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

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KEYWORDS
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Diffuse alveolar damage;
Lymphoid interstitial pneumonia

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.

Abbreviations

AML	acute myeloid leukemia
ALL	acute lymphoid leukemia
BAL	bronchoalveolar lavage
CT	computed tomography
DAD	diffuse alveolar damage
DL_{CO}	diffusion capacity for carbon monoxide
FEV_1	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