Late-onset noninfectious interstitial lung disease after allogeneic hematopoietic stem cell transplantation

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Summary

Background: Various late-onset noninfectious pulmonary complications may occur after allogeneic hematopoietic stem cell transplantation (HSCT). Interstitial lung diseases (ILD) are often overlooked, and few data are available.

Methods: We retrospectively analyzed the clinical features, pulmonary function tests, radiological features and outcomes of allogeneic HSCT recipients who were diagnosed with a noninfectious ILD and were managed in our center between 2001 and 2010.

Results: Forty patients were analyzed. The median time from transplant to ILD was 11.3 months. The donor hematopoietic stem cell source was peripheral blood stem cells in 75% of the cases. Seventy percent of the patients had extra-thoracic chronic graft versus host disease at ILD diagnosis. We identified two lung computed tomography (CT) scan patterns according to the predominance of ground glass opacities or alveolar consolidations. Restrictive ventilatory defect was the main pulmonary function pattern. Lung histology was available for seven patients and showed diffuse alveolar damage, non-specific interstitial pneumonia, organizing pneumonia or lymphoid interstitial pneumonia. Thirty-five patients (87.5%) were treated with systemic steroids. Thirteen patients died (32.5%), 10 of respiratory failure. The median survival rate at 24 months was 61%.

Conclusion: This study highlights the existence of noninfectious post-allogeneic HSCT ILD and provides new insights into the characteristics of these illnesses. © 2014 Elsevier Ltd. All rights reserved.

Keywords
Interstitial lung disease; Bone marrow transplantation; Organizing pneumonia; Nonspecific interstitial lung pneumonia; Diffuse alveolar damage; Lymphoid interstitial pneumonia

Abbreviations
AML acute myeloid leukemia
ALL acute lymphoid leukemia
BAL bronchoalveolar lavage
CT computed tomography
DAD diffuse alveolar damage
DLCO diffusion capacity for carbon monoxide
FEV1 forced expiratory volume in 1 s
FVC forced vital capacity
GVHD graft-versus-host disease
HRCT high-resolution computed tomography
HSCT hematopoietic stem cell transplantation
ILD interstitial lung disease
IPS idiopathic pneumonia syndrome
IQR inter-quartile range
LIP lymphoid interstitial pneumonia
LONIPC late-onset non-infectious pulmonary complication
PFT pulmonary function test
NYHA New York Heart Association
NSIP non-specific interstitial pneumonia
OLD obstructive lung disease
OP organizing pneumonia
PBSC peripheral blood stem cells
RLD restrictive lung disease
SLB surgical lung biopsy
TBI total body irradiation
TLC total lung capacity

Background

Late onset noninfectious pulmonary complications (LONIPCs) might follow allogeneic hematopoietic stem cell transplantation (HSCT) and have a significant effect on patient outcomes [1–3]. Previous publications have focused on bronchiolitis obliterans (BO), which is the most common LONIPC [4–6]. Some epidemiological retrospective studies [2,7–9] have reported interstitial lung diseases (ILD) among LONIPCs. Although individual cases of post allogeneic HSCT ILD have been published [10–13], no series have described the spectrum of these ILD using an overall pulmonologic approach. Post HSCT noninfectious ILD are likely misdiagnosed and overlooked. Conversely to BO [6], ILD is characterized by the presence of diffuse lung parenchymal opacities on a CT scan. In the current practice, an infectious cause is first considered. Concomitantly, the patient might be diagnosed with an extra thoracic graft versus host disease (GVHD) and treated with corticosteroids. In this context, these patients are usually treated with a combined treatment associating empirical antimicrobiological drugs and steroids that may explain why these noninfectious ILD are misdiagnosed.

