


The Diagnosis of Extranodal Marginal Zone B-Cell Lymphoma of Mucosa-Associated Lymphoid Tissue

To the Editor:

We read with great interest the case report by Cadavid et al in a recent issue of CHEST (January 2011). Although Cadavid et al reported an excellent case of extranodal marginal zone B-cell lymphoma (MZBL) of mucosa-associated lymphoid tissue (MALT), we would like to raise some concerns about the diagnosis of extranodal MZBL of MALT. To our knowledge, the optimal diagnosis of the disease requires careful integration of morphologic, immunohistochemical, and molecular information, given the non-specific nature of clinical manifestation, physical examination, and radiographic features. It is worth noting that this case report presented only one endobronchial biopsy specimen demonstrating extensive infiltration of the mucosa and submucosa by a homogeneous population of lymphocytes. We question whether it is sufficient to diagnose the disease by histologic examination only. The histologic differentiation between extranodal MZBL of MALT and reactive lymphocytic proliferation may sometimes be difficult. This is the reason why some of the patients with extranodal MZBL of MALT are given a misdiagnosis of pneumonia, pulmonary tuberculosis, or interstitial lung disease. Furthermore, extranodal MZBL of MALT typically expresses B-cell-associated antigens, such as CD20 and CD79a, but lacks CD5, CD10, CD23, and cyclinD1. Thus, immunophenotyping is used to exclude B-chronic lymphocytic leukemia/small lymphocytic lymphoma, mantle cell lymphoma, and follicular lymphomas to aid in the correct diagnosis. We would propose that the authors of this case report supplement immunohistochemistry and/or examine gene rearrangement to validate the diagnosis of extranodal MZBL of MALT.

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REFERENCES


IV Delivery of Fluorescent Beads

To the Editor:

Cell-based therapies using induced pluripotent stem (iPS) cells have emerged as potential novel approaches for several devastating and otherwise incurable lung diseases like emphysema, pulmonary fibrosis, pulmonary hypertension, and ARDS. The article by Yang et al in a recent issue of CHEST (November 2011) evaluating the role of iPS cells in the treatment of endotoxin-induced acute lung injury revealed a possible protective effect mediated by iPS cells, which significantly diminishes the histopathologic changes of acute lung injury and the lung injury score. Moreover, it was shown that the protective effects were not replicated by control cell therapy carried with fibroblasts.

However, in our opinion, the strength of the article would be enhanced substantially by a more precise evaluation of the area of iPS cell integration into the lung and by an assessment of the iPS cell dynamic through different parenchymal organs. The latter will help to establish iPS cell lung-homing capacity.

To illustrate the importance of these points, we will describe the results of a recent experiment performed in our laboratory. A total of $1 \times 10^5$ fluorescent beads (FBs) (2.5 μm, ex: 630-660 nm, em: 670-720 nm; Invitrogen) were suspended in 50 μL of phosphate-buffered saline and injected into the tail vein of Cby.CgFoxn1nu/J 1-month-old nude mice (Charles River). Location of FBs was registered by in vivo fluorescent imaging (Pearl-Impulse; LI-COR Biotechnology), at different times after the injection: 5 min, 1, 2, 3, and 4 weeks. After 4 weeks, the mice were killed according to approved methods, and their internal organs inspected for fluorescent emission. In order to localize with more precision the location of the beads, 10-μm tissue sections were analyzed by standard fluorescent microscopy (DMI 6000B; Leica Microsystems).

In agreement with our previous findings in nude rats, 5 min after injection many of the FBs were localized in the breast area of animals (Fig 1A). However, a week after the injection almost all the FBs were present in the abdominal part of the body (Fig 1B). This image remained unaltered at 4 weeks after the injection. The analysis of autopy material (Fig 1C, 1D) clearly shows that almost all the FBs were located in spleen and liver, being undetectable in kidney, heart, and lung.

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Analyses of time dynamics of iPS distribution through the parenchymal organs might allow for the quantification of their relative homing capabilities in the organ of interest and, thereby, better clarification of their role in the different pathologic processes.

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Response

To the Editor:

We thank Drs Tokalov and Bachiller for their interest in our recent article in CHEST. Dr Tokalov and colleagues have studied the role of fluorescent beads (FBs) to trace the distribution of FBs in vascular space and parenchymal organs in small animals. We have shown that IV delivery of induced pluripotent stem (iPS) cells provided a beneficial effect in attenuating the severity of endotoxin-induced acute lung injury (ALI) and resulted in a decrease in physiologic impairment. As shown by in vivo radionuclide imaging and in vitro Hoechst-labeled fluorescent staining, an increase in iPS cells in the lungs of mice with ALI was evident when compared with control mice.

We agree with Drs Tokalov and Bachiller’s recommendations that analyses of time dynamics of the distribution of iPS cells through the parenchymal organs may allow the quantification of the relative homing capabilities in the organ of interest. In our article, we have demonstrated an early-phase homing potential of iPS cells, evident by more 131I-IdUrd-labeled iPS cells accumulated over the lung area in mice with endotoxin-induced ALI than in control mice (in vivo radionuclide imaging). In addition, to explore the microscopic fate of transplanted iPS cells, we labeled iPS cells with Hoechst and located Hoechst-positive cells in lung tissue. In agreement with the findings of radionuclide imaging, after 24 h of iPS cell delivery, we found Hoechst-labeled cells were more scattered in the injured lung sections of mice with ALI when compared with lung sections of control mice. However, long-term dynamic distribution of iPS cells in different parenchymal organs may be related to the safety and efficacy of iPS cell-based therapy applied in different lung diseases and therefore requires further studies.

Notably, Drs Tokalov and Bachiller showed that FBs were initially located in the breast area of nude mice after the tail vein injection followed by the abdominal part of the body after 1 week. This elegant finding provided a novel approach to monitor the long-term dynamic distribution of FBs in vivo. In line with Drs Tokalov and Bachiller’s suggestion, this FBs-derived platform may play a role in iPS cells and other stem cell research, and further investigation of its function on migration, proliferation, differentiation, and programmed death is warranted. However, the material properties of tracer including biodegradability, biosafety, and nano-sized scale for delivery need to be examined in molecular imaging-based diagnosis and stem cell transplantation in the future.

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