Primary Extranodal Lymphoma of the Thorax

Seth J. Kligerman, MD[a,b,*], Teri J. Franks, MD[c], Jeffrey R. Galvin, MD[a,b,d]

KEYWORDS

• Lymphoma • Thorax • Extranodal • Primary • MALT • Thymus • Pleura

KEY POINTS

- Primary pulmonary lymphomas (PPLs) represent a pathologically heterogeneous group of disorders that often share imaging features, which include peribronchovascular nodules and masses or areas of nonresolving consolidation.
- Primary mediastinal B-cell lymphoma is an extranodal non-Hodgkin lymphoma (NHL) seen in younger patients that has imaging and pathologic features that demonstrate some degree of overlap with Hodgkin lymphoma (HL).
- Primary lymphomas of the pleural space are rare and associated with concomitant viral infections.

INTRODUCTION

Neoplasms originating in lymphoid tissue are common, 2015, it is estimated that there will be approximately 72,000 newly diagnosed cases of non-Hodgkin lymphoma (NHL) and 9000 newly diagnosed cases of hodgkin lymphomas (HLs) in the United States.[1] A vast majority of these cases represent systemic diseases that arise from and spread to lymphoid tissue throughout the body and most commonly involve lymph nodes, bone marrow, and spleen. Lymphoid tissue exists, however, in numerous places throughout the body and, therefore, malignant and nonmalignant lymphoid proliferations can be seen in and isolated to various organs and tissues. Although uncommon, these primary extranodal lymphomas occur throughout the thorax and can involve the lung, mediastinum, and pleura.

PRIMARY PULMONARY EXTRANODAL NEOPLASTIC LYMPHOID PROLIFERATIONS

Lymphomatous lesions of the lung can occur through 3 mechanisms. In most instances, either HL or NHL seeds the lung through hematogenous dissemination or directly invades the pulmonary parenchyma via extension from adjacent hilar or mediastinal lymph nodes. These secondary malignant manifestations are more common than primary pulmonary lymphoproliferative disorders because secondary pulmonary involvement can occur in up to 24% of patients with NHL and up to 38% of patients with HL.[2] The third mechanism, which is the least common, occurs when there is a primary clonal lymphoid proliferation that originates in the lung.[3] These primary pulmonary lymphoproliferative disorders are rare and represent only 0.3% of all primary pulmonary malignancies,

Disclaimer for T.J. Franks: The views expressed in this article are those of the author and do not reflect the official policy of the Department of Defense or the United States Government.

[a] Chest Imaging, Department of Radiology and Nuclear Medicine, University of Maryland School of Medicine, 22 South Greene Street, Baltimore, MD 21201, USA; [b] Chest Imaging, American Institute for Radiologic Pathology, 1010 Wayne Ave, Suite 320, Silver Spring, MD 2091, USA; [c] Pulmonary and Mediastinal Pathology, Department of Defense, Joint Pathology Center, 606 Stephen Sitter Ave, Silver Spring, MD 20910-1290, USA; [d] Pulmonary and Critical Care Medicine, Department of Internal Medicine, University of Maryland School of Medicine, 22 South Greene Street, Baltimore, MD 21201, USA

* Corresponding author. Department of Radiology and Nuclear Medicine, University of Maryland School of Medicine, 22 South Greene Street, Baltimore, MD 21201.

E-mail address: skligerman@umm.edu

Radiol Clin N Am 54 (2016) 673–687

http://dx.doi.org/10.1016/j.rcl.2016.03.002

0033-8389/16/$ – see front matter

less than 1% of all NHL cases and only 3% to 4% of all extranodal manifestation of NHL.[4]

Primary pulmonary lymphomas (PPLs) represents a monoclonal proliferation of lymphoid tissue in the lungs in patients with no detectable extrathoracic lymphoma for at least 3 months after initial diagnosis.[2] These lesions arise from bronchus-associated lymphoid tissue (BALT), which is 1 component of the complex pulmonary lymphatic system. BALT is a specific type of mucosa-associated lymphoid tissue (MALT) in the lungs that is involved with the body's immune response to inhaled antigens. BALT represents an organized cluster of central B cells surrounded by a peripheral rim of T cells and lacks germinal centers when antigenic stimulation is absent. Although afferent lymph channels are absent, BALT drains to regional lymph nodes via efferent lymphatic channels.