The process of achieving a multidisciplinary diagnosis in a patient with ILD requires close communication between clinician, radiologist, and when appropriate, pathologist [14]. The multidisciplinary approach usually allows to determine whether the noninvasive approach based on clinical, radiological, lung function, bronchoalveolar lavage (BAL) and laboratory findings is informative enough or if a lung biopsy is needed [14]. Besides idiopathic ILD, several medical settings such as exposure or collagen vascular diseases have been shown to cause ILD. In these contexts, knowledge of the clinical characteristics of these ILD has led to an improvement in their management with a dramatic decrease in the indications for lung biopsies [14–19]. In the setting of allogeneic HSCT, two pathological studies identified 6 cases of diffuse alveolar damage (DAD) 8 cases of organizing pneumonia (OP), one case of lymphoid interstitial pneumonia (LIP) and 13 cases of non-classified
ILD [20,21]. In HSCT recipients, ILD management based on surgical lung biopsies is, however, questionable: first, a lung biopsy is an invasive and high-risk procedure in this setting [22,23]; second, no correlation between pathological findings and prognosis exists for post allogeneic HSCT ILD that would allow to guide the treatment; and third, the efficient microbiological tools applied to samples obtained from less invasive techniques such as BAL or nasal aspirate often help differentiate ILD from infectious pneumonia [24–26].

Because post HSCT ILD are infrequent, it was important to retrospectively analyze the patients diagnosed with an ILD to describe their clinical presentations based on the pulmonary investigation techniques used in clinical practice and to analyze the outcomes of these patients.

Patients and methods

This retrospective study was approved by the institutional review board of the French learned society for respiratory medicine CEPRO 2011-055. All of the allogeneic HSCT recipients diagnosed with a noninfectious ILD in our center between 2001 and 2010 were eligible for this study. In addition, patients who underwent an allogeneic HSCT in another French bone marrow transplantation department and who were referred to our respiratory diseases department for the management of an ILD were included. We collected data from individual medical records.

Diagnosis of noninfectious ILD

A noninfectious ILD was diagnosed when infiltrative opacities were present on HRCT and 1) no pathogens were identified in the respiratory samples (BAL and/or nasal aspirate and/or sputum); and/or 2) no clinical or radiological improvements were observed despite broad antimicrobial treatment; and/or 3) clinical and radiological improvements occurred after initiating or increasing the immunosuppressive treatment; and/or 4) no pathogens were found on the lung biopsy (if it was performed).

Clinical characterization of ILD

As is conventional in pulmonology practice, ILD were characterized by clinical symptoms, high-resolution computed tomography (HRCT), pulmonary function testing (PFT), BAL analysis, and lung histology. HRCT scans performed at the time of ILD diagnosis and during follow-up were reviewed by an experienced radiologist (CDB) and two pulmonologists (FS and AB). The following features were noted: alveolar consolidations, ground glass opacities, septal thickening, subpleural reticulations, honeycombing, bronchiectasis, bronchial thickening and pleural abnormalities. To assess lesion distribution, each lung was divided into three areas (upper/medial/lower) from the lung apices to the domes of the diaphragm. Conclusions were reached by consensus. The clinical data, PFT and BAL findings were collected. An extensive search for viruses (as described in the e-appendix), bacteria (direct examination and culture) and fungi (immunofluorescence and molecular biology for Pneumocystis jiroveci; direct examination and culture for other species) was performed on the BAL. When bronchoscopy could not be performed, bacteria and fungi were searched for in the sputum. P. jiroveci was searched for in induced sputum samples and respiratory viruses were searched for in nasal aspirates (e-appendix). The total and differential cell counts in the BAL were analyzed. Pulmonary function tests were performed using a body plethysmograph (Jaeger Masterscreen Body; Jaeger, GMBH; Wurzburg, Germany). The diffusing capacity of carbon monoxide (DL_{CO}) was measured using the single breath method, and the results were adjusted to the last available hemoglobin level. Predictive values were determined as previously described [27]. Obstruction was defined as an FEV1/FVC ratio <0.7 [28], and restriction was defined as a TLC <80% of the predicted value. A DL_{CO} <80% of the predicted value was considered abnormal. An experienced pathologist (VM) analyzed the lung tissue specimen from patients who underwent a surgical lung biopsy. The diagnosis and severity of GVHD were reported based on the clinical grading scores [29,30].

