Abstract

Pulmonary complications after hematopoietic stem cell transplantation (HSCT) are common and involve both infectious and non-infectious etiologies. Although the infectious complications are the most common, the non-infectious complications are associated with high rates of mortality and can affect patient quality of life for several years after transplantation. These complications can occur early or late after HSCT and in many instances are challenging to treat. An understanding of the uncommon late pulmonary complications after HSCT is necessary for Pulmonologists to facilitate the early diagnosis and treatment of these complications. Improvements in the knowledge of the underlying mechanisms and etiologies for these non-infectious pulmonary complications after HSCT will allow for the identification of biomarkers to diagnose and follow these patients and in the design of targeted therapies for treatment in the future. This review will discuss some of the newer observations regarding pulmonary infectious complications after HSCT but will focus on the non-infectious complications and in particular the rarer forms of these complications.

Keywords: pulmonary complications, hematopoietic stem cell transplantation

Introduction

Hematopoietic stem cell transplantation (HSCT) is an increasingly common procedure undertaken to treat both hematological malignancies and select genetic disorders. At present over 150,000 HSCT are performed each year worldwide [1,2]. Although HSCT are lifesaving in the treatment of hematologic malignancies, the post-transplant course for patients can be challenging due to the complications associated with HSCT, particularly those who underwent allogeneic transplants. A common organ involved in post-HSCT complications is the lung where 30-60% of patients undergoing HSCT develop lung complications [1,3,4]. Lung associated complications can occur from either infectious or non-infectious etiologies with the non-infectious etiologies significantly affecting long-term quality of life, particularly at later stages after transplant. In this paper we will review the pulmonary associated complications after HSCT with a primary focus on the non-infectious complications after HSCT with a few highlights on some of the newer observations regarding infectious complications.
Infectious Complications

The major focus of this review will be on the non-infectious complications after HSCT however several newer observations regarding infectious complications after HSCT will also be discussed. By frequency, as well as the overall number of occurrences, pulmonary infectious complications after HSCT are the most common post-HSCT lung complication and involve infections from all classes of infectious agents including bacterial, viral, fungal, and Mycobacterial species [5-8]. Prior to HSCT, the treatment of patients with hematologic malignancies involves the use of chemotherapeutic agents with these agents commonly causing neutropenia and thereby increasing the risk of pulmonary infectious complications secondary to an immunocompromised state. In addition to bacteria, other infections, particularly fungal and Mycobacterial, can occur prior to transplant with these infections potentially recurring after HSCT. This can also be true for hospitalized acquired bacterial organisms that can colonize these patient’s respiratory tract. Accordingly, a detailed history of pre-transplant infections needs to be obtained to assist in guiding the diagnostic work-up and treatment of infectious complications that arise after transplant. After transplant use of immunosuppressive agents (e.g. corticosteroids, cyclosporine) are known to increase the risk for developing infectious complications [9-11]. One effect of these immunosuppressive agents is on immunoglobulin production by B cells. A delayed recovery in immunoglobulin production increases the risk of developing an infectious complication and may delay its resolution. This effect has been recognized but has not been well studied in this patient population. In those post-HSCT patients with infectious complications at our institution, we routinely monitor total immunoglobulin levels and administer replacement for levels<400 gm/dl.

In the past several years, the spectrum of respiratory viral infections after HSCT has changed with the emergence of new viruses. With advancement of diagnostic testing using polymerase chain reaction (PCR) techniques, newer viral strains are being isolated along with an increased sensitivity for detection of the more established viruses known to cause infection [12]. While infection with influenza, parainfluenza, and respiratory syncytial virus remain the most common and clinically relevant viral pathogens isolated in post-HCT patients, special mention needs to be made of newer viral pathogens including human metapneumovirus (HPV) and human herpes virus 6 (HHV6). Finally, the role of Rhinovirus infection resulting in lower respiratory tract infections with associated morbidity and mortality in this patient population needs to be discussed.

