Diffuse large B-cell lymphoma of the lung in a 63-year-old man with left flank pain

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Diffuse large B-cell lymphoma (DLBCL) of the lung is a rare entity, and although the prognosis is favorable, its biological features, clinical presentation, prognostic markers, and treatment have not been well defined.[1,2] It is the second most common primary pulmonary lymphoma (PPL) after mucosa-associated lymphoid tissue (MALT). PPL itself is very rare; it represents 3%-4% of extranodal non-Hodgkin lymphoma, < 1% of NHL, and 0.5%-1.0% of primary pulmonary malignancies.[2,3] A review of the literature indicates a lack of data on pulmonary DLBCL. The objective of this case report is to highlight areas in which further research may be pursued to better understand this disease.

Case presentation

A 63-year-old man presented to the emergency department with the complaint of shortness of breath on minimal exertion, chronic nonproductive cough, and worsening left lower chest and flank pain. The shortness of breath had been worsening progressively over the past several months and at the time of presentation it significantly limited his activities of daily living. The chest and flank pain had appeared during the previous week and was described as a constant dull ache. He had a 60 pack year smoking history and his past medical history was significant only for prostate cancer treated with proton beam radiotherapy.

Physical examination at the time of initial presentation was remarkable for decreased air entry at the left lung base and mild left-sided lower chest wall tenderness. Initial lab investigations, including complete blood count with differential, basic metabolic panel, and hepatic function tests were unremarkable. A chest radiograph showed a wedge-shaped opacity within the left lung base and a subsequent computed tomography (CT) scan of the chest confirmed the presence of a soft tissue mass of 8 × 4 × 5 cm that abutted the left pleura (Figure 1). A CT-guided core biopsy was done on the following day.

The flow cytometry and cytomorphology of the tissue sample was consistent with a diagnosis of DLBCL (Figure 2). Flow cytometric analysis of the lung mass tissue revealed a large lymphoid population which was positive for HLA-DR, CD19, CD20, CD38, CD10 and lambda light chain. The CD10 positivity was indicative of a follicular cell origin for this tumor. To complete the staging, a bone marrow aspirate smear and biopsy with flow cytometric analysis were done and they revealed no overt evidence of a B-cell lymphoproliferative disorder.

Further investigations aimed at staging and determining the patient's prognosis using the Revised International Prognostic Index (R-IPI) were done. This included obtaining a lactate dehydrogenase level and evaluating for extranodal spread of the disease with a positron emission tomography–computed tomography scan. The PET–CT scan demonstrated avid fluorodeoxyglucose (FDG) uptake in the left lower lobe mass with a maximal standardized uptake value (mSUV) of 37.24 and it also showed a small non-FDG avid left pleural effusion (Figure 3).

The patient was calculated as having an R-IPI score of 2, which indicated a good prognosis based on his age (older than 60 years), a good performance status, an LDH level greater than upper limit of normal (271), no extranodal sites of spread, and stage II disease. He was subsequently started on an R-CHOP (rituximab, cyclophosphamide, doxorubi-

