Reviewer's report

Title: Clinical and Radiological Characteristics of Patients with Late-Onset Severe Restrictive Lung Defect After Hematopoietic Stem Cell Transplantation

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Reviewer: Veronica Alfieri

Reviewer's report:

In the paper by Namkoong et al, entitled "Clinical and radiological characteristics of patients with late-onset severe restrictive lung defect after hematopoietic stem cell transplantation", the authors described the clinical and radiological features in patients with late-onset idiopathic pneumonia syndrome (IPS) with severe restrictive ventilatory defect (defined as VC% less than 60%). Twelve of 453 patients were enrolled for the analysis (2.6%). The underlying disease was acute leukemia in 8 patients and myelodysplastic syndrome in 1. Ten of 12 patients had total body irradiation as conditioning regimen. All patients received Cyclosporin A or Tacrolimus with a short course of Methotrexate as GVHD prophylaxis. Eleven of 12 patients developed acute GVHD and all chronic GVHD. HRCT showed findings consistent with PPFE in 7 patients, airway-predominant disease in 3 patients and unclassifiable interstitial pneumonia in 2. The value of DLco was reduced after the diagnosis of IPS while the RV/TLC ratio was increased.

The research topic is of interest, however in my opinion the manuscript has some points that need to be improved and clarified.

Major points:

- Methods/Patients (page 6): the authors have chosen to include in the study patients with diagnosis of late-onset IPS with severe restrictive defect (VC% less than 60%) because they aim to exclude heterogeneous case of mild to moderate restrictive ventilatory defect. Regarding to the choice of VC%<60% as cut off, a few considerations should be done. A restrictive ventilatory defect is defined by a reduction in TLC, even if in interstitial lung disease the use of FVC, together with DLCO, is commonly used to assess the severity of the disease, the efficacy of treatments and for the follow up of patients, but a cut off of 60% has not been reported. Furthermore, the results show the presence of airway dominant disease in 3 of 12 patients at the CT, and the figure 4a shows that at least 3 patients have an obstructive or mixed ventilatory defect (FEV1/FVC < 70%).

It is my opinion that the choice of the cut off of 60% seems arbitrary and need better clarification.
- Methods/Radiological evaluation (page 6): the authors should provide a description of the radiological features noted by the two pulmonologists and the radiologist. I suppose the conclusions were reached by consensus, but I think it should be clarified.

- Results/Characteristics of severe late-onset IPS (page 8): The description of the radiological features and the Table 2 should reflect the methodology. The authors suggest the identification of 3 groups/pattern (also used in the results) that should be clarified here.

- Discussion: should be reviewed according to the changes in methods and results.

Minor points:

- Results/Clinical features of patients with severe late-onset IPS (page 8): I do not understand how many patients had chronic GVHS, the text suggests not all ("All the patients who had") but Table 1 indicates that all patients had extensive chronic GVHD (page 8 line 26 and Table 1).

- Results/Pulmonary function changes (page 9): I suggest to change "pulmonary function test" with "lung volumes and DLco" at page 9 line 38. Adding a table with the pulmonary function test according to the HRCT pattern could improve the description of the patients analyzed.

- Tables: Table 1 could be improved adding the smoking history and the history of infections (any time and between HSCT and IPS). The explanation of the abbreviation TAC and MTX is missing. The fact that one pediatric patients (n.3, age at HSCT: 12) has been included should be disclosed.

Table 2 could be completed adding the history of pneumomediastinum.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

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