Human metapneumovirus is a recently identified viral pathogen with a prevalence that appears to be increasing [13-16]. This increase is most likely due to the availability to detect the virus with modern PCR viral testing systems and less likely due to an actual increase in the presence of disease. The true incidence of HPV in post-HSCT patients compared to the more common viral infections of influenza or RSV has not been fully described. Overall the incidence has been reported as 2.5-7% in all post-HSCT patients with a higher incidence in those who underwent allogeneic transplant [17-19]. This prevalence in those patients presenting with LRTI, however, may be higher as reported by Egli et al. wherein almost 9% of their patients with LRTI due to a viral infection were found to by HPV positive [20]. Importantly the risk for progression of URTI to a LRTI in those positive for HPV appears to be high with over 20% (21-40%) of patients presenting with a URTI going on to develop a LRTI [17,18,21]. Early reports of HPV in patients with hematologic malignancies or post-HSCT suggested a challenging clinical course with associated high rates of morbidity and mortality (up to 80%) [19,22,23]. In later studies [17,18,20] and in our own observations (Unpublished observations) mortality rates seem much lower (<10%) and are similar to those with Influenza or RSV infection. At present treatment for HPV is supportive with no effective anti-viral agents available and no randomized studies to guide therapy. Although the use of ribavirin and immunoglobulin supplementation have been suggestive as treatment modalities, no conclusive evidence for their effectiveness in treating HPV has been published [20,24].
The role of HHV6 in causing respiratory illness after HSCT remains unclear. HHV6 is a ubiquitous infection with an almost 100% exposure rate by age 17 [25]. The presence of HHV6 in the blood is commonly found after HSCT (up to 46%) and represents re-activation [25,26]. Although, HHV6 can cause life threatening encephalitis in post-HSCT patients, at present there is some controversy regarding if HHV6 is the cause of pneumonitis or if its detection in the lung is only due to an artifact of testing [26-29]. Mariotte et al. reported that respiratory co-pathogens, well established in causing pneumonitis, were present in 86% of patients with pneumonitis and HHV6 found in BAL fluid suggesting that HHV6 may not have been the cause of respiratory failure [28]. In support of this is that HHV6 isolated in BAL fluid may not represent actual viral shedding from the lung parenchyma and therefore active infection [28]. HHV6 can become integrated in the cellular DNA, particularly in monocytes, the predominant cell present in the alveolar space [26,30]. As such, its identification by PCR testing in BAL fluid may only represent monocyte cell lysis and not true viral shedding. To explore this possibility, we examined total BAL fluid and post centrifugation BAL cell free supernatant for HHV6 by PCR. Although total BAL fluid HHV6 levels by PCR were over 1 million, HHV6 levels in the BAL supernatant were under 20,000, thereby suggesting a lack of true HHV6 infection in the alveolar space (Unpublished observations). Further studies need to be performed examining the role of HHV6 in pulmonary infection after HSCT.

A final observation regarding viral infection in this patient group is the potential severity of Rhinovirus infection. Although human rhinovirus is one cause of the common cold with associated symptoms usually restricted to the upper respiratory tract, in immunocompromised patients, including post-HSCT patients, it can also result in lower respiratory tract infections (LRTI) that may lead to respiratory failure with significant hypoxia and even death [31,32]. Typical chest CT findings for post-HSCT patients with Rhinovirus induced LRTI are bilateral patchy ground glass infiltrates. Rhinovirus-induced LRTI is associated with significant mortality in these patients with reported mortality rates of 20-100% [21,31,32]. Typically, treatment for Rhinovirus associated LRTI in post-HSCT patients is supportive, however one caveat is that although not usually confirmed by lung biopsy, GGO on CT imaging of these patients may represent areas of cryptogenic organizing pneumonia (COP). In our experience, these patients require the use of high dose corticosteroids for clinical improvement.

The spectrum of fungal infections has also changed in post-HSCT patients in the past 20 years with emerging fungal species being identified. Infections with Aspergillus species (most commonly Aspergillus fumigatus and niger) were the most frequently isolated fungal species identified in the lung from patients with either hematologic malignancies or after HSCT [7,33]. With the use of prophylactic azoles after transplant, however, the overall incidence of infections due to Aspergillus has decreased and other fungal isolates are being commonly identified [8]. These include Geotrichum, Beauveria Chaetomium, and Paecilomyces [8]. The clinical significance of positive cultures for these newer isolates, particularly in the outpatient setting, is unclear. There remain very few studies describing the clinical presentation and outcomes of post HSCT patients infected with non-Aspergillus fungal species. Published studies have predominately focused on pediatric patients with acute leukemia who are severely ill with significant disease found on CT imaging [34,35]. The role of these infections in less ill patients, especially outpatients, and if anti-fungal treatment is necessary for these isolates, is not clear. Future studies are to needed answer these questions.

