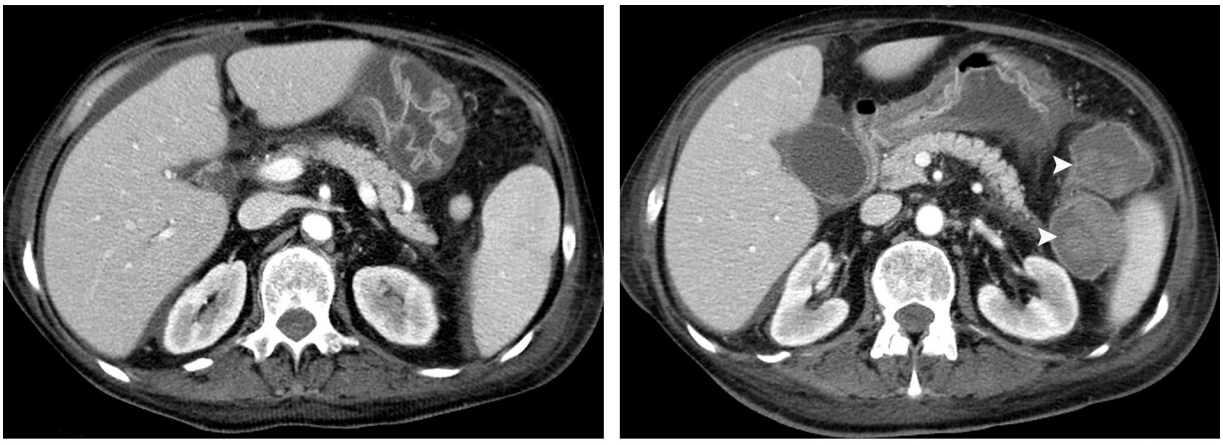


Figure 13. Hemorrhagic cystitis following stem cell transplantation. Transverse US image through the bladder shows echogenic intravesicular debris and diffuse bladder wall thickening.

reveal hyperemic granulation tissue surrounded by lower-attenuation outer bowel wall layers, resulting in the "halo sign" (21). Patients with gastrointestinal GVHD may not tolerate orally administered contrast material well; therefore, CT protocols that make use of oral contrast material will result in poor bowel loop enhancement in these patients. However, the lack of intraluminal enhancement or the use of a negative contrast agent such as water may be advantageous for identifying mucosal hyperemia and the halo sign (21). When adequate intraluminal enhancement is achieved with oral contrast material, prolonged



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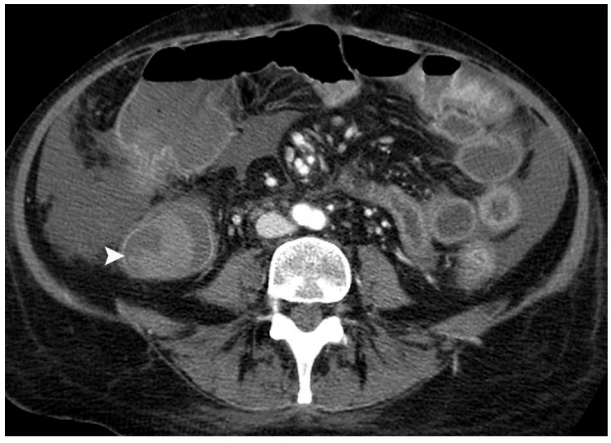

c.

Figure 14. Acute gastrointestinal GVHD. Contrast-enhanced CT scans through the upper **(a)**, middle **(b)**, and lower **(c)** abdomen demonstrate fluid-filled bowel loops, ascites, and mucosal enhancement. Severe mucosal damage has resulted in intraluminal hemorrhage (arrowheads in **b** and **c**).

barium adherence to mucosal ulcers can lead to the incorporation of contrast material into the bowel wall (23,24). Other CT findings in gastrointestinal GVHD include fluid-filled bowel loops, bowel fold thickening, bowel loop separation, and mesenteric stranding (Fig 14) (21,23–25). Similar imaging findings in a recent transplant recipient may also be caused by infection, inflammatory bowel disease, and radiation enteritis; however, the overall extent of bowel involvement tends to be greater in GVHD (23,26). From a management standpoint, differentiation of GVHD from infectious enteritis is essential, since the treatment for GVHD usually involves immunosuppressive drugs such as steroids or methotrexate. For this reason, diagnostic tissue sampling is often necessary to confirm the diagnosis. Finally, it is worth noting that because GVHD damages gut mucosa, impairs mucosal lymphoid intestinal immunity, and is treated with immunosuppression, GVHD patients are susceptible to the development of concomitant gastrointestinal infections.

