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Nodular AL Amyloidosis — An Unusual Etiology of a Solitary Pulmonary Nodule

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INTRODUCTION

Solitary pulmonary nodules (SPN) are defined as single intraparenchymal opacities less than 3 centimeters. The differential diagnosis of the SPN is broad. AL amyloidosis is a protein conformational disease which occurs when certain monoclonal light chains develop an unstable tertiary structure with resultant polymerization of insoluble amyloid fibrils that deposit in the extracellular space of sundry tissues. In the lung, diffuse interstitial amyloid deposition is the most common form of the disease.

A 76-year-old man and current smoker has a medical history including stage IIC prostate cancer in remission and active stage pT1N0 distal esophageal adenocarcinoma. As a part of his oncologic evaluation, chest CT captured a well-circumscribed, non-spiculated 2.1cm mass without calcifications adjacent to the major fissure in the right middle lobe (RML). The patient underwent navigational bronchoscopy and transbronchial biopsy of the RML nodule. Pathology revealed a small number of plasma cells showing lambda light chain restriction. Liquid chromatography tandem mass spectrometry detected a peptide profile consistent with amyloid light-chain (AL) amyloidosis. The overall findings were most consistent with nodular pulmonary amyloidosis. The patient underwent a bone marrow biopsy, which showed monoclonal kappa positive plasma cells but negative Congo red stain, consistent with MGUS.

Nodular pulmonary amyloidosis is an uncommon cause of SPN, and an extremely rare form of amyloidosis, constituting only 1.4% of the total amyloidosis cases found at autopsy. Treatment generally necessitates chemotherapy with a goal of suppressing the formation of light chains. Widespread disease, limited response to therapy, and presence of cardiac involvement all portend worse prognosis. Amyloidosis continues to be a great mimicker and it remains important to keep it on a differential diagnosis.

CASE DESCRIPTION

A 76-year-old Caucasian man and current 60 pack-year smoker has a past medical history including hypertension, hyperlipidemia, chronic kidney disease, permanent atrial fibrillation, stage IIC prostate cancer status-post radiation and androgen deprivation therapy, and active stage pT1N0 distal esophageal adenocarcinoma status-post endoscopic submucosal dissection.

As a part of his oncologic evaluation, chest computed tomography imaging captured a well-circumscribed, non-spiculated 2.1cm mass without calcifications adjacent to the major fissure in the right middle lobe. A subsequent positron emission tomography scan to evaluate the probability of malignancy did not show fludeoxyglucose avidity of the nodule. Given the history of two malignancies, the decision was made to pursue a tissue diagnosis. The patient underwent navigational bronchoscopy and transbronchial biopsy of the right middle lobe nodule. Pathology revealed fragments of amyloid and a small number of plasma cells showing lambda light chain restriction (**Figure 1**). Liquid chromatography tandem mass spectrometry detected a peptide profile consistent with amyloid light-chain (AL) amyloidosis. The overall findings were most consistent with nodular pulmonary amyloidosis. Cardiac magnetic resonance imaging showed abnormal, delayed gadolinium enhancement in a pattern consistent with cardiac amyloidosis. Given that nodular pulmonary amyloidosis is frequently associated with underlying indolent B-cell lymphoma[1], the patient underwent a bone marrow biopsy, which showed monoclonal lambda-positive plasma cells but negative Congo red stain, consistent with monoclonal gammopathy of undetermined significance (MGUS). The patient was referred to pulmonology, cardiology, and oncology for management of his pulmonary amyloid, cardiac amyloid, and MGUS, respectively.