**Non-Infectious Complications**

The most worrisome pulmonary complications after HSCT are the ones not related to infection as these non-infectious complications can significantly affect long-term quality of life and survival. The overall prevalence of these complications is fortunately low (<10% of the post-HSCT population) but due to their significant potential long-term
effects, an understanding of their clinical presentation must be appreciated by lung specialists. This understanding will hopefully facilitate an earlier recognition, diagnosis, and treatment of these complications. Non-infectious complications after HSCT can be divided into those occurring in the early (day<30), middle (Days 31-100) or late (Day>100) phases after transplant [36,37]. A common feature of most of the non-infectious pulmonary complications after HSCT is that their etiology remains idiopathic, although their clinical presentation and outcomes have been well described. For several etiologies an infectious cause has been proposed but a direct link to infection has not been proven. In addition, patients with hematologic malignancies receive chemotherapeutic agents prior to, and while undergoing, HSCT. Several of these agents have been implicated in causing lung complications, including organizing pneumonia (COP) and other interstitial pneumonias [38,39]. Accordingly, a detailed history of prior chemotherapeutic exposure needs to be taken at the time of initial evaluation to exclude the possibility of drug toxicity. Similar concerns are present for whole body irradiation used in the conditioning regimen prior to transplant. Below we will describe the most common non-infectious pulmonary complications seen after HSCT with discussion regarding potential causes and a focus on clinical management.

**Diffuse alveolar haemorrhage**

The most common early to middle phase pulmonary complications after HSCT are diffuse alveolar hemorrhage (DAH) and the idiopathic pneumonia syndrome (IPS) [2,6,40,41]. Both are associated with the development of respiratory failure, the high likelihood of needing mechanical ventilation and critical care monitoring, as well as high mortality rates. Etiologies for both entities are not fully understood. Diffuse alveolar hemorrhage has been reported to occur in 5-12% of patients after HSCT although its incidence may be decreasing with recent estimates being at 5% [40,41]. Currently it is thought that DAH may be induced after an infectious insult, be due to drug toxicity associated with the transplant pre-conditioning regimen (chemotherapeutic agents and/or total body irradiation (TBI)) or is associated with the immune reaction present in acute graft versus host disease [2,40-42]. The median time to onset of DAH is 19 days post HSCT [40]. The diagnosis of DAH is made by bronchoscopy with the presence of an increasingly bloodier return upon administration of subsequent aliquots of bronchoalveolar lavage fluid. Alternatively, the presence of over 20% hemosiderin laden macrophages in BAL fluid is also highly suggestive of the diagnosis. The diagnostic methods utilized, particularly that of a progressively bloodier return on BAL fluid, however, has been questioned. The presence of blood or hemosiderin macrophages in BAL fluid from post-HSCT is non-specific as this can also be seen in post-HSCT patients due to thrombocytopenia, defects in coagulation, or pulmonary hypertension. In addition, Agusti et al. found that only 50% of patients with findings of DAH on autopsy had increasingly bloody bronchoalveolar lavage fluid on bronchoscopy [43]. Accordingly, the diagnosis of DAH in this patient group requires careful clinical correlation in addition to the findings from bronchoscopy. The standard treatment for DAH is corticosteroids, with the dosages utilized varying among several studies [1,3]. Patients appear to do better with low dose (<250 mg/day) compared to medium (250-1000 mg/day) or high dose (or >1000 mg/day) corticosteroids. Accordingly, the steroid dosages utilized should be limited to prevent complications due to opportunistic infections, muscle weakness, and the other known complications associated with the use of corticosteroids. Mortality rates remain high in DAH, up to 85% in those admitted to the intensive care unit [3,41,42]. Due to this high rate of mortality, even with corticosteroid treatment, trials have been completed evaluating the effectiveness of adjuvant therapies used alongside corticosteroids. These have explored attempts to regulate coagulation or clot stability using aminocaproic acid, tranxemic acid, and recombinant Factor VIIa (rFVIIa) [1,3,42,44]. Outcomes from these studies have been disappointing, as no differences in mortality were found between the combined therapy groups in comparison to treatment with corticosteroids alone.
**Idiopathic pneumonia syndrome**