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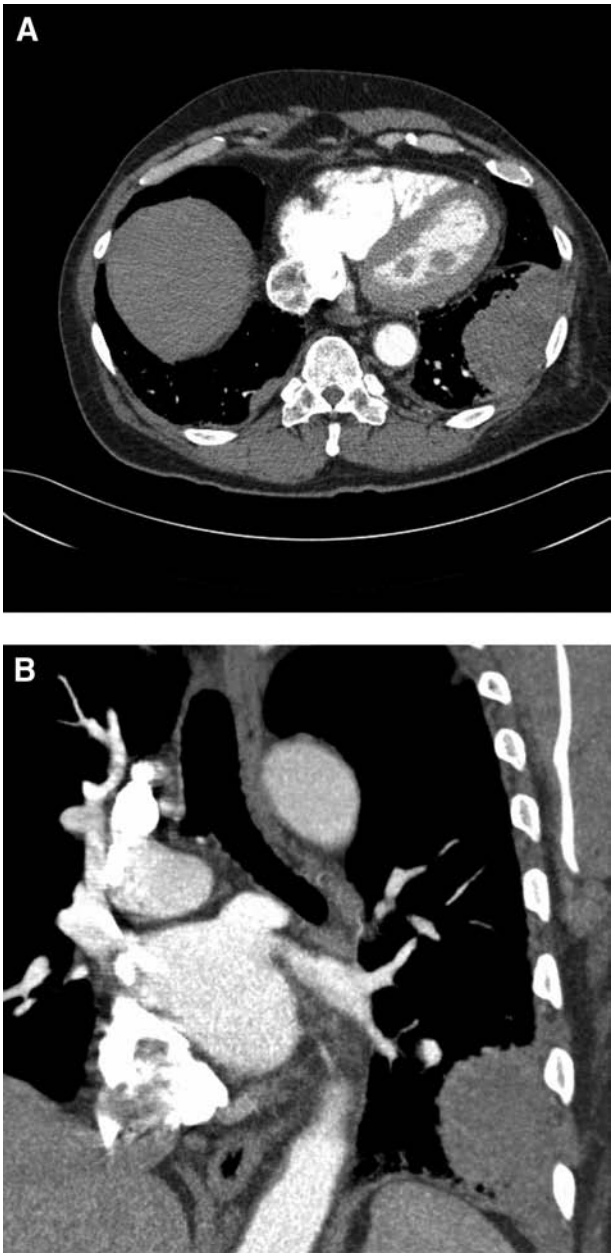

FIGURE 1 A, A computed tomography angiogram of the chest showing a large soft tissue mass within the inferior left hemithorax measuring approximately 3.2 × 1.6 in. B, A CT angiogram of the chest showing left apical pleural thickening and a very small left pleural effusion. Within the left lower lobe laterally is a soft tissue mass of 3.3 × 1.6 × 2.2 in. that abuts the pleural surface and demonstrates acute angles with the chest wall.

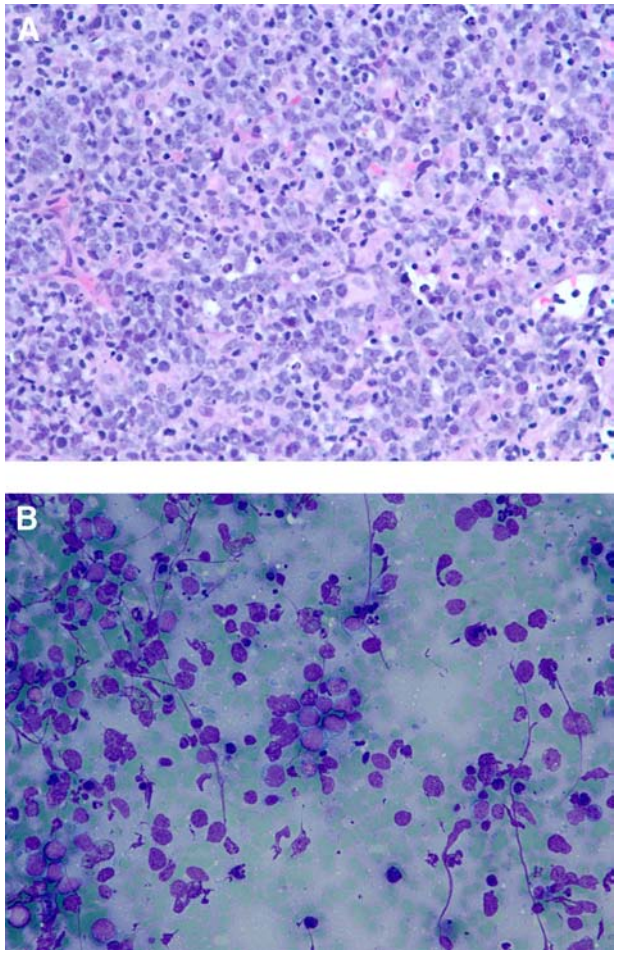

FIGURE 2 A, Diffuse large B-cell lymphoma, histopathologic view; note loose, dispersed arrangement of monomorphic large lymphoid cells that are larger than smaller darker background normal lymphocytes. These sheets of cells efface the underlying alveolar architecture of the lung (hematoxylin and eosin stain, original magnification x40). B, Imprint smear cytology shows dyscohesive, monomorphic round cells with basophilic cytoplasm. This favors a lymphoid population, most likely a lymphoma, diffuse large cell variant (Diff-Quik-stained smear, original magnification x40).

cin, vincristine, prednisone) regime followed by involved field radiation.