Statistical analyses

Descriptive statistics are presented as the median and inter-quartile range (IQR) [IQR: 25 to 75th percentiles] for continuous parameters and as the number and percentage for non-continuous and qualitative parameters. Survival after ILD diagnosis and ILD incidence were estimated using the Kaplan–Meier method. The prognostic analysis of post-ILD survival was univariate, based on a log rank test for non-continuous parameters or logistic regression with a Cox model for continuous parameters. Given the sample size and number of observed events, no multivariate analyses were performed. Every statistical analysis had a bilateral formulation, and P < 0.05 was considered significant.

Results

Patient characteristics

Between 2001 and 2010, 1277 allogeneic HSCTs were performed in our center, including 35% using a myeloablative conditioning regimen, and 65% using a nonmyeloablative conditioning regimen with stem cell sources as followed: 60% peripheral blood stem cells, 25% bone marrow and 15% cord blood.

Thirty-one allogeneic HSCT recipients were identified as having a noninfectious ILD (2.4%). Three patients from a previous study were included [11]. Nine additional patients, referred to our department because of an ILD during the study period, were included. Sixteen patients were diagnosed between 2001 and 2007 and 24 patients between 2008. The clinical characteristics of the patients are summarized in Table 1. All ILD occurred within the first three years after allogeneic HSCT. The median time from transplantation to ILD was 11.3 months [IQR: 5.9–19.2]. Most of the patients had received prior chemotherapy, and 30% had experienced a prior autologous transplantation. The donor hematopoietic stem cell sources were peripheral blood stem cells in 75% of the cases, and the conditioning regimen was non-myeloablative in 57.5% of the cases.
Clinical characteristics

The most frequent clinical symptoms were dyspnea (n = 35, 87.5%; New York Heart Association (NYHA) ≥ 3: n = 12, 40%), fever (n = 20, 50%), and cough (n = 24, 60%).

Hematological diseases

Table 1 Clinical characteristics of the 40 patients at ILD diagnosis.

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Median [IQR]; N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at transplant, years</td>
<td>40.5 [27.5–51.5]</td>
</tr>
<tr>
<td>Male</td>
<td>28 (70)</td>
</tr>
<tr>
<td>Smoking history</td>
<td>17 (43)</td>
</tr>
<tr>
<td>Age at ILD, years</td>
<td>40.6 [28.5; 51.8]</td>
</tr>
<tr>
<td>Time from transplantation to ILD, months</td>
<td>11.3 [5.9–19.2]</td>
</tr>
<tr>
<td>History of an infectious pneumonia in the time between the transplant and ILD</td>
<td>11 (27.5)</td>
</tr>
</tbody>
</table>

Table 2 Lung HRCT findings in patients at diagnosis of ILD after allogeneic hematopoietic stem cell transplantation.

<table>
<thead>
<tr>
<th>Imaging finding</th>
<th>N (%) of patients (N = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar consolidations</td>
<td>30 (75)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>19 (63)</td>
</tr>
<tr>
<td>Ground glass opacities</td>
<td>29 (72)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>24 (83)</td>
</tr>
<tr>
<td>Involvement of &gt;3 lung areasa,b</td>
<td>15 (37)</td>
</tr>
<tr>
<td>Exclusive upper lung area involvementb</td>
<td>5 (12)</td>
</tr>
<tr>
<td>Exclusive lower lung area involvementb</td>
<td>9 (22)</td>
</tr>
<tr>
<td>Reticulation</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Septal thickening</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Honeycombing</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Bronchial thickening</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Pneumomediastinum</td>
<td>3 (7)</td>
</tr>
</tbody>
</table>

ILD characteristics

The most frequent clinical symptoms were dyspnea (n = 35, 87.5%; New York Heart Association (NYHA) ≥ 3: n = 12, 40%), fever (n = 20, 50%), and cough (n = 24, 60%).
Bronchoalveolar lavage cell count

