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Special issue on diagnosis of primary hematolymphoid disease of the lung and pleura

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ABSTRACT

This special issue is dedicated to the pathologic diagnosis of commonly encountered pulmonary hematolymphoid tumors and the reactive mimickers. The articles focused on the interesting topics of primary malignant hematolymphoid diseases of the lung and pleura. We hope this update is educational for general surgical pathologists and hematopathologists when dealing with challenging pulmonary lesions of lymphoid infiltrates in their daily practices.

Lymphoproliferative disorders detected as primary lesions in the lung are rare, representing only 0.3% of all primary pulmonary malignancies, 1.0% of all the cases of non-Hodgkin lymphoma and 3.0–4.0% of all extra nodal manifestations of non-Hodgkin lymphoma.[1,2] With advancements in the technology of CT scan-guided biopsy and/or microcoil insertion followed by VATS resection of lung nodules, more specimens are available for pathological evaluation. This increase in specimen availability may lead to an increase in reported Lymphoproliferative disorders detected as primary lesions in the lung. Additionally, the endobronchial ultrasound and electromagnetic navigation bronchoscopy improves the sensitivity of transbronchial biopsy in the diagnosis of peripheral lung nodules.

"At first glance the lungs may seem uncomplicated, but many wise men have gone astray in their labyrinths," as quoted by Dr. Aveill A. Liebow, who was considered the "founding father" of modern pulmonary pathology, in a foreword to the first edition of "Spencer's Pathology of the Lung" in 1962. The lesson we learned from the pioneers are still instructive for our today's practice in regards to the diagnosis of primary pulmonary lymphoma and mimickers.[3]

The pulmonary lymphoid system is well developed and complex, which is composed of two main compartments: the pulmonary primary lymphatics and the bronchus-associated reactive lymphoid tissue (BALT) .[4] The local pulmonary lymphoid tissues are critical for initiation of the adaptive immune responses to various stimuli such as virus or bacterial infection, autoimmune disorders and/or foreign antigens. Many other cells with coordinating function in the pulmonary lymphoid system include dendritic cells, Langherhans cells, macrophages, and plasma cells.[4] The understanding of normal lymphoid anatomy of the lung as well as its immunology and pathophysiology is helpful in diagnosis of the radiologic and pathologic findings of the pulmonary lymphoid lesions.

The classification of the spectrum of pulmonary lymphoproliferative disorders is evolving, and the World Health Organization (WHO) classification of lymphoid neoplasm recently emphasized the importance of immunophenotypes in correlation with clinical features.[1] The first comprehensive study of pulmonary lymphomas, published by Dr. Saltzstein in the 1963, used the term "pseudolymphoma" of the lung to describe a lymphoid lesion that consisted predominantly of lymphocytes, often with numerous reactive follicles.[5] He concluded that the low-grade cytologic appearance of many lymphocytic masses in the lung, the presence of germinal centers, the infrequency of lymph node involvement, and the indolent clinical behavior were the result of a reactive lymphoid process masquerading as lymphoma.[5,6]

The benign lymphoproliferative disorders of the lung include benign intraparenchymal lymph nodes, nodular lymphoid hyperplasia, follicular bronchiolitis, lymphocytic interstitial pneumonia (LIP) and IgG4-related sclerosing disease.[1,2] These conditions represent distinct histologic patterns that are characterized by hyperplasia of the bronchial-associated lymphoid tissue (BALT). LIP and follicular bronchiolitis often present as diffuse parenchymal lung diseases, mimicking interstitial lung disease. Intraparenchymal lymph node and nodular lymphoid hyperplasia commonly present as pulmonary nodules, mimicking malignancy.[5,6]

This special issue is dedicated to the pathologic aspects of common encountered pulmonary lymphomas and the mimickers of reactive conditions. The primary goal of this special edition is to give an update on the diagnostic features incorporated with the current WHO criteria.[1] We invited a group of experts in the field to share their perspectives about the diagnostic histopathological features, differential diagnosis, and recent classification, while also provide up-to-date guidance on the

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application of immunohistochemistry and molecular testing of commonly encountered primary hematolymphoid lesions in the lung, adjacent pleural or mediastinal locations with emphasis on their clinical relevance for treatment.

1 In the first article, Dr. Fiona E. Craig and Dr. Katalin Kelemen from Mayo Clinic review the recent progress in the diagnosis of pulmonary B-cell lymphoma including pulmonary extranodal marginal zone lymphoma (MALToma) and DLBCL, and the main differential diagnosis such as nodular lymphoid hyperplasia (pulmonary pseudo-lymphoma).
2 The second article is contributed by Dr. Flavia Rosado from UTSW and Dr. Ling Guo from Ohio state University to update the criteria in the diagnosis of Hematolymphoid neoplasms with a plasma cell phenotype including extramedullary plasmacytoma, amyloidoma, plasmoblastic lymphoma (PBL), and primary effusion lymphoma (PEL).
3 The third article is contributed by Dr. Pan Zengguan and Dr. Mirna Xu from Yale University to discuss the most recent progress in the diagnosis of T- cell lymphomas including PTCL, ALCL and NK/ T-cell lymphoma of nasal type.
4 The fourth article is contributed by Dr. Joo Song and colleagues at City of Hope to summarize the reactive lymphoproliferative disorders in the lung and mimickers of lymphoma including Lymphomatoid granulomatosis(LYG), IgG4 related disease, Castleman disease, graft-versus-host disease (GvHD), and post-transplant lymphoproliferative disorders (PTLD).
5 The fifth article is contributed by Dr. Weina Chen from UTSW and Dr. Joseph Khoury from MD Anderson to overview myeloid neoplasms involving the lung and pleural space.
6 The final article is written by Dr. Frankin Fuda and Dr. Weina Chen from UTSW will introduce the significance of application of flow cytometry as an ancillary test in the diagnosis and differential diagnosis of hematolymphoid disease in the lung and pleural space.

The diagnosis of pulmonary lymphoid lesions can be challenging, as broad differential exists with a spectrum of pathological interface from benign reactive proliferative and atypical proliferation to neoplastic lesions. The practical diagnostic approach will integrate clinical, radiologic and pathologic findings. The routine histopathology is combined with immunophenotyping by flow cytometry or immunohistochemistry and molecular pathology analysis, which are helpful in the diagnosing all types of pulmonary lymphomas and guidance of appropriate treatment.

In summary, this special issue is dedicated to the pathologic aspects of commonly encountered pulmonary hematolymphoid tumors. We thank all the authors who contribute articles on these interesting topics of primary malignant hematolymphoid diseases of the lung and pleura. We hope this update is educational for general surgical pathologists and hematopathologists when dealing with challenging pulmonary lesions of lymphoid infiltrates in their daily practices.

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