Pulmonary Complications in Adult Blood and Marrow Transplant Recipients*

Autopsy Findings

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Study objective: To describe the pulmonary findings at autopsy of blood and bone marrow transplant (BMT) recipients.

Design: Retrospective.

Setting: An academic medical center.

Patients: Seventy-one deceased adult BMT recipients.

Interventions: None.

Measurements: Antemortem and postmortem pulmonary findings.

Results: The transplants were allogeneic in 39 patients (55%), with a peripheral stem cell source in 43 patients (61%). Death occurred at a median of 1.30 months after transplant. Ninety-six pulmonary complications were noted in 63 patients (89%): 27 infectious (bacterial bronchopneumonia, n = 11; pulmonary aspergillosis, n = 11; cytomegalovirus pneumonia, n = 2; and Candida bronchopneumonia, n = 1) and 69 noninfectious (diffuse alveolar damage, n = 35; diffuse alveolar hemorrhage [DAH], n = 10; amyloidosis, n = 9; pulmonary embolism, n = 5; lymphoma/leukemia, n = 4; bronchiolitis obliterans, n = 2; bronchiolitis obliterans organizing pneumonia, n = 1; pulmonary alveolar proteinosis, n = 1; aspiration pneumonia, n = 1; and acute and organizing pneumonia, n = 1). Twenty-seven of the 96 complications (28%) were diagnosed antemortem. Infectious complications were more likely to be diagnosed antemortem compared to noninfectious complications (48% vs 20%, p = 0.006). Six of the 13 patients with bronchopneumonia (46%), 5 of the 11 patients with pulmonary aspergillosis (45%), and 7 of the 8 patients with DAH (88%) at autopsy were not receiving treatment for these conditions at the time of death. Ten patients being treated for suspected pulmonary aspergillosis, 7 patients treated for suspected pulmonary cytomegalovirus infection, 22 patients treated for suspected bacterial pneumonia, 2 patients treated for suspected Pneumocystis carinii pneumonia, and 12 patients treated for DAH at the time of death had no evidence of these conditions at autopsy. The most common immediate cause of death was respiratory failure (n = 37, 52%).

Conclusions: Pulmonary complications, the majority not diagnosed antemortem, are the most common cause of death in BMT recipients. As the result of underdiagnosis, BMT recipients may not receive appropriate therapy for potentially treatable pulmonary complications.

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Key words: aspergillosis; autopsy; bone marrow transplantation; bronchiolitis obliterans; bronchiolitis obliterans organizing pneumonia; cause of death; pneumonia

Abbreviations: BMT = blood and bone marrow transplant; BO = bronchiolitis obliterans; BOOP = bronchiolitis obliterans organizing pneumonia; DAH = diffuse alveolar hemorrhage; IQR = interquartile range; FCP = Pneumocystis carinii pneumonia

Tens of thousands of patients receive blood and bone marrow transplants (BMTs) annually to treat otherwise potentially fatal diseases.1 Earlier publications2,3 have suggested that pulmonary complications occur in approximately 30 to 60% of BMT recipients. Because of the absence of graft-vs-host disease and the infrequent use of immunosuppressive medications and radiation therapy, pulmonary complications are less common in autologous compared to allogeneic BMT recipients.4–6 The spectrum of pulmonary complications in BMT recipients might be expected to change with advances in supportive care, increased application of BMT for older patients, widespread application of prophylactic antibiotics, and newer antiviral and antifungal agents.1,7,8
Both infectious and noninfectious findings are frequently found at autopsy of BMT recipients.9–12 In a 1995 report,13 one or more infectious complications were identified in the majority of 56 BMT recipients at autopsy, and most of the nonbacterial infections were not identified antemortem. Despite the availability of effective prophylaxis, Pneumocystis carinii pneumonia (PCP) has been identified in approximately 18% of immunocompromised patients without AIDS, including BMT recipients.14,15 Noninfectious pulmonary complications also develop commonly in BMT recipients.16 In an autopsy study12 of umbilical cord blood transplant recipients, diffuse alveolar damage (DAD) was found in approximately one half of the patients. Idiopathic pulmonary syndrome, bronchiolitis obliterans (BO), and pulmonary veno-occlusive disease are among the noninfectious pulmonary complications that have been diagnosed at autopsy in a significant number of BMT recipients.17–19

While a significant concordance was noted between premortem clinical diagnosis and postmortem findings in a study9 of 28 critically ill BMT recipients, minimal data are available on the correlation of autopsy findings and antemortem clinical suspicion, diagnosis, and treatment of pulmonary complications. Most of the previous studies9,11–13,19–21 of autopsy in BMT recipients were not focused on pulmonary complications, or included predominantly allogeneic recipients for whom bone marrow was the stem cell source. The purpose of this study was to describe the pulmonary findings at autopsy of BMT recipients during a recent time period, in a population including both autologous recipients and a peripheral stem cell source.