BAL was performed in 30 patients. The total and differential cell counts are shown in Table 4. Except for three patients (10%) who had normal BAL cell counts, all patients had an alveolitis. Lymphocytic alveolitis (defined by a lymphocyte count ≥15% of total cells) was the most frequent and was found in 20 patients (67%). Among these patients, the median percentage of alveolar lymphocytes was 40% [IQR: 21–56%] and seven patients had a concomitant neutrophil count ≥10% of total cells. Three other patients had a neutrophil count ≥10% of total cells (median 20%, [IQR: 15–33%]). Four patients had an eosinophil count ≥10% of total cells, including two with an eosinophil count ≥20% of total cells, suggesting an eosinophilic pneumonia.

Lung histology

Eleven lung biopsies were available for 10 patients. Four patients had CT scan-guided percutaneous lung biopsies, and seven patients had surgical lung biopsies (six with video-assisted thoracoscopy). Four of these 10 patients (40%) experienced postoperative morbidity or mortality; two patients required prolonged chest tube aspiration (one required another surgery), and two patients died within 15 days following surgery (one from respiratory failure and the other from septic shock with multisystem organ failure). A

Both PFT and BAL results were similar whether patients had a ground glass opacities HRCT pattern or an alveolar consolidation pattern.
definite histological diagnosis was obtained in 7/10 (70%) patients and consisted of DAD (n = 2), nonspecific interstitial pneumonia (NSIP) (n = 2), OP (n = 2) and LIP (n = 1). Patients diagnosed with DAD had either an alveolar consolidation or a ground glass opacities HRCT pattern. The two patients diagnosed with OP and the patient diagnosed with LIP had an alveolar consolidations pattern; both of the patients diagnosed with NSIP had a ground glass opacities HRCT pattern.

### Treatment and outcome

The median follow-up after diagnosis of ILD was 9.3 months [IQR: 2.1–32]. The patients of both HRCT phenotypes were treated similarly. Thirty-five patients (87.5%) received systemic steroids for the treatment of ILD. The lung histology available for two of these patients showed DAD for one and NSIP for the other. The three other patients died of refractory gut cGVHD associated with severe sepsis, septic shock and encephalopathy syndrome. The survival rate was estimated at 77% [IQR: 64–92%], 70% [IQR: 56–88%] and 61% [IQR: 45–82%] at 6, 12 and 24 months, respectively, after ILD diagnosis (Fig. 2).

### Evolution of HRCT and PFT

Although the overall prognosis of ILD was poor, a significant number of patients had a favorable outcome regarding HRCT and PFT. We did not find any association between the evolution of both HRCT and PFT and the HRCT scan pattern at ILD diagnosis.

Among the survivors, at least two serial HRCT scans were available for 18 patients (alveolar consolidations HRCT pattern). Thirteen patients died (33%). Ten patients died of respiratory failure; these patients were receiving systemic steroids for ILD treatment. The lung histology available for two of these patients showed DAD for one and NSIP for the other. The three other patients died of refractory gut cGVHD associated with severe sepsis, septic shock and encephalopathy syndrome. The survival rate was estimated at 77% [IQR: 64–92%], 70% [IQR: 56–88%] and 61% [IQR: 45–82%] at 6, 12 and 24 months, respectively, after ILD diagnosis (Fig. 2).

### Table 3 Pulmonary function testing in overall patients and according to the lung HRCT pattern at the time of ILD diagnosis.

<table>
<thead>
<tr>
<th></th>
<th>Median [IQR]</th>
<th>FEV$_1$ (L)</th>
<th>% pred</th>
<th>FVC (L)</th>
<th>% pred</th>
<th>FEV$_1$/FVC %</th>
<th>TLC (L)</th>
<th>% pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground glass pattern</td>
<td>1.675 [1.54–2.25]</td>
<td>52.5</td>
<td>21.8 [1.82–2.55]</td>
<td>52</td>
<td>81.9</td>
<td>4.04</td>
<td>63.5</td>
<td>43</td>
</tr>
</tbody>
</table>

- Lung CT scan pattern; FEV$_1$, forced expiratory volume in 1 s; FVC, forced vital capacity; TLC, total lung capacity; DL$_{CO}$, diffusing capacity of carbon oxide; pred, predicted.

