

Rare primary  
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## Rare Primary Pulmonary Marginal Zone Lymphoma Presenting with Incidental Pulmonary Nodules

### Introduction:

Primary pulmonary lymphoma (PPL) is a rare neoplasm accounting for 0. 5-1% of pulmonary malignancies [1]. It can present with nonspecific symptoms, or in some cases, it can be detected as an incidentaloma during surveillance of other thoracic pathologies. Here, we present a case of an elderly male who was seen at his primary care physician's (PCP) office for follow up of ascending aortic aneurysm. Computed tomography (CT) of the chest without contrast revealed pleural-based right upper lobe, central right lower lobe, and left upper lobe pulmonary nodules. Pathology confirmed the diagnosis of low-grade B-cell non-Hodgkin's lymphoma (NHL) consistent with marginal zone lymphoma.

### Case Presentation:

An 83-year-old male with past medical history of mild Alzheimer's dementia, non-ischemic cardiomyopathy, aortic regurgitation, and an ascending aortic aneurysm measured at 4. 1 cm presented to the pulmonology clinic with an abnormal CT of the chest. He was seen by his PCP recently for follow up of ascending aortic aneurysm and had a CT chest without contrast performed which showed 14. 8 mm pleural-based nodular density in the posterior medial right upper lobe, irregular 20. 5 mm right lower lobe nodule, and a 2 mm left upper lobe partially calcified nodule. He had no respiratory or constitutional symptoms. He was a lifelong non-smoker without any significant occupational exposures. [ <sup>18</sup> F]Fluorodeoxyglucose-positron

emission tomography with CT (  $^{18}\text{F}$  -FDG PET/CT) was performed showing multiple  $^{18}\text{F}$  -FDG avid nodules in the right upper lobe, right lower lobe, and left upper lobe. Initially thought to be inflammatory in nature, a 3-month follow up CT chest was recommended however, patient opted for CT-guided transthoracic biopsy. Histopathology revealed low-grade B-cell NHL consistent with marginal zone lymphoma. Patient was referred to oncology for further management.

### Discussion:

Primary pulmonary lymphoma (PPL) is a rare clinicopathologic entity, which comprises less than 0.3% of all primary lung malignancies, less than 1% of all cases of NHL, and 3% to 4% of all extranodal NHL [2-4]. It is defined as a lymphoma localized to the lung in a patient with no prior history of extrapulmonary disease at the time of diagnosis or up to 3 months thereafter [2, 5].

The most common type of PPL is the marginal zone lymphoma (MZL) of mucosa-associated lymphoid tissue (MALT), otherwise known as MALT lymphoma or “ MALToma,” which comprises 70-80% of all cases of PPL [6]. These MALT lymphomas are thought to arise from clonal proliferation of marginal zone B cells of bronchial-associated lymphoid tissue (BALT) [2]. Approximately 40-50% of pulmonary MALT lymphomas are positive for t(11; 18)(q21; q21) [7]. This unique translocation is responsible for the creation of a fusion RNA transcript from the *API2* (*apoptosis inhibitor 2*) and the *MALT1* genes which induces activation of the NF- $\kappa$ B pathway resulting in cell proliferation [8, 9]. Unlike gastric MALT lymphoma which is associated with

*Helicobacter pylori*, MALT lymphoma of the lung has not been linked to any infectious or specific autoimmune conditions, although there have been case reports associated with tuberculosis [10]. Like gastric MALT lymphoma, it is postulated that pulmonary MALT lymphoma can progress to high-grade diffuse large B-cell lymphoma (DLBCL), however, this has not been well studied [1].

The clinical presentation is highly variable. Most patients are clinically asymptomatic or present with constitutional symptoms, cough, hemoptysis, or dyspnea; B-symptoms are uncommon. Median age at time of diagnosis is 60 years, however, it has also been diagnosed in younger individuals who are usually immunocompromised [2]. One-third of patients have concurrent autoimmune conditions such as rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus and up to 40% of patients have monoclonal gammopathy as well [11].

Radiographic appearance is variable, ranging from consolidations to inconspicuous nodules or masses. The presence of ground glass opacities, air bronchograms, and bronchiectasis may confound the diagnosis suggesting an infectious or inflammatory process. Presence of air bronchograms is due to relative airway-sparing nature of the disease [2]. Hilar lymphadenopathy is present in approximately 30% of cases [12].

Histologic confirmation is required for definitive diagnosis and is characterized by reactive lymphoid follicles with diffuse infiltration by small lymphocytes and lymphoid proliferation which leads to expansion of the marginal zone; lymphoepithelial lesions (infiltrates of 5 or more neoplastic B-

cells into the bronchial epithelium) support the diagnosis but are not required for diagnosis [2]. Lymphoepithelial lesions can be detected with immunohistochemical stains for cytokeratin (which highlights epithelial cells only but not lymphocytes) and CD20 (which highlights lymphocytes but not epithelial cells). As the MALT lymphoma grows, the bronchial wall and adjacent lung parenchyma can be replaced but necrosis or airway obstruction is rare [2].

Primary pulmonary MALT lymphoma is associated with a good prognosis; 5-year and 10-year survival rates are 90% and 70% respectively [13, 14]. Currently, there are no established guidelines for the management of pulmonary MZL. Considering the indolent course of disease, observation and treatment for symptomatic disease are both reasonable options. Treatment can be considered for symptomatic patients. Therapeutic options include surgical resection, chemotherapy, and radiation therapy. Localized or peripheral lesions can be treated with surgical resection or moderate-dose radiation therapy [15, 16]. Patients with widespread disease not amenable to resection may be treated with single agent chemotherapy, such as rituximab, which has been shown to be effective [17]. Combination chemotherapy with cyclophosphamide, vincristine, and prednisone (CVP) can be considered as well [18]. There is no consensus on whether surgical resection is associated with better outcomes. Further prospective clinical research is greatly needed to determine the optimal treatment modality.

### Conclusion:

Nonspecific presentation and indolent course makes the diagnosis of primary pulmonary lymphoma very challenging and often leads to misdiagnosis or delayed diagnosis. This diagnosis should especially be suspected in individuals who present with lung nodules but lack usual risk factors for primary non-small cell and small cell lung cancer, similar to our patient.

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