**Materials and Methods**

In this retrospective, cohort study, we reviewed the medical and autopsy records of BMT recipients who died at Mayo Medical Center, Rochester, MN. Mayo Medical Center is a tertiary care medical center with two hospitals, Rochester Methodist and Saint Marys, with a total of approximately 1,900 beds. Patients who received autologous or allogeneic BMT and underwent a postmortem autopsy from August 1996 through May 2003 were included in the study. We excluded from the study patients <18 years old and those who did not authorize their medical records to be reviewed for research. Patients who died at other institutions were also excluded.

Data collected included demographics, reason for BMT, date of transplant, type of BMT (autologous or allogeneic), source of stem cell (bone marrow or peripheral blood), conditioning regimen, clinical premortem diagnoses, postmortem pulmonary findings, and causes of death. We also noted whether the pulmonary findings at autopsy were diagnosed antemortem. Neutropenia was defined as absolute neutrophil count <0.5 × 10^9/L. Antemortem clinical diagnoses were determined from physician notes, hospital discharge summaries, laboratory studies, radiologic examinations, and pathology reports. For the antemortem clinical diagnosis of the pulmonary complications, we used the objective criteria outlined in their definitions below. Bacterial bronchopneumonia was defined by the presence of new or worsening pulmonary infiltrate on chest radiograph and the growth of a bacterial pathogen from respiratory specimen associated with two of the following: temperature >38.5°C or <35°C, leukocyte count >10,000/μL or <3,000/μL, purulent sputum, or change in the character of the sputum. PCP was diagnosed by the identification of P carinii in stain or direct fluorescent antibody. Candida pneumonia was defined by the histopathologic or cytopathologic demonstration of the fungus in lung tissue. Aspergillus pneumonia was defined by the histopathologic demonstration of aspergillus or the isolation of aspergillus in respiratory specimen in the presence of a compatible clinical and radiographic pattern. Cytomegalovirus was considered to be pathogenic if it was isolated by cell cultures from a respiratory specimen or when inclusion bodies were present on histopathologic evaluation. Diffuse alveolar hemorrhage (DAH) was defined by the presence of a widespread alveolar injury (as evidenced by multilobar infiltrates, symptoms and signs of pneumonia, abnormal pulmonary physiology with increased alveolar-to-arterial oxygen gradient); cytopathologic, pathologic, microbiologic, or virologic studies excluding infection compatible with the diagnosis; and BAL fluid returns becoming progressively bloodier or showing iron-laden macrophages ≥20%.20 BO was defined by the presence of obstructive airways with suspected bronchiolitis due to chronic graft-vs-host disease or the demonstration of new-onset airflow obstruction in a BMT recipient without pulmonary symptoms.18 Bronchiolitis is suspected by the presence of cough, wheezing, dyspnea, or hypoxemia with normal chest radiograph findings. Acute lung injury and ARDS were defined by the criteria of the North American/European consensus conference.21 We used the 1993 National Heart Lung and Blood Institute workshop summary criteria to define idiopathic pulmonary syndrome.24

All autopsies were performed by the Mayo Clinic Department of Pathology. Causes of death were obtained from the death certificates filed by the pathologist and based on autopsy findings. All reports and histologic slides were reviewed. Histologic diagnostic categories included infection as determined by the presence of acute bronchopneumonia, invasive fungal infection, and DAD with identification of organism. DAH was defined by the presence of alveolar hemorrhage involving multiple lobes in the absence of another etiology. If the alveolar hemorrhage did not involve multiple lobes, it was not considered diffuse. Bronchiolitis obliterans organizing pneumonia (BOOP) was diagnosed by the presence of patchy intraluminal fibrosis, consisting of polyoid plugs of immature fibroblasts, resembling granulation tissue embedded in a myxoid matrix.18 BO was diagnosed when bronchiolar lumen narrowing by concentric fibrous tissue was present. We defined DAD as a pattern of acute lung injury characterized by the presence of a widespread alveolar injury...
by an exudative phase with cell necrosis, edema, and hyaline membrane formation and a proliferative phase with organizing interstitial fibrosis. 25, 26