The idiopathic pneumonia syndrome (IPS) is another early to mid-phase pulmonary complication after allogeneic HSCT [2,40]. Similar to DAH, IPS is associated with respiratory failure and frequently the need for intensive care monitoring and mechanical ventilation. Mortality rates, like those in DAH, are high [2,40,45]. IPS has been strictly defined as a non-infectious complication and as such requires an invasive work-up to exclude infection and to also rule out other potential causes of respiratory failure including as cardiac dysfunction or volume overload [40]. Recently the description of IPS as a non-infectious complication has been challenged. Seo et al. re-examined banked bronchoalveolar lavage fluid from an older cohort of IPS patients and explored these BAL samples for infection using state of the art technology. In their report they identified infection in over 50% of the patients, for whom infection was previously excluded at the time of initial diagnosis [6]. The majority of these infections were viruses, including human herpes virus 6 (HHV6), rhinovirus, and cytomegalovirus. Overall this study suggests that IPS may in fact be an infectious mediated complication with earlier attempts at identifying infections impeded by the techniques used in their detection. One limitation of the study, however, concerns the potential role of some of these viruses, particularly HHV6, in inducing lower respiratory tract disease, and in particular, IPS. These findings need to be confirmed in additional data sets using banked BAL fluid from other IPS patients.

Risk factors for the development of IPS include an indication for HSCT of acute myelogenous leukemia or myelodysplastic syndrome, preconditioning regimen using high dose cyclophosphamide or total body irradiation, older age, and acute graft versus host disease [40,46-48]. The pathogenesis for IPS is currently unknown. Based on animal models it appears to be driven by host monocyte and donor T lymphocyte infiltration into the lung interstitium and alveolar space inducing alveolar epithelial cell apoptosis, an elevation in inflammatory cytokines, and an increase in endothelial permeability partially due to endothelial cell apoptosis [49,50]. In addition to the influx of inflammatory cells and direct inflammatory cell tissue injury, several inflammatory mediators are also thought to play a role in IPS, including circulating tumor necrosis alpha (TNF-α) and reactive oxygen intermediates [49-51]. Evidence for the role of TNF-α in IPS is supported by its involvement in major histocompatibility complex expression, cell mediated cytotoxicity, and endothelial cell apoptosis, as well as the effectiveness of its blockade in reducing lung inflammation in animal models of IPS [40,51,52]. The mainstay of treatment for IPS, like DAH, has been corticosteroids. Due to the suspected mechanistic implications of elevated TNF-α levels in the pathophysiology of IPS, recent studies have also examined the effectiveness of TNF-α blockade using Etanercept [2,53]. Use of Etanercept in IPS, however, has been disappointing as the largest randomized study examining its effect was closed early due to a lack of significant benefit [53]. Future studies will need to focus on improving the understanding of the underlying pathophysiology for IPS, as well as DAH, in post-HSCT patients, with results from these studies used to design targeted therapies for treatment. A limitation for these future studies is the lack of biologic lung samples to explore mechanisms and biomarkers, as only a limited number of these patients undergo surgical lung biopsy.

**Bronchiolitis obliterans syndrome**

The most feared non-infectious pulmonary complication after HSCT is cGVHD of the lung, also known as the bronchiolitis obliterans syndrome (BOS). This is a late stage complication after allogeneic HSCT and occurs in 5-10% of transplant recipients [54-57]. As currently defined, BOS occurs in the setting of established non-pulmonary cGVHD, although it has been suggested to be the initial manifestation of cGVHD in a small number of patients [56]. The diagnosis of BOS is established by the detection of airflow obstruction on either pulmonary function testing (PFT), showing a decrease in the ratio of the forced expiratory volume in one second (FEV-1) over the forced vital capacity (FVC)/(FEV-1/FVC) or an increase in the residual volume, or by the presence of air trapping on expiratory CT images of the lung as shown by the presence of lung mosaicism [54,55]. In our experience the decrease in the FEV-1
and the FEV-1/FVC ratio in patients with post-HSCT BOS is profound (average of 40-60% reduction compared to pre-transplant PFT’s) with a lesser decrease suggesting the possibility of another etiology causing the decrease in airflows or the presence of air trapping on CT imaging. Other etiologies that need to be excluded include post-infectious bronchiolitis (common after viral infections), exposure to environmental toxins, or new onset asthma or reactive airway disease. Cases of new onset allergies and asthma have been described in post-HSCT patients, so the development of atopy needs to be evaluated [58]. Such cases of new onset atopy after HSCT have been thought to be due to donor derived reactive T cells. Accordingly, obtaining a donor history for a past diagnosis of allergies or asthma is important to exclude this possibility.

