

bone marrow transplant: infectious complications [created by Paul Young 02/10/07]

### bacterial

Risk factors:  
- The main risk factors for bacterial infections following HSCT are:  
(i) neutropenia,  
(ii) mucositis or skin breakdown,  
(iii) gastrointestinal problems associated with acute GVHD,  
(iv) intravenous catheters

Clinical features:  
- Severe bacterial infections in the ICU usually present as pneumonia, bacteremia, or septic shock.  
- Surveillance blood cultures may be necessary to detect occult blood stream bacterial infections in HSCT recipients, especially those who are receiving systemic corticosteroids

Organisms:  
- Gram-negative pathogens such as Pseudomonas and Klebsiella should be given important consideration during the neutropenic phase.  
- Gram positive organisms such as MRSA, Streptococcus viridans, and enterococci are being increasingly identified as the main cause of severe bacterial infections following HSCT

General  
- Fungal infections are increasingly identified in critically ill HSCT recipients.  
Candida species is the most commonly isolated fungal infection in this patient population.

Epidemiology:  
- Aspergillus is a leading cause of severe fungal infection following HSCT. The prevalence of IPA has been rising and currently ranges between 2% and 26%.

Time Course  
- The onset of IPA has a bimodal distribution, with an early peak during the neutropenic phase and a late phase during the treatment of chronic GVHD

Clinical features  
- The lung is the primary site of Aspergillus infection, leading to severe pneumonia with vascular invasion, necrosis, and hemorrhage. IPA disseminates to other organs, especially the brain, kidney, liver, and skin. In the lungs, the presentation is nonspecific, and fever may be absent. Pleuritic chest pain and hemoptysis, though nonspecific, should alert to the possibility of IPA

Investigation:  
- Two radiologic signs that are highly suggestive, but not pathognomonic, of IPA on HRCT of the chest are the Halo sign and air crescent sign. These signs are demonstrated in 33–60% of patients with proven IPA  
- Sputum cultures and BAL are positive in 45–62% of patients with IPA. Isolation of Aspergillus species from sputum or BAL fluid has a high predictive value of 82% for IPA in this patient population, although these tests are negative in 70% of patients with proven IPA

Treatment:  
- the treatment of choice for patients with IPA is voriconazole, and in the case of breakthrough therapy, caspofungin is an alternative

Prognosis:  
- The mortality rate of IPA is very high (74–92%)

### fungal

#### Invasive pulmonary aspergillus

#### Candida

#### PCP

Epidemiology  
The prevalence of invasive candidal infection is estimated to be 1.3–10%, with mortality reaching 50%

Clinical features  
- Candidemia is the most common serious manifestation of this infection; however, other internal organs may be affected, including hepatic and splenic infections. Primary candidal pneumonia is extremely rare.

Risk factors:  
- The main risk factors for serious candidal infections in HSCT recipients are :  
(i) advanced age,  
(ii) unmatched donor,  
(iii) neutropenia,  
(iv) acute GVHD,  
(v) underlying disease,  
(vi) corticosteroid therapy,  
(vii) duration of candidemia

Treatment  
- The treatment of candidemia and deep infection is primarily fluconazole; however, if there is evidence of endophthalmitis or resistant organisms, then caspofungin is the treatment of choice

Epidemiology:  
- P. carinii Pneumonia. P. carinii pneumonia (PCP) is rarely seen following HSCT due to the effective prophylaxis using trimethoprim-sulfamethoxazole

Clinical Features:  
- The clinical presentation of PCP in HSCT recipients is more severe and fulminant than in HIV patients; however, response to therapy is good if instituted early.

Investigations:  
- BAL is the procedure of choice for the diagnosis of PCP, with positive yield in 90% of cases

### general

- estimated to be the reason for ICU admission in approximately 25%  
- susceptible to a wide range of infections including opportunistic infections such as invasive pulmonary aspergillosis (IPA), CMV, and PCP

- Viral infections are common following HSCT and may occasionally result in critical illness. These viruses include CMV, herpes zoster virus, respiratory syncytial virus, human herpes simplex virus 6, and adenovirus.

- The most serious complication of these viral infections is pneumonitis with acute respiratory failure; however, they may lead to other organ dysfunctions such as hepatitis, encephalitis, and bone marrow suppression.

General:  
- CMV is the most important viral infection following HSCT, and pneumonitis is the most severe manifestation of this infection.

Epidemiology:  
- Recently prevalence of CMV has decreased due to:  
(i) routine prophylaxis against CMV using ganciclovir in high-risk patients in the first 100 days following HSCT.  
(ii) preemptive treatment of patients with subclinical viremia detected by surveillance pp65 antigenemia or polymerase chain reaction assay

Clinical features:  
- CMV pneumonia usually presents a median of 7 wks after transplantation, with nonproductive cough, dyspnea, fever, and hypoxemia that quickly progresses to acute respiratory failure

Risk Factors:  
(i) transplant from a seropositive donor to a seronegative recipient  
(ii) older age,  
(iii) transplantation for hematologic malignancy,  
(iv) total body irradiation,  
(v) antithymocyte globulins,  
(vi) neutropenia,  
(vii) GVHD  
(viii) CMV seroconversion

Treatment:  
- Treatment of CMV pneumonia using ganciclovir and immunoglobulins, especially when started early in the course of the illness, results in significant improvement in survival. However, it is important to note that ganciclovir treatment is associated with significant side effects, including neutropenia, nephrotoxicity, seizures, and retinal detachment. Foscarnet is an alternative that may also lead to acute renal failure.

#### CMV:

#### RSV

#### HSV-6

#### Herpes Zoster

Clinical features  
- begins with URTI symptoms that progress to lower respiratory symptoms.

Investigation:  
- The diagnosis is made by detecting the virus by nasal wash or BAL fluid culture.

Treatment:  
- Uncontrolled trials suggest that the combination of aerosolized ribavirin and intravenous immunoglobulins decrease mortality, especially if started before the onset of acute respiratory failure

Prognosis:  
- Once pneumonia develops, mortality is very high and approaches 80%.

General:  
- Human herpes simplex virus 6 is another severe viral infection following HSCT and may cause pneumonitis, marrow suppression, and encephalitis.

Treatment:  
- Treatment is by ganciclovir or foscarnet

General:  
- Herpes zoster virus infection following HSCT is rare but may lead to a disseminated disease with pneumonia, hepatitis, skin rash, encephalitis, and disseminated intravascular coagulation.

Treatment:  
High-dose acyclovir is the treatment of choice.