From the clinical notes, we noted whether patients were being treated antemortem for suspected or documented pulmonary complications. We used the mean and SD to describe normally distributed continuous data, median and interquartile range (IQR) to describe nonnormally distributed continuous data, and percentages to describe categorical data. When comparing different groups, we used χ² test and Fisher Exact Test for categorical variables, Mann-Whitney U test for nonnormally distributed continuous variables, and Student t test for normally distributed continuous variables; p < 0.05 was considered significant.

**Results**

During the 9-year study period, 1,470 patients underwent BMT at our institution; 636 of these patients died. There were no statistically significant differences in gender and age between patients with and without autopsy. The autopsy rate was 28.2% in allogeneic BMT recipients, compared to 8.9% in autologous BMT recipients (p < 0.001). Patients with autopsy died at a median of 2.60 months (IQR, 1.10 to 9.25 months) after transplantation, compared to 8.80 months (IQR, 4.13 to 18.23 months) of the patients who did not have autopsy (p < 0.001). Autopsy was performed in 30.7% of patients who had bone marrow grafts, compared to 10.4% of those with peripheral blood stem cell grafts and 21.4% of those with both bone marrow and peripheral blood stem cell grafts (p < 0.001).

Excluding patients who died at other institutions, patients < 18 years old, and those who did not authorize their medical records to be reviewed for research, 71 BMT recipients who underwent autopsy at our medical center were identified. All patients except one were white (mean age, 48.4 years; SD, 12.5 years). Thirty-three of the patients (46%) had a history of smoking cigarettes, but only 2 patients (13%) were smoking at the time of evaluation for transplantation.

The indications for BMT were hematologic disorders in all 71 patients. The transplants were autologous in 32 patients (45%), and the source of stem cells was peripheral blood in 43 patients (61%). Death occurred at a median of 1.30 months (IQR, 0.78 to 6.21 months) after transplant. The immediate causes of death were respiratory in 37 patients (52%), sepsis in 10 patients (14%), cardiac in 9 patients (13%), and bleeding, liver failure, worsening of underlying disease, multiple organ failure, and neurologic failure each in 3 patients (4%). Among the 37 patients with a respiratory-related cause of death, the immediate cause of death was attributed to DAD in 22 patients (infection, n = 8; aspiration, n = 1; and unknown cause, n = 13), pneumonia in 6 patients, aspergillosis in 4 patients, pulmonary embolism in 2 patients, hemorrhagic pulmonary edema in 1 patient, airway hemorrhage in 1 patient, and BO in 1 patient. No mortality was attributed to pulmonary amyloidosis or DAH.

Pulmonary complications were noted at autopsy in 63 of the 71 patients (89%). The characteristics of the 63 patients with pulmonary complications are listed in Table 1. A total of 96 pulmonary complications were identified at the time of autopsy, of which 69 complications (72%) had not been diagnosed antemortem (Table 2). Most of the pulmonary complications affected both allogeneic and autologous BMT recipients (Table 3). The timing of death following transplant for each of the pulmonary complications is listed in Table 2. Noninfectious etiologies accounted for 69 of the 96 autopsy findings (72%) [Table 2]. Four of the five patients with pulmonary embolism also had deep venous thrombosis at autopsy. One patient had deep venous thrombosis without pulmonary embolism. The most common infectious and noninfectious complications were bacterial bronchopneumonia and DAD, respectively (Table 2). Thirteen of the 27 infectious complications at autopsy (45%) had been diagnosed antemortem, compared to 14 of the 69 noninfectious complications (20%; p = 0.006) [Table 2]. Twenty-one of the 33 patients with a smoking history (64%)...
had DAD at autopsy, compared to 14 of the 38 without a smoking history (37%; p = 0.024). Twenty-three of the 35 patients with DAD (66%) received a conditioning regimen containing total body irradiation, compared to 14 of the 36 patients without DAD (39%; p = 0.024). Seven of the 25 patients with neutropenia (28%) had DAD at autopsy, compared to 28 of the 46 patients without neutropenia (61%; p < 0.008). Twelve of the 35 patients with DAD at autopsy met the clinical criteria for acute lung injury or ARDS antemortem. The most common pulmonary findings associated with DAD at autopsy were of infectious etiology, found in 10 of 35 patients (29%) [Table 4]. No associated finding was identified in 19 of the 35 patients with DAD (54%) and in the 1 patient with acute and organizing pneumonia. These 20 patients can be considered as having idiopathic pneumonia syndrome.