Although absent at birth, BALT begins to develop in infants and young children due to antigenic stimulation. Although this tissue regresses in healthy adults, it reappears in those who undergo acute or chronic antigenic stimulation and can be seen in adults with acute or chronic infection, chronic bronchial inflammation (asthma), collagen vascular diseases, or AIDS and in cigarette smokers (**Fig. 1**).[5,6] It is the chronic antigenic stimulation of BALT that leads to a variety of benign and malignant lymphoid lesions that are visualized on imaging. In some instances, chronic stimulation of BALT can lead to various types of lymphoid lesions, such as follicular bronchiolitis, lymphocytic interstitial pneumonia, and MALT lymphoma, arising in a single patient.[6–9]

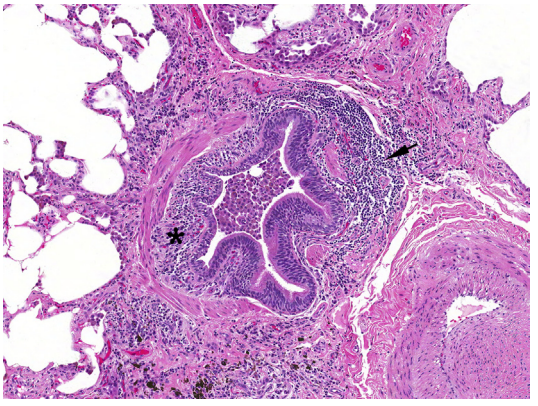

Fig. 1. Smoking-related BALT hyperplasia. Medium-power microscopic image (original magnification, ×100; hematoxylin-eosin stain) demonstrates a small airway with submucosal and adventitial lymphoid infiltrates (*arrow*) typical of BALT hyperplasia. This is associated with smoking-related small airway injury, including respiratory bronchiolitis, characterized by luminal accumulation of yellow-brown pigmented macrophages; submucosal organization; and chronic inflammation (*asterisk*).

The most common type is the more indolent low-grade marginal zone B-cell lymphoma of MALT lymphoma, which represents between 60% and 80% of cases of PPL.[10,11] The more aggressive diffuse large B-cell lymphomas (DLBCLs) represent approximately 10% to 25% of cases and are the second most common form of PPL.[6,12] Other rarer causes of PPL include follicular lymphoma, Burkitt lymphoma, and T-cell lymphoma. Primary pulmonary HL PPHL is extremely rare and usually arises from direct extension of mediastinal disease or is associated with disseminated disease. Fewer than 70 cases of PPHL have been reported in the literature since 1927.[13] Lymphomatoid granulomatosis (LG) is a rare form of PPL with a poor overall survival. Although it is generally accepted as a lymphoproliferative disorder, controversy exists in regards to its diagnosis, taxonomy, and relationship to other forms of PPL.[14]

MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA (LOW-GRADE MARGINAL ZONE B-CELL LYMPHOMA OF MUCOSA-ASSOCIATED LYMPHOID TISSUE)

As discussed previously, MALT lymphoma is the most common PPL to involve the lung. Most patients are in their sixth to seventh decades of life and slightly more than half of patients are women.[11,15] At the time of diagnosis, approximately half of the patients are asymptomatic. When symptoms are present, they are usually nonspecific and include cough, mild dyspnea, chest pain, and hemoptysis. Extrapulmonary manifestations, which are restricted to general signs, such as fever and weight loss, given the definition of PPL, occur in less than one-quarter of patients.[3]

A majority of patients have some form of chronic antigenic stimulation, which is associated with growth of BALT.[16] In 1 large meta-analysis, 45% of patients had a history of smoking, 9% of patients had a history of exposure to toxic substances, and 19% had a known preexisting lung disease.[15] Collagen vascular diseases are seen in approximately 10% to 29% of patients with MALT lymphoma, a majority of which have Sjögren syndrome.[17–19] Although usually associated with the development of more aggressive lymphomas, MALT lymphoma can also be seen in patients with systemic lupus or patients with rheumatoid arthritis (RA), particularly in those with RA treated