Hepatic GVHD damages the biliary epithelium and results in hyperbilirubinemia, jaundice, and hepatic dysfunction, findings that overlap with those in hepatic VOD (21,22,27). US findings of gallbladder wall thickening and gallbladder sludge in hepatic GVHD may also be seen in patients with hepatic VOD and calculous or acalculous cholecystitis, which may necessitate liver biopsy for histologic diagnosis (28).

Neutropenic colitis (typhlitis) is a rare complication of stem cell transplantation. Imaging findings include inflammation of the distal small bowel, cecum, and right colon and are usually accompanied by adjacent fat stranding and free intraabdominal fluid (Fig 15) (15,17,23,25,26). Patients present with fever, bloody or watery diarrhea, and right lower quadrant pain. Severe typhlitis can result in gut ischemia and perforation. Treatment consists of bowel rest, antibiotics, and aggressive fluid and electrolyte replacement.

Benign pneumatosis intestinalis is occasionally encountered in stem cell transplant recipients (Fig 16). It is thought to be caused by steroid-induced hypertrophy of Peyer patches that results in mucosal defects through which gas can track. Pneumatosis can also arise in conjunction with typhlitis or CMV enteritis.

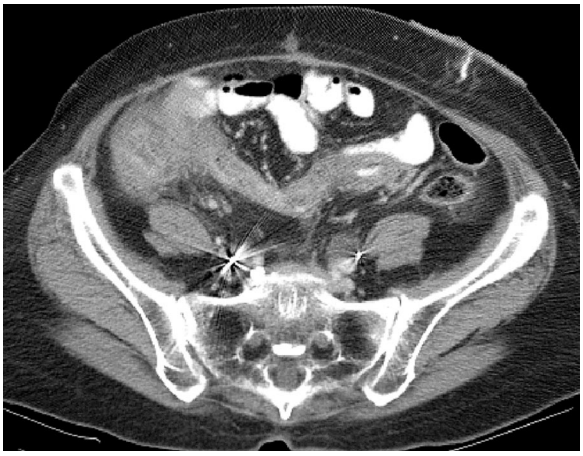

Figure 15. Typhlitis (neutropenic colitis). Contrast-enhanced CT scan demonstrates a shaggy cecum and inflammation of the cecum and terminal ileum.

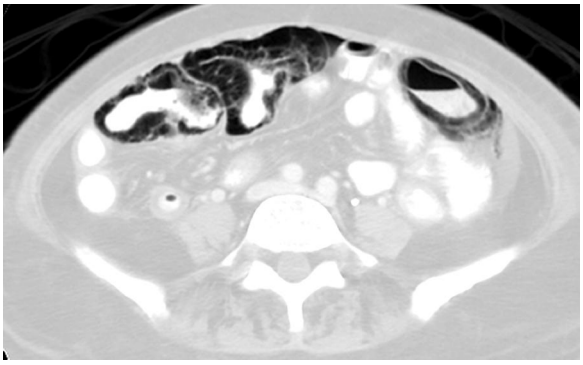

Figure 16. Benign pneumatosis intestinalis following stem cell transplantation. Contrast-enhanced CT scan (lung window) demonstrates pneumatosis intestinalis.

Late Posttransplantation Period (Beyond Day 100)

The most common abdominal complication that arises in the late posttransplantation period is chronic GVHD. Transplant recipients with acute GVHD often develop chronic GVHD, although the acute form of the disease is not a requirement for developing the chronic form. The risk factors for acute and chronic GVHD are similar. Chronic GVHD occurs more commonly in recipients of unrelated allogeneic transplants, having a prevalence of 47%–72% in unrelated matched transplants compared with 27%–50% in sibling-matched transplants. Treatment for chronic GVHD consists of administration of cyclosporine, tacrolimus (FK506), or steroids (27,29). Prolonged steroid therapy can lead to significant long-term morbidity, including osteoporosis, steroid-induced diabetes, opportunistic infections, and avascular necrosis. Skin changes in chronic GVHD include hyperpigmentation and scleroderma-like tightening of the skin. Chronic GVHD can manifest as esophageal strictures or webs. Bowel abnormalities can persist at CT well after GVHD has been treated because of chronic infection and malabsorption resulting from persistent impaired mucosal immunity (Fig 17). Development of small bowel or colonic strictures is uncommon (27). Chronic hepatic GVHD can result in "vanishing bile duct" syndrome, in which extrahepatic ducts develop strictures similar to those seen in primary sclerosing cholangitis (30,31).

