Pulmonary mantle cell lymphoma: a rare manifestation of an uncommon condition

Zachary S. DePew, Robert Vassallo

Department of Medicine, Division of Pulmonary/Critical Care Medicine, Mayo Clinic, Rochester, MN, USA

Abstract

Herein we describe the case of a 64-year old man with a history of mantle cell lymphoma found to have evidence of pulmonary parenchymal involvement by recurrence of his lymphoma. While lung involvement is not necessarily uncommon with Non-Hodgkin's lymphomas as a group, it is very rare for mantle cell lymphoma to involve the lung parenchyma. In addition, the radiographic manifestation of his pulmonary lymphoma as a discrete FDG-avid ground-glass lesion on chest imaging was also distinctly uncommon for pulmonary lymphoma which classically appears in one of three patterns: scattered ill-defined nodules, a bronchovascular/lymphangitic process, or pneumonic/alveolar consolidation effectively indistinguishable from bacterial pneumonia. Due to significant underlying lung disease our patient was not a candidate for high-dose conditioning and autologous stem cell transplantation. He was ultimately treated with rituximab and cladribine therapy and had early signs of clinical response at last correspondence.

Case Report

A 64-year-old man with a history of Non-Hodgkin's lymphoma (NHL) was referred for evaluation of dyspnea and an indeterminate lung lesion. Two years prior to presentation he was diagnosed with mantle cell lymphoma by bone marrow biopsy demonstrating B-cells with consistent flow markings and 11;14 translocation by fluorescent in-situ hybridization (FISH) analysis. He was subsequently treated with 6 cycles of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) and achieved remission by positron emission tomography - computed tomography (PET/CT) imaging and bone marrow biopsy. He was evaluated for autologous stem cell transplant but this was deferred due to limited pulmonary reserve. He was treated with rituximab maintenance therapy until a follow-up PET/CT showed concern for recurrence at which point he was treated with 6 cycles of bendamustine, bortezomib, and rituximab. Repeat PET/CT imaging again showed persistence of FDG-avid lymphadenopathy within his neck, chest, abdomen, and pelvis, as well as a ground-glass opacity in the left lung for which he was referred for pulmonary consultation.

During the pulmonary consultation the patient noted that he had dyspnea on exertion to the point of limiting his ability to walk more than one block without resting. This was chronic and related to his history of chronic obstructive pulmonary disease. Other than lower back pain and a mild non-productive cough, the rest of his review of symptoms was negative. He specifically denied weight loss, night sweats, fevers, chills, myalgias, and hemoptysis.

Vital signs were as follows: temperature 35.6ºC; heart rate 94/min; BP 139/78 mmHg, respirations 16/min; BMI 26.4 Kg/m^2. Pertinent findings on physical exam included a small palpable lymph node in the left submandibular region and mild fine bibasilar crackles on lung exam without wheezing. The remainder of the exam was unremarkable.

Laboratory studies including complete blood count with differential cell count, electrolytes, renal and liver function tests were all within normal limits. Pulmonary function testing revealed mild irreversible obstruction with normal lung volumes. The diffusing capacity was reduced and there was oxygen desaturation with minimal activity. A high resolution computed tomography scan of the chest (Figure 1A) showed an isolated area of ground-glass opacification in the left lower lobe which was highly FDG-avid on positron emission tomography (Figure 1B). Flexible bronchoscopy with broncho-alveolar lavage of the left lateral basal segment was performed. The effluent was sent for microbiologic analysis for routine and opportunistic pathogens. All microbiologic data was ultimately unrevealing. Iron stain was performed and showed no hemosiderin-laden macrophages. Cytologic evaluation showed no evidence of malignancy. Transthoracic fine needle aspiration of the lesion was ultimately performed and showed an atypical population of CD-20 positive B-cells (Figure 2A) coexpressing CD-5, blc-2, and cyclin D1 (Figure 2B) consistent with pulmonary mantle cell lymphoma.

After confirmation of relapse of his mantle cell lymphoma the patient returned to his hematologist to discuss therapeutic options. Unfortunately, due to his underlying pulmonary disease he was not felt to be a candidate for high-dose conditioning and autologous stem cell transplant. The decision was made for the patient to proceed with rituximab and cladribine therapy. Review of recent correspondence from his local providers indicates he is tolerating chemotherapy well with early signs of clinical response.

Correspondence: Robert Vassallo, Division of Pulmonary/Critical Care Medicine, Mayo Clinic Rochester, 201 First St. SW, Rochester, MN 55905., USA. Tel./Fax: +1.507.266.4372.
E-mail: vassallo.robert@mayo.edu

Key words: mantle cell lymphoma, pulmonary lymphoma, non-Hodgkin's lymphoma.

Conflict of interest: no potential conflicts of interests to declare.

Received for publication: 10 November 2011.
Accepted for publication: 4 December 2011.

Rare Tumors 2012; 4:e11
doi:10.4081/rt.2012.e11

Discussion

Pulmonary infiltrates in immunosuppressed patients are frequently encountered given the increased use of immunosuppressive chemotherapeutics and transplant procedures performed over the past few decades. Infectious etiologies are certainly the foremost concern in immunosuppressed patients presenting with respiratory symptoms and new pulmonary infiltrates on chest imaging. Flexible bronchoscopy with bronchoalveolar lavage is frequently employed as a diagnostic tool in the evaluation of these patients. Bronchoalveolar lavage of the affected region allows for multiple microbiologic diagnostic studies including varied stains, cultures, and genetic studies for bacteria, mycobacteria, fungi, and viruses, as well as cytologic evaluations for malignancy and diffuse alveolar hemorrhage. While infectious processes represent a significant portion of the pulmonary infiltrates in immunocompromised patients, non-infectious etiologies must also be considered.