### Table 4 Bronchoalveolar lavage cell counts in overall patients and according to the lung HRCT pattern.

<table>
<thead>
<tr>
<th></th>
<th>Median [IQR]</th>
<th>Total cell count/mm$^3$</th>
<th>Ma</th>
<th>Ly</th>
<th>Neu</th>
<th>Eo</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
<td>280 [180–460]</td>
<td>54</td>
<td>20.5</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Ground glass pattern</td>
<td>250 [150–280]</td>
<td>67</td>
<td>19</td>
<td>5</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Alveolar consolidations pattern</td>
<td>315 [225–465]</td>
<td>50</td>
<td>23</td>
<td>7</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

- Lung CT scan pattern; Ma, macrophages; Ly, lymphocytes; Neu, neutrophils; Eo, eosinophils.
pattern \((n = 11)\), ground glass opacities HRCT pattern \((n = 7)\)). For these patients, the last available HRCT scan was performed at a median time of 10.3 months after ILD diagnosis \([IQR: 2–23]\). At last follow-up, complete resolution of radiological abnormalities was observed in five patients (alveolar consolidations pattern \((n = 4)\)) and persisted in 13 patients (ground glass opacities pattern \((n = 6)\), alveolar consolidations \((n = 7)\)). After being characterized as having a particular phenotype by a CT scan at the time of diagnosis, none of the patients evolved to the other phenotype.

All the patients who had PFT at ILD diagnosis had two or more PFTs during the follow-up with a similar distribution between both HRCT pattern; for these patients, the last available PFT was performed at a median time of 7 months \([IQR: 3–18]\) after the first PFT. Fourteen patients (45%) showed greater than 10% improvement of FVC or FEV\(_1\), relative to the baseline.

**Prognostic analysis**

In the univariate analysis, no prognostic factor was identified to be associated with survival (e-Table 1). The patients with an alveolar consolidation pattern tended to have better survival than those with a ground glass opacity pattern (78% vs. 60% at 12 months, 71% vs. 48% at 24 months), although the difference did not reach statistical significance \((p = 0.19; \text{e-Fig. 1})\).

**Discussion**

This retrospective study is the largest series on allogeneic post-HSCT non-infectious ILD. Our study highlights the existence of post-allogeneic HSCT non-infectious ILD and provides new insights into the clinical characteristics of this complication. Previous studies have focused on epidemiological data and anecdotal reports. We observed the following: 1) post-allogeneic HSCT ILD typically occur within the first 3 years after transplantation and are frequently associated with extra pulmonary GVHD manifestations; 2) ILD include different histological entities; 3) two distinct lung HRCT patterns were observed according to the predominance of ground glass opacities or alveolar consolidations; 4) lung function restriction and BAL lymphocytic alveolitis were frequent; and 5) the prognosis was globally poor, although in some cases, ILD might improve or resolve with corticosteroids.

In the context of allogeneic HSCT, the occurrence of ILD is often attributed to idiopathic pneumonia syndrome (IPS) or to OP \([4,31]\). IPS is not a well-defined pulmonary disease and includes various conditions \([31,32]\). The diagnosis of IPS, which has recently been reviewed, relies on diffuse lung opacities on the chest X-ray and the exclusion of several diagnoses, such as lung infection or pulmonary edema \([31]\). The median time of onset for IPS is reported to be 19 days (range, 4–106 days) after HSCT. The intensity and type of HSCT conditioning have been associated with the development of IPS, which is consistent with data generated from mouse models \([31]\). The ILD described in our study differ in various respects from IPS. ILD occurred later after transplantation, predominantly in patients who underwent non-myeloablative conditioning. Only 60% of our patients underwent pre-transplant total body irradiation, and none of our patients received carmustine; both of these factors are associated with IPS. Thus, the ILD we described do not match the current IPS criteria. Conversely, the time of onset after the HSCT and the clinical, pulmonary and radiological characteristics of some of our patients were similar to the characteristics described in cases of post-allogeneic HSCT OP \([13,33]\). However, based on the lung biopsy results, other ILD entities (NSIP, DAD and LIP) were observed in our patients.