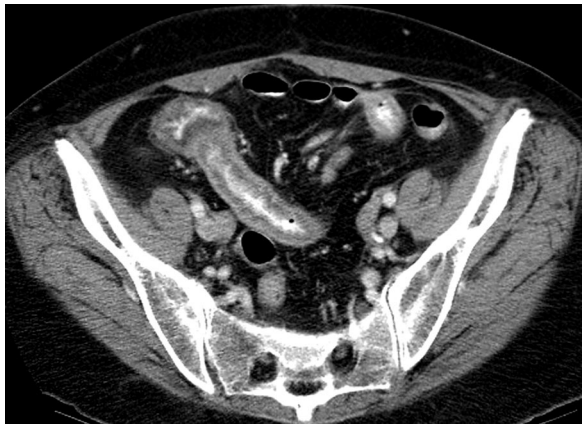

Figure 17. Chronic gastrointestinal GVHD. CT scan shows concentric bowel wall thickening.

Posttransplant lymphoproliferative disorder (PTLD) is rare following stem cell transplantation, with a prevalence of 0.45% and 1.4% in recipients of matched allogeneic grafts and unmatched grafts, respectively. PTLD results from Epstein-Barr virus–induced proliferation of engrafted B lymphocytes that goes unchecked because of pharmacologic T-cell oversuppression (32). In its most severe form, PTLD manifests clinically as a lymphoma with intraabdominal lymphadenopathy, hepatosplenomegaly, and ascites (15–17). On a cellular level, PTLD can range from polyclonal lymphoid hyperplasia to malignant monoclonal lymphoma (15). Determination of the PTLD histologic subtype is clinically relevant because the polyclonal lymphoid hyperplasia form typically responds well when immunosuppression therapy is reduced, whereas the monoclonal lymphoma form tends to require more aggressive therapy for disease control and has a high mortality rate (32,33). Reduced immunosuppression leads to PTLD regression in 23%–65% of patients (32).

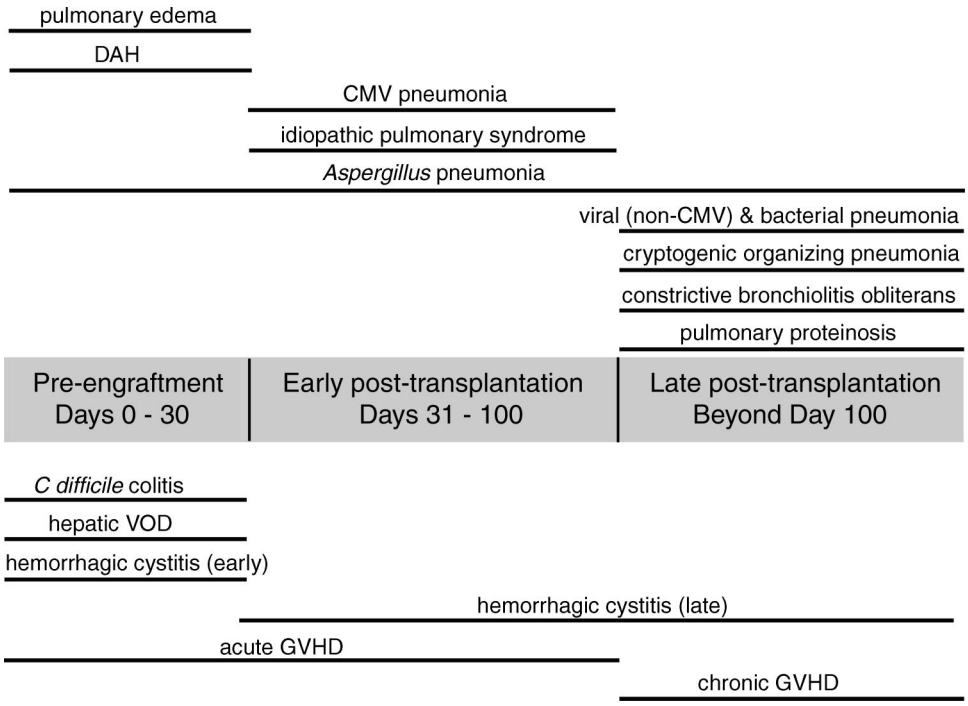

Figure 18. Chart illustrates when specific pulmonary and abdominal complications are most likely to occur following hematopoietic stem cell transplantation.

Conclusions

Patients who undergo the potentially life-saving therapy of hematopoietic stem cell transplantation are at risk for infectious and immune-mediated complications. Timely, accurate diagnosis is essential because these complications ultimately determine the success or failure of the transplantation, and radiology serves as the cornerstone for diagnostic evaluation. Analyzing clinical factors—the type of transplant and the point of time during the posttransplantation course—aids the radiologist in determining which complications are most likely to be encountered (Fig 18). Allogeneic transplant recipients develop GVHD; autologous and syngeneic transplant recipients do not and have fewer chronic or late posttransplantation complications. Nonmyeloablative transplant recipients are less likely to develop opportunistic infections and other complications in the period immediately following transplantation, but are at risk for developing chronic GVHD and other more chronic complications. Combining these clinical factors with characteristic imaging features yields the most specific and accurate differential diagnosis for radiologic findings in stem cell transplant recipients.

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