Parenchymal lung involvement in Non-Hodgkin's lymphoma (NHL) is uncommon and is reported to be present in less than 5% of patients at the time of diagnosis. It is important to note, however, that the prevalence of parenchymal lung involvement increases over time and may be present in as many as 24% of patients during their disease course. This is in contrast to Hodgkin's lymphoma in which nearly 10% of patients have lung involvement at presentation and 35-40% will develop parenchymal disease during their disease course.[1] Interestingly, lung parenchymal involvement in NHL frequently occurs in the absence of significant thoracic adenopathy. As

with all other features of NHL, the prevalence of lung involvement is highly dependent on the specific pathologic cell type.

Radiographic features of pulmonary lymphoma on chest CT imaging are varied but classically present in one of three patterns. The most common appearance is that of scattered ill-defined nodules with lower lobe predominance. These nodules frequently include air-bronchograms; cavitations with or without air fluid levels are also possible. The second most common pattern is a bronchovascular/lymphangitic process with coarse linear and reticulonodular shadows extending outwards from the hilum in a perivascular and peribronchial distribution. When extensive this pattern can appear very similar to consolidative bronchopneumonia. The third pattern is described as pneumonic/alveolar and is effectively indistinguishable from bacterial pneumonia. It can be a segmental or lobar process. The only discerning feature is an absence of volume loss which would be consistent with a consolidative process.[2] Ground-glass opacification is a distinctly uncommon presentation of pulmonary lymphoma and not classically described.

Mantle cell lymphoma (MCL) is a mature B-cell NHL characterized by proliferation of B-cells resembling those found in the follicular mantle zones and accounts for approximately 5% of NHL. It is most often a very aggressive disease typically presenting in the sixth decade with a male predominance.[3,4] Cyclin D1 nuclear staining is positive in over 90% of cases. Cyclin D1 overexpression is strongly associated with the t(11;14), however this translocation is present by karyotyping in only 50%-65% of patients.[5] The majority of patients with MCL present with advanced disease with over 75% of patients having extranodal involvement at presentation. The most common sites of extranodal involvement include the bone marrow, peripheral blood, GI tract, Waldeyer's ring, and liver in descending order. In one study 25% of patients with MCL had an extranodal site as the primary site of involvement at presentation, though none of these patients had parenchymal lung disease.[3] Despite the frequency of extranodal disease in MCL it is still distinctly uncommon for the lung parenchyma to be involved. Nonetheless, the presence of a non-infectious metabolically active infiltrate found on radiographic chest imaging in any patient with NHL, including MCL, should prompt efforts to establish a tissue diagnosis of pulmonary lymphoma.

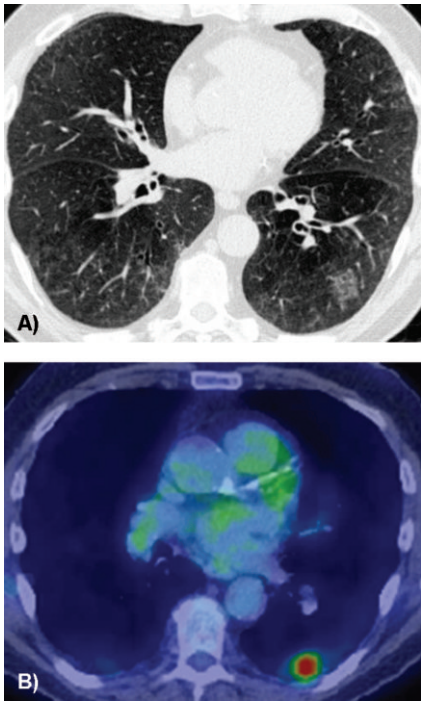

Figure 1. A) Non-contrast chest computed tomograohy scan showing left lower lobe ground-glass opacification; B) chest positron emission tomography - computed tomography image demonstrating FDG-avidity of left lower lobe opacity.

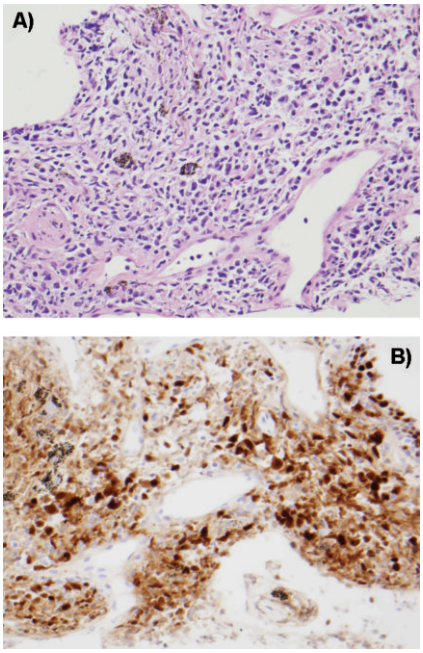

Figure 2. Transthoracic needle aspiration biopsy specimens from left lower lobe ground-glass opacity, original magnification ×400, with hematoxylin-eosin (A) and cyclin D1 (B) stains depicting an atypical population of CD-20 positive B-cells coexpressing CD-5, blc-2, and cyclin D1.

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