There were no statistically significant differences in smoking history and neutropenia between patients with and without alveolar hemorrhage. Of the 11 patients with alveolar hemorrhage, 10 patients (91%) had multilobar involvement. Among the 10 patients with multilobar alveolar hemorrhage, no other pulmonary condition was found in 8 patients (80%) at autopsy, and bronchopneumonia and pulmonary aspergillosis were identified in the other 2 patients. The eight patients with multilobar alveolar hemorrhage with no infectious etiology are considered as having DAH.

There were no statistically significant differences in smoking history and neutropenia between patients with and without pulmonary aspergillosis. Ten of the 16 patients (63%) who were being treated for suspected pulmonary aspergillosis at the time of death did not have any evidence of pulmonary aspergillosis at autopsy. Five of the 11 patients (45%) with pulmonary aspergillosis at autopsy were not being treated for it at the time of death.

**Table 2—Pulmonary Complications Identified at Autopsy of 71 BMT Recipients*  

<table>
<thead>
<tr>
<th>Pulmonary Complications</th>
<th>Autopsy</th>
<th>Antemortem</th>
<th>Months After BMT, Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial bronchopneumonia</td>
<td>13 (18)</td>
<td>8</td>
<td>1.30 (0.79–4.50)</td>
</tr>
<tr>
<td>Aspergillosis</td>
<td>11 (15)</td>
<td>4</td>
<td>0.84 (0.78–3.61)</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>2 (3)</td>
<td>1</td>
<td>8.55</td>
</tr>
<tr>
<td>Candida bronchopneumonia</td>
<td>1 (1)</td>
<td>0</td>
<td>16.50</td>
</tr>
<tr>
<td>Noninfectious</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAD</td>
<td>35 (49)</td>
<td>12</td>
<td>1.80 (0.90–5.08)</td>
</tr>
<tr>
<td>Alveolar hemorrhage</td>
<td>10 (14)</td>
<td>1</td>
<td>3.32 (0.70–7.70)</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>9 (13)</td>
<td>0</td>
<td>0.84 (0.40–1.15)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>5 (7)</td>
<td>0</td>
<td>0.82 (0.37–1.75)</td>
</tr>
<tr>
<td>Leukemia/lymphoma</td>
<td>4 (6)</td>
<td>0</td>
<td>5.75 (3.40–9.15)</td>
</tr>
<tr>
<td>BO</td>
<td>2 (3)</td>
<td>0</td>
<td>29.55</td>
</tr>
<tr>
<td>Pulmonary alveolar proteinosis</td>
<td>1 (1)</td>
<td>0</td>
<td>17.90</td>
</tr>
<tr>
<td>BOOP</td>
<td>1 (1)</td>
<td>0</td>
<td>11.80</td>
</tr>
<tr>
<td>Acute and organizing pneumonia</td>
<td>1 (1)</td>
<td>0</td>
<td>1.86</td>
</tr>
<tr>
<td>Aspiration pneumonia</td>
<td>1 (1)</td>
<td>1</td>
<td>2.20</td>
</tr>
</tbody>
</table>

*Data are presented as No. (%) or No.