With regards to chest CT imaging in post-HSCT BOS, separate from the presence of air trapping, there are no other chest CT findings diagnostic for BOS. In those patients with abnormal CT findings (separate from mosaicism due to air trapping) or a less than 40% decline in FEV-1, it is our opinion that additional investigation and testing is necessary before confirming a diagnosis of BOS. Findings on chest CT of ground glass opacities or nodular infiltrates are suggestive of a potential infectious or other non-infectious inflammatory (i.e. cryptogenic organizing pneumonia) condition as the cause for the observed airway obstruction. Further diagnostic testing by bronchoscopy or lung biopsy is necessary to exclude these possibilities, particularly viral infections. Recently exhaled nitric oxide (FeNO) levels were suggested to be useful in the diagnosis of BOS in post-HSCT patients [37]. In contrast to patients with asthma or patients with BOS after lung transplantation, wherein FeNO levels are high [59,60], levels in post-HSCT BOS were reportedly to be low, with levels of <15 ppm thought to be diagnostic of post-HSCT BOS [37]. This was a small study with only FeNO levels provided at the time of diagnosis. Accordingly, additional confirmatory studies, and in particular the use of serial FeNO levels to determine disease progression, are necessary prior to using FeNO as a diagnostic tool in post-HSCT BOS.

Unlike other forms of cGvHD in HSCT patients, BOS is difficult to treat with patients’ symptoms and decline in airflow changing little over time based on the experience at our institution. The lack of an animal model that accurately mimics post-HSCT BOS limits advancement in the understanding of the underlying pathophysiology of post-HSCT BOS and therefore the discovery of new effective agents to be used in its treatment. To date there have been no randomized controlled studies showing a survival benefit with any treatment modality in post-HSCT BOS patients. At present the mainstay of treatment for BOS has been systemic corticosteroids, although other immunosuppressives have been tried including sirolimus, rituximab, and TNF-α blockade [54,61,62]. To avoid the systemic toxicity of immunosuppressives, several studies have examined the use of novel agents including the macrolide antibiotic azithromycin, the prostaglandin inhibitor montelukast, and inhaled corticosteroids [63-65]. Each individually has shown a benefit in the treatment of BOS with a recent small non-randomized retrospective study showing benefit using all three agents in combination [63,64]. An ongoing multicenter randomized control is underway to confirm results from these smaller trials regarding the effectiveness of combined therapy in this patient population. In addition to the use of immunosuppressive, extracorporeal photophoresis has been tried in post-HSCT BOS [66]. Results from these trials have shown that lung function stabilizes with this treatment but does not significantly improve. Overall, outcomes in patients with post-HSCT associated BOS appear to be better than those of post-lung transplant associated BOS with the latter having a progressive decline in FEV-1 with a median survival of 3 years after the initial diagnosis of BOS [60]. This suggests that the inciting event or underlying pathophysiology of BOS in these two patient groups may be distinctly different. Those patients that do progress, even with the treatment using corticosteroids or combination therapy, should be evaluated for lung transplantation, which has been shown to be effective in this group [4].
Serositis

A recently described but poorly understood late complication after HSCT is the development of serositis. Although pleural and pericardial effusions are commonly observed in the early phase after HSCT these resolve over a short period of time [67 and unpublished observations]. Estimates are that post-HSCT serositis occurs in <5% of all patients after allogeneic HSCT. The true incidence is not fully known as there have only been a few large case series published describing this complication. In our review of post-HSCT serositis at our institution, it appears that the overall incidence is around 4% (Unpublished observations) with the review by Modi et al. confirming these observations by reporting an incidence of less than 2% [67]. Most cases of serositis occur in the setting of established pre-existing cGvHD, although rarely serositis can be the initial presentation of cGvHD. Unlike other non-infectious pulmonary complications after HSCT, a significant lag time can occur between the initial onset of pleural or pericardial effusions and the development of symptomatic disease (up to over 200 days) [67 and unpublished observations]. Clinical presentation includes the development of acute or sub-acute shortness of breath, chest pain, abdominal distention, dizziness, or syncope. These symptoms occur due to the accumulation of fluid in the peritoneal, pleural, or pericardial spaces and the resulting organ dysfunction. Most concerning are patients presenting with the rapid accumulation of fluid in the pericardial space leading to tamponade. These patients require immediate evacuation of the fluid for stabilization. In contrast, pleural effusions, based on our experience, develop slowly over several months prior to the development of symptoms and seldom require emergent evacuation (Unpublished observations).