Discussion

Primary pulmonary lymphoma is defined as clonal lymphoid proliferation that affects 1 or both lungs (parenchyma and/or bronchi) in a patient with no detectable extrapulmonary involvement at diagnosis or during the subsequent 3 months of diagnosis.[4]

The incidence of primary pulmonary non-Hodgkin's lymphoma (PPNHL) peaks in the sixth and seventh decades of life, and the ratio of males to females is close to 1.[5] PLL-DLBCL often occurs in patients with underlying immunosuppression such as human immunodeficiency virus or those that have undergone solid organ (heart or lung) transplantation with cyclosporine A or OKT3 immunosuppression.[4] However, as in this case, PLL-DLBCL has been identified in nonimmunosuppressed patients and does not show any clinical difference

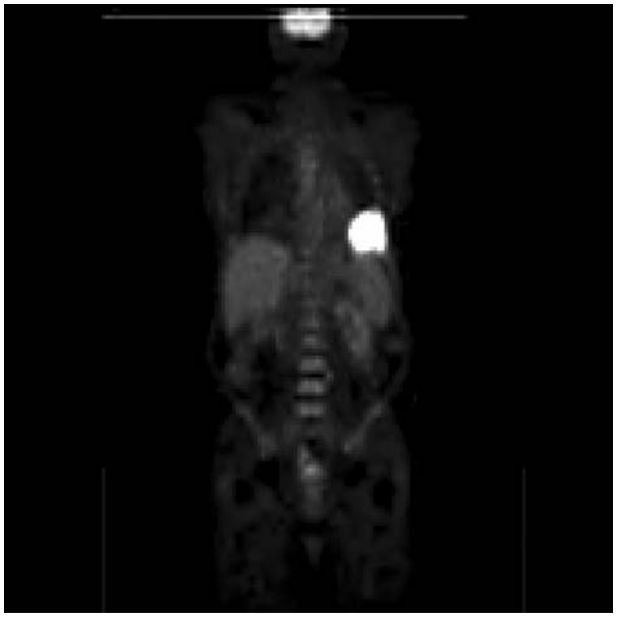

FIGURE 3 Fused PET-CT scan revealing that previously seen left lower lobe mass demonstrates avid FDG uptake with maximal standardized uptake value of 37.24. The mass appears stable in size and is about 3 × 2.1 in. There is small non-FDG avid left pleural effusion.
Abbreviations: FDG, fluorodeoxyglucose; PET-CT, positron emission tomography-computed tomography.

to the clinical presentation in the immunosuppressed setting.[2]

This case describes a patient who presented primarily with the respiratory symptoms of cough and shortness of breath with left-sided chest pain. Based on the current literature, cough, and dyspnea were the most frequently reported symptoms of primary NHL of the lung. However a significant percentage of patients presented with constitutional symptoms such as fever, weight loss, or fatigue and a smaller subset were asymptomatic at the time of diagnosis.[1]

The radiographic appearance of primary pulmonary lymphoma can show a variety of findings from nodule or mass (single or multiple) to atelectasis.[6] In various studies of patients with pulmonary DLBCL, the most common radiologic findings were a pulmonary infiltrate or mass lesion. Pleural effusion is also often present.[1,4] In this case, the patient was found to have a pulmonary mass and pleural effusion. However, any radiological abnormality of the lung parenchyma contains the possibility of lymphoma.[6]