**Table 4—Pulmonary Findings Associated With DAD in 35 BMT Recipients**

<table>
<thead>
<tr>
<th>Pulmonary Findings</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar hemorrhage</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Bacterial bronchopneumonia</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Pulmonary aspergillosis</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Alveolar hemorrhage and bacterial bronchopneumonia</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Pulmonary aspergillosis and alveolar hemorrhage</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Cytomegalovirus pneumonia</td>
<td>1 (3)</td>
</tr>
<tr>
<td>None</td>
<td>19 (54)</td>
</tr>
</tbody>
</table>
treated for aspergillosis at the time of death. Seven patients who were being treated for suspected cytomegalovirus pneumonia at the time of death did not have any evidence of pulmonary cytomegalovirus at autopsy. None of the two patients with cytomegalovirus pneumonia at autopsy were receiving treatment for cytomegalovirus infection at the time of death. Twenty-two of the 29 patients (76%) who were being treated for suspected bacterial pneumonia at the time of death did not have any evidence of bacterial pneumonia at autopsy. Seven of the 13 patients with bacterial bronchopneumonia at autopsy (54%) were receiving antibiotics for bacterial infection at the time of death. No patient was found to have PCP at autopsy. Two patients were being treated for suspected PCP at the time of death. Twelve of the 13 patients (92%) who were being treated with corticosteroids for suspected DAH at the time of death did not have any evidence of alveolar hemorrhage at autopsy. Only one of the eight patients with DAH of noninfectious etiology (13%) was being treated with corticosteroids for documented DAH at the time of death.

**Discussion**

In this study, we found that 89% of BMT recipients had pulmonary complications at autopsy. The majority of the pulmonary complications detected at autopsy were not diagnosed before death. Compared to infectious pulmonary complications, noninfectious complications were more common and less likely to be diagnosed antemortem. Bacterial bronchopneumonia and aspergillosis were the most common infectious pulmonary complications. Most of the patients who were being treated for suspected infections did not have the suspected infections at autopsy. DAD and DAH were the most common noninfectious pulmonary findings. BOOP and BO were rare. No one was found to have PCP. The majority of patients who were being treated for suspected DAH at the time of death did not have evidence of alveolar hemorrhage at autopsy, and most of the patients with evidence of DAH at autopsy were not receiving treatment at the time of death.

Pulmonary complications develop frequently in BMT recipients and are major causes of mortality. A study by Chandrasekar et al showed infectious pulmonary complications to be present in 22 of 56 BMT recipients (39%) at autopsy, and 11 of the 22 patients had two or more pulmonary infections. It also showed the lungs to be the organs most commonly affected by noninfectious abnormalities, DAD being the most frequent finding and a common immediate cause of death. In the present study, pulmonary complications were found in the overwhelming majority of the patients, and respiratory failure was the most common immediate cause of death. Some of the patients had multiple pulmonary complications. Although > 90% of the transplants in our institution are autologous, only 45% of the current study population received autologous BMT, reflecting the high mortality rate associated with allogeneic transplant. Severe infectious and noninfectious pulmonary complications have been reported more often with allogeneic than autologous BMT recipients. However, we found that pulmonary complications occur with high frequency in both allogeneic and autologous BMT recipients when they die.

Despite advances in diagnostic technology, fewer than half of the potentially treatable, nonbacterial, pulmonary infections found at autopsy were diagnosed prior to death. Although an autopsy study of critically ill BMT recipients has shown a significant concordance between clinical diagnoses and postmortem findings, conditions with impact on therapy may be more likely to be underdiagnosed in transplant recipients. Only two cases of cytomegalovirus pneumonia and no cases of PCP were found at autopsy in our patients, probably reflecting the impact of prophylactic and preemptive therapy. This contrasts favorably with two earlier autopsy reports showing cytomegalovirus pneumonia in 18% and 38% of BMT recipients, respectively. However, aspergillus pulmonary infection was a significant problem undiagnosed antemortem or persisting despite diagnosis and treatment. Compared to other infectious complications, there has not been as much success in the prevention and treatment of invasive aspergillosis in BMT recipients. In an earlier study, pulmonary aspergillosis was documented at autopsy in 20% of BMT recipients. In a more recent study of 56 BMT recipients, 6 patients (11%) had aspergillus at autopsy, four of which were not diagnosed antemortem. The lung is the organ most commonly infected by aspergillus. Even with appropriate therapy, the cure rate of invasive aspergillosis in BMT recipients is very low. The current study confirms the need for better preventive, diagnostic, and therapeutic strategies for aspergillosis pulmonary infection.