The underlying pathophysiology of post-HSCT induced serositis is poorly understood with only limited clinical markers available that are suggestive of an increased risk for developing serositis. In addition, currently there are no fluid biomarkers available to diagnose or risk stratify patients with post-HSCT serositis or to use to target therapy or predict outcomes. The rarity of this complication limits investigation into the pathogenesis and mechanism of disease. One study examining biomarkers has suggested that an increase in circulating monocytes or an acute decrease in serum albumin may identify patients at risk [68]. In addition, some reports have suggested that serositis may be induced after a viral respiratory infection [67] and we have also seen this association in a small number of our patients. Finally, no published reports have characterized the pleural or pericardial fluid in these patients. Such analysis may point to potential mechanisms underlying the pathogenesis of this complication.

In regard to treatment, there have been no clinical trials describing the management of post-HSCT associated serositis. At present the mainstay of treatment is drainage of symptomatic effusions with augmentation in immunosuppression using corticosteroids, tacrolimus and/or sirolimus [67,68]. Other modalities tried have included extracorporeal photophoresis, etanercept, and rituximab [67]. Although augmentation in immunosuppression was reported to be successful in over 60% of the patients as reported by Modi et al., it has been effective in only about a quarter of the patients at our institution [67 and Unpublished observation]. Treatment in those unresponsive to augmentation in immunosuppression alone involves repeated thoracentesis for symptom control. Further research is necessary to determine the etiology, mechanisms, and treatment for this uncommon but significant post-HSCT pulmonary complication.

Pulmonary eosinophilia

We [36] and others [69-72] have identified post-HSCT patients who present with cough, SOB, and acute hypoxia. Chest imaging by CT is abnormal showing GGO which were upper lobe predominant in our series. This disease occurs mainly in those who have undergone allogeneic transplant and have been diagnosed with cGvHD [36,69,70,72], however, there has been one report of eosinophilic pneumonia occurring after autologous transplant.
Overall it appears that eosinophilic pneumonia is a late phase complication after HSCT with only two patients described who were diagnosed with eosinophilic pneumonia prior to day 100 after transplant [72]. Establishment of the diagnosis of pulmonary eosinophilia resides in results from bronchoscopy showing an elevated number of eosinophils in the absence of infection. Although the level of eosinophilia does not always reach the strict criteria of 25% used to diagnose acute eosinophilic pneumonia (AEP) in non-HSCT patients, all of the patients in our series had BAL fluid eosinophils levels of at least 10% or higher [36]. The lack of the cut-off value of 25% eosinophilia in BAL fluid in our series was thought to be due to the current use of corticosteroids in most of our patients at the time of bronchoscopy [36]. In addition to an elevation in the number of eosinophils in the lung, most of the patients described have also had peripheral eosinophilia, including those in our case series [36,70-72].

The pathogenesis of eosinophilic pneumonia after HSCT is currently unknown. The presence of peripheral eosinophilia has been suggested to correlate with the presence of acute GVHD after HSCT and may be a clinical marker of severity of aGVHD [72-74]. In addition, tissue infiltration of eosinophils in the liver or lung of solid organ transplant recipients has been indicative of transplant rejection [75,76]. Taken together, pulmonary eosinophilia in post-HSCT patients may be just a marker of cGVHD of the lung. However, the lack of BOS, the sin qua non of pulmonary cGVHD, either prior to or subsequent to the diagnosis of eosinophilic pneumonia, would suggest that it represents a separate disease. In the several years of follow-up in our patient group, no patient developed BOS [36]. Treatment for post-HSCT associated eosinophilic pneumonia is corticosteroids, with patients typically responding quickly after their initiation. The dosages utilized are typically high (500-1000 mg/day), with such high dosages used to treat the acute respiratory failure common in these patients. Lower dosages (1 mg/kg per day) have also been used with a good clinical response [36,69,72]. Unique to eosinophilic pneumonia after HSCT compared to those with AEP is that several patients have been described that relapsed upon steroid taper [36]. These patients have required a longer treatment course with corticosteroids, including two in our series that required lifelong daily steroids [36]. Another interesting observation is that in our series most patients had persistence of the upper lobe GGO abnormalities even though symptoms had resolved [36].

References