At present, only biopsy-proven BO has been firmly recognized as a manifestation of lung GVHD based on epidemiological studies that show a strong association between BO and extra-thoracic chronic GVHD. In several studies, OP has also been associated with GVHD \([4,13,15]\). A feature of our findings is that almost all patients who developed late onset ILD had a history of acute and/or chronic GVHD. Unfortunately, due to the retrospective design of our study, we could not evaluate the incidence of GVHD in our population of HSCT recipients who did not develop ILD during the study period. Thus, although our findings suggest that the ILD spectrum may reflect lung GVHD, we could not formally conclude. However, the presence of an OLD in some of our patients, suggesting BO associated with ILD, further strengthens this hypothesis. Although the history of the patients was not suggestive, the role of drug pulmonary toxicity in patients receiving multiple treatments cannot be formally ruled out.

One finding of our study is that, conversely to what is known for the treatment of BO \([6,34]\), a significant proportion of our patients who were treated with steroids had either complete resolution of their ILD or a significant improvement in their PFT. These data emphasize the importance of identifying these ILD to promptly administer steroids. However, only a randomized study could demonstrate the efficacy of steroids in post allogeneic non-infectious ILD.

The retrospective design and the relatively small number of patients did not allow us to reach firm conclusions on several points. First, we could not correlate the radiological and clinical diagnosis with the underlying histological disease because of the small number of patients who underwent a surgical lung biopsy. Of note, in our few patients who underwent a lung biopsy, alveolar consolidations HRCT pattern could be associated with either DAD, OP or LIP whereas ground glass opacities pattern was associated with NSIP or DAD. Second, during the follow-up period, we did not report any changes in the HRCT scan patterns. However, follow up HRCT scans were not available for all of the patients. Thus, we could not firmly exclude that both HRCT scan patterns are a spectrum of the same lung disease entity. Third, we could not identify any prognostic factors, although the patients with an alveolar consolidation pattern tended to have better survival than the patients with a ground glass opacities pattern.

In summary, because of the increasing number of long-term HSCT survivors, an understanding of new late onset noninfectious complications is important. Herein, we described the characteristics of ILD occurring after allogeneic HSCT according to the usual approach of ILD. As typically occurs in clinical practices, the majority of these
patients did not undergo lung biopsies. Our data provide information regarding the management of these patients. Further studies are needed to clarify the physiopathology, identify the risk factors and optimize the treatment of these lung disorders to improve the prognosis.

Authors’ contribution

FS: Data acquisition, analysis and interpretation, drafting the article, final approval of the version to be published. SC: Statistical analysis of the data, drafting the article, final approval of the version to be published. GL: Data analysis and interpretation, final approval of the version to be published. CDB: Data acquisition, final approval of the version to be published. RPDL: Data analysis and interpretation, final approval of the version to be published. WM: Data acquisition, final approval of the version to be published. MM: Data acquisition, final approval of the version to be published. EH: Data acquisition, final approval of the version to be published. BW: Data acquisition, final approval of the version to be published.

VH: Data acquisition, final approval of the version to be published. SMA: Data acquisition, final approval of the version to be published. GS: Data analysis and interpretation, final approval of the version to be published. AT: Study conception and design, data analysis and interpretation, final approval of the version to be published. AB: Study conception and design, data acquisition, analysis and interpretation, drafting the article, final approval of the version to be published.

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Conflict of interest

None declared.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmed.2014.09.006.

References


Forslow U, Remberger M, Nordlander A, Mattsson J. The clinical importance of bronchoalveolar lavage in allogeneic SCT patients with pneumonia. Bone Marrow Transplant 2010;45:945–50.