An earlier autopsy study reported noninfectious pulmonary complications to be less common than infectious complications in BMT recipients. As a result of effective prophylactic and preemptive therapies of some infections in BMT recipients, the relative frequency of noninfectious pulmonary complications has increased. BO, BOOP, DAH, and idiopathic pneumonia syndrome are among the non-infectious complications.
infectious pulmonary complications that develop in BMT recipients. Clinically, BO affects allogeneic BMT recipients with a frequency of approximately 8.3%. Yokoi et al have reported BO in 8 of 81 autopsies (10%). In our study, autopsy confirmed the presence of BO in two of the 30 allogeneic BMT recipients. There are isolated case reports of BOOP in BMT recipients. In the current study, BOOP was found in only one patient at autopsy. Palmas et al reported the incidence of BOOP to be 1.7% among long-term survivor allogeneic BMT recipients from our institution. In a recent study of 19 BMT recipients who underwent open-lung biopsy, histologic evidence of BOOP was documented in 5 patients (26%). This higher frequency likely reflects the selection bias in patients undergoing lung biopsy.

DAD is a nonspecific finding at autopsy. It is associated with various infectious and noninfectious etiologies, such as shock, aspiration, sepsis, drug toxicity, and radiation. The current study shows that the risk for the development of DAD is increased in patients with smoking history and total body irradiation, but not with neutropenia. The association of smoking with DAD is consistent with a finding suggesting a relationship between cigarette smoking and ARDS. In BMT recipients, DAD can be found in noninfectious pulmonary complications such as DAH, periengraftment respiratory syndrome, and idiopathic pneumonia syndrome. No infection was identified in most of the patients with DAD in the current study. Idiopathic pneumonia syndrome develops in approximately 10% of BMT recipients and is characterized by the presence of alveolar injury and the absence of active lower respiratory tract infection. The histologic findings of idiopathic pneumonia syndrome include DAD, organizing or acute pneumonia, and interstitial lymphocytic inflammation. No associated infectious pulmonary complications were found in 19 of our patients with DAD and 1 patient with acute and organizing pneumonia, suggesting idiopathic pneumonia syndrome may have occurred in 28% of the current study population. However, we cannot exclude empirically treated previous infections as causing the histologic changes.

DAH develops in approximately 5% of both autologous and allogeneic BMT recipients. DAH is found in approximately 10% of BMT recipients at autopsy. In the current study, we identified DAH of unknown etiology in 11% of the patients. Our findings are consistent with a study showing an increase in the incidence of DAH. Most of the patients with DAH at autopsy did not receive a diagnosis antemortem. In retrospective studies of BMT recipients, corticosteroid therapy has been associated with better outcome of DAH. A study from our group has shown improved outcome over time for BMT recipients with DAH, probably as a result of early corticosteroid therapy. The findings in the present study highlight the need for high index of suspicion and early intervention in the management of DAH. The absence of alveolar hemorrhage at autopsy in the patients who were being treated for DAH at the time of death may reflect treatment success or misdiagnosis.

Our study showed a discrepancy between clinical diagnosis and autopsy findings of potentially treatable pulmonary complications such as bacterial bronchopneumonia, CMV pneumonia, pulmonary aspergillosis, and DAH. Resolution of these complications as a result of appropriate treatment may partly explain the discrepancy. However, a significant number of the patients with potentially treatable pulmonary complications did not have the correct diagnosis antemortem and were not receiving appropriate therapy at the time of death.

This study has several limitations. Since the analysis was limited to one medical center with predominantly white patients, our results may not be generalizable to other populations. Although hundreds of patients who underwent BMT at our institution died during the study period, most of them were referred from elsewhere, and only a minority underwent autopsy at our institution. This low rate of autopsy may introduce potential bias to our findings. In the current study, the antemortem definition of bacterial pneumonia included the presence of leukocytosis or leukopenia and purulent sputum. Quantitative cultures of BAL fluid or protected specimen brush were rarely performed for the diagnosis of bacterial pneumonia in our study population. This practice has led us to apply criteria with probably low sensitivity and specificity for the diagnosis of bacterial pneumonia. Our study highlights the fact that many pulmonary complications are not diagnosed antemortem. However, it is not easy to determine the importance of underdiagnosis since a significant number of our patients may have preferred comfort care and would not have wanted invasive diagnostic interventions because of their poor prognosis. Further, infections such as disseminated aspergillosis may occur as late complications of a terminal illness.

Conclusions

The current study shows that pulmonary complications develop in the overwhelming majority of dying BMT recipients and are the most common immediate cause of death. Most of these infectious and noninfectious pulmonary complications are not diagnosed and thus not treated antemortem.
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