Pulmonary Manifestations of Lymphoma and Leukemia

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KEYWORDS

• Hematologic malignancies • Cancer • Pleural disease • Lymphoma • Leukemia
• Pulmonary hypertension • Lymphadenopathy

KEY POINTS

- Malignant lymphoma typically originates in the lymph nodes, but concomitant or primary presentations may also include parenchymal, endobronchial, or pleural disease.
- Myeloid sarcoma is an extramedullary manifestation of myeloid leukemia, which may occur before, during, or after cancer diagnosis. It may rarely present in the form of a pulmonary mass, endobronchial disease, pleural disease, or intrathoracic lymphadenopathy.
- Confirmation with cytology and/or flow cytometry is recommended to diagnose malignant pleural effusions in lymphoma and leukemia.
- After infection is excluded, pleural effusions in acute leukemia and myelodysplastic syndrome are often related to malignancy.
- Venous thromboembolism may present in patients with leukemia and lymphoma despite the presence of thrombocytopenia.

INTRODUCTION

Pulmonary disease can occur across the entire disease spectrum of hematologic malignancies. Although infectious processes are common in these immunosuppressed individuals, noninfectious causes account for up to half of the pulmonary manifestations found in hematologic malignancies and should be kept in mind when evaluating enigmatic pulmonary findings in this population.

Significant overlap exists among variants of lymphoma and leukemia. Lymphoid neoplasms may evolve into a leukemic picture, and leukemia may present with a mass lesion, more classically suggestive of a lymphoma. Intrathoracic disease is common in lymphoid disorders. In fact, 85% of individuals with Hodgkin lymphoma (HL) and 66% of those with non-Hodgkin lymphoma (NHL) may have pulmonary findings.[1] Although the most common abnormality affecting the respiratory system in myeloid disease includes infection, myelogenous leukemia and its precursors have distinct pulmonary presentations as well. This review highlights prominent noninfectious pulmonary complications of lymphoma, leukemia, and their precursors.

Mediastinal Lymphadenopathy

Malignant lymphomas are neoplasms of the lymphatic system that include HL and a heterogeneous group of tumors referred to as NHL. These malignancies initially affect lymph node groups with subsequent spread to other organs. Lymphoma typically affects the anterior mediastinum

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and may be part of more diffuse disease. The distribution of mediastinal lymphoma includes about 50% to 70% HL and 15% to 25% NHL.[2] Primary mediastinal lymphoma is rare and comprises 10% of lymphomas in the mediastinum. The 3 most common subtypes of mediastinal lymphoma include nodular sclerosing HL, lymphoblastic lymphoma, and large B-cell lymphoma.

HL and NHL are markedly different in tumor biology, clinical presentation, and therapeutic approach. HL has a bimodal incidence with a peak in young adulthood and again after the age of 50 years.[2] Reed-Sternberg cells are pathognomonic, and the nodular sclerosing subtype commonly affects the mediastinum.

Lymphoblastic lymphoma is a high-grade aggressive subtype of NHL that commonly affects the mediastinum at a mean age of 28 years.[2] Although blastic involvement of the bone marrow is common, if there is nodal predominant disease with less than 25% involvement in the bone marrow, it is categorized as a lymphoblastic lymphoma. Alternatively, if the disease burden is predominantly noted in the marrow and circulation with little nodal involvement, then it is categorized as T-cell acute lymphoblastic leukemia (ALL).[3]

Primary mediastinal B-cell lymphoma is a diffuse large B-cell lymphoma derived from the thymus, and it is the most common type of NHL involving the mediastinum in adults, with distinct clinical and biologic characteristics when compared with other lymphomas. It mainly affects young adults with a mean age of presentation of 30 years and a slight female predilection.[2,4] It accounts for 5% of aggressive lymphomas and typically presents with a rapidly growing anterior or superior mediastinal mass often resulting in tracheal compression.[5,6] HL and primary mediastinal B-cell lymphoma share several similarities, including similar genetic mutations and prominent fibrosis, but the presence of Reed-Sternberg cells and tumor markers enables histologic differentiation.[6] Patients may present with superior vena cava (SVC) syndrome, phrenic nerve palsy, dysphagia, hoarseness, bilateral breast swelling or chest pain, and productive cough.[4] Although initial involvement of the bone marrow or extrathoracic structures is not common, primary mediastinal B-cell lymphoma often invades within the thoracic cavity to the lungs, pleura, or pericardium.

The pattern of mediastinal involvement in HL is distinct compared with NHL (**Table 1**). Approximately 85% of patients with HL will have intrathoracic lymphadenopathy at the time of initial diagnosis, compared with 50% of individuals with NHL.[7,8] Intrathoracic disease may be incidentally detected on imaging studies due to a lack of respiratory symptoms, while occasionally symptoms related to compression of mediastinal structures ranging from mild cough to SVC syndrome may prompt the workup.

Other lymphoid neoplasms including ALL and chronic lymphocytic leukemia (CLL) may affect the mediastinum similar to lymphoma. Hilar and mediastinal involvement by CLL has been reported in autopsy and radiographic series.[9] Although it is classically an indolent disease, CLL may also evolve into malignant lymphoma. Richter syndrome is described in up to 10% of patients and is characterized by transformation into

Table 1
Radiographic patterns of lymphoma

Characteristics of	Hodgkin Lymphoma	Non-Hodgkin Lymphoma
Mediastinal disease	Nodular sclerosis most common abnormality Progressive and contiguous Asymmetric pattern Unilateral disease and single lymph node involvement less common	Large B-cell and lymphoblastic lymphoma most common abnormality Less predictable progression Less bulky Frequently not contiguous Single lymph node involvement may occur
Mediastinal predilection	Anterior mediastinum Superior mediastinum (prevascular, paratracheal), hilar, subcarinal, cardiophrenic, posterior mediastinum, internal mammary	Anterior mediastinum Posterior mediastinum Paracardiac node
Parenchymal disease	Often associated with mediastinal or hilar adenopathy	Frequently occurs in the absence of mediastinal disease

Data from Refs.[1,20,22,24,101,102]