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Case Report

Amyloid nodule and primary pulmonary lymphoma in the same lung: Radiologic-pathologic correlation of a rare combination

Andrei Jipa, MD^{a,*}, Jonathan Glaab, MD^b

^a Radiology Resident, MetroHealth Medical Center and Case Western Reserve School of Medicine, Cleveland, OH, USA

^b Department of Radiology, MetroHealth Medical Center and Case Western Reserve School of Medicine, Cleveland, OH, USA

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ABSTRACT

A 61-year-old man presented for lung cancer screening with low dose CT. A spiculated right apical nodule suspicious for primary lung malignancy and an indeterminate small basilar consolidation were identified. PET/CT was notable for increased FDG uptake in the basilar consolidation. Transthoracic needle biopsy of both lesions was performed which lead to pathologic diagnoses of pulmonary amyloid nodule for the apical nodule and pulmonary extramarginal zone lymphoma of the mucosa associate lymphoid tissue for the basilar consolidation. While incidental findings are common in lung cancer screening CT, exceedingly rare diagnoses or combinations of