An adequate tumor sample was obtained by a CT-guided transthoracic needle biopsy in our patient. Various case series report that surgical procedures such as video-assisted thorascopic surgery or open thoracotomy are required to make a definitive diagnosis in a large proportion of patients. A few studies have suggested that molecular techniques such as flow cytometry using bronchoalveolar lavage fluid may establish the diagnosis. However, more invasive approaches are superior for confirmatory diagnosis as there are a number of nonmalignant reactive conditions that can simulate the immunohistochemical findings in malignant lymphoma.[1,6]

TABLE 1 Staging classification for extranodal lymphomas[1]

Stage	Description
I E	Involvement of lung only (can be bilateral)
II 1E	Lung and hilar lymph nodes
II 2E	Lung and mediastinal lymph nodes
II 2EW	Lung and adjacent chest wall or diaphragm
III	Involvement of lung and of lymph nodes below diaphragm
IV	Diffuse involvement of 1 or more extralymphatic organs or tissues

In the current case, clinical staging workup was completed by bone marrow aspiration and PET and CT scans, which showed no evidence of extrathoracic lymphoma at the time of diagnosis. PET and CT has emerged as a highly sensitive and specific tool for the detection and localization of Hodgkin lymphoma and aggressive non-Hodgkin lymphoma. The current data indicate that mSUVs are much higher in DLBCL than in other primary pulmonary lymphomas.[7] In our case, the lung tumor displayed avid FDG uptake with an mSUV of 37.24. Further studies may be required to evaluate whether FDG uptake by pulmonary lymphomas has prognostic significance.

DLBCL of the lung is currently staged by using the Ann Arbor staging system with Cotswold modification, which was originally developed for staging of Hodgkin lymphoma and has been adapted for staging NHL.[8] The staging classification used for these extranodal lymphomas is shown in Table 1.[1] In our case the patient presented with stage I E as it involved lung parenchyma only.

The prognosis of patients with primary pulmonary NHL is known to be relatively favorable.[6] However, further studies are required to identify specific prognostic factors. A poor overall survival rate in patients with primary pulmonary lymphoma was found in patients with an elevated serum LDH level, non-MALT PPL, hilar/mediastinal LAP, B symptoms, or stage II disease or greater.[9] In various studies, the histological subtype of PPL (ie, MALT vs non-MALT subtype) has been considered the most important survival factor for all these

patients with the non-MALT tumors such as DLBCL having a worse prognosis.[6,7,9]

Although there are several treatment modalities available for pulmonary DLBCL including tumor resection, radiation, surgery followed by adjuvant treatment or chemotherapy alone, the therapeutic consensus has not been clearly established.[6,7] Our case describes a patient with limited stage DLBCL of the lung defined by Ann Arbor stage I. Most patients with nonbulky limited stage DLBCL regardless of tumor location are treated with combined modality therapy consisting of abbreviated systemic chemotherapy (ie, 3 cycles of CHOP [cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone]), the recombinant anti-CD20 antibody rituximab, and involved field radiation therapy.[10] More studies are required to evaluate the optimal modality of treatment for pulmonary DLBCL and in particular the role of early surgical intervention for nonbulky limited stage disease. Surgery may be considered the treatment of choice in the localized form of PPL if complete resection can be achieved.[11]

The patient described in this report was started on systemic chemotherapy with R-CHOP and completed 2 cycles before his treatment course was complicated by neutropenic fever and pneumonia. He did not tolerate treatment well, so his chemotherapy regime was eventually stopped.

Conclusion

DLBCL of the lung is a rare entity in terms of biological features, clinical presentation, and prognostic markers. Therapeutic options for this disease have not been well defined. Although the prognosis is relatively favorable, based on the current literature there is no therapeutic consensus on the optimal modality of treatment for DLBCL of the lung. We reviewed pertinent literature, and found that PET and CT scans may have a role in follow-up after treatment to enable us to distinguish between responding and nonresponding patients. This case also highlights the role of surgical intervention in decreasing tumor burden and consequently treatment related morbidity and mortality for nonbulky limited stage disease.

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