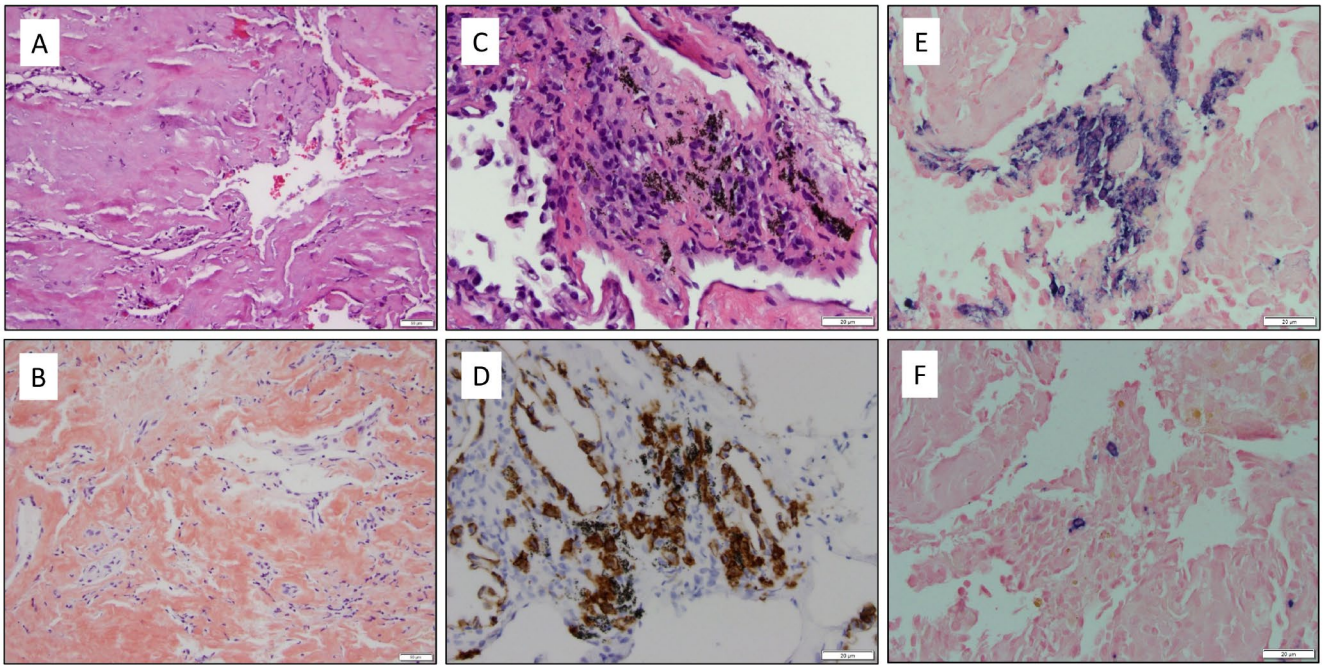

Figure 1: Fine needle aspiration from the right middle lobe nodule revealed fragments of amorphous eosinophilic material consistent with amyloid (A, hematoxylin & eosin, 40x). The amyloid was positive for Congo red stain (B, 40x) and showed apple green birefringence under polarized light. In the biopsy specimen, there was a plasma cell infiltrate associated with the amyloid and within the lung parenchyma (C, hematoxylin & eosin, 40x). The plasma cells were positive for CD138 immunohistochemical stain (D, 40x) and showed lambda light chain restriction by in situ hybridization (ISH) (E, lambda ISH, 40x; F, kappa ISH, 40x).

Solitary pulmonary nodules (SPN) are most commonly defined as single intraparenchymal opacities less than 3 centimeters, whereas lesions greater than 3 centimeters are defined as a 'mass' and are more commonly malignant; however, no size criteria reliably distinguishes benign versus malignant SPN.[2] The differential diagnosis of the SPN is broad, including neoplastic, inflammatory, infectious, vascular, traumatic, and congenital etiologies.[2,3] See **Table 1**. History of smoking, advanced age, and prior diagnosis of malignancy all increase the probability that the SPN may be malignant.[3,4]

DISCUSSION

AL or primary amyloidosis is a protein conformational disease which occurs when certain monoclonal light chains develop an unstable tertiary structure with resultant polymerization of insoluble amyloid fibrils that deposit in the extracellular space of sundry tissues.[5] With an average age of diagnosis of 65 years, it is most typically seen as an systemic disease with multiorgan involvement.[5] In the lung, diffuse interstitial amyloid deposition is the most common form of the disease.[5] Nodular pulmonary amyloidosis is an uncommon cause of SPN, and an extremely rare form of amyloidosis, constituting only 1.4% of the total amyloidosis cases

Table 1: Differential diagnosis of the solitary pulmonary nodule

Malignant neoplasms	• Bronchogenic carcinoma • Carcinoid tumor • Pulmonary lymphoma • Pulmonary sarcoma • Solitary metastasis
Benign neoplasms	• Hamartoma • Adenoma • Lipoma • Chondroma
Infectious inflammatory	• Granuloma (tuberculous or fungal) • Nocardia • Round pneumonia • Abscess
Non-infectious inflammatory	• Rheumatoid arthritis • Granulomatosis with polyangiitis • Sarcoidosis • Amyloidosis
Vascular	• Arteriovenous malformations • Infarction • Hematoma
Congenital	• Bronchial atresia
Miscellaneous	• External object • Pseudotumor • Pleural thickening

Adapted from Erasmus et al.[7] and Mosmann et al.[8]

found at autopsy.[6] Treatment generally necessitates chemotherapy with a goal of suppressing the formation of light chains.[5] Widespread disease, limited response to therapy, and presence of cardiac involvement all portend worse prognosis.[5]

In our patient, given two active malignancies, longstanding tobacco use, and older age, it was prudent to obtain a tissue diagnosis to rule out a neoplastic etiology of SPN in this high-risk patient. Amyloidosis continues to be a great mimicker and it remains important to keep it on a differential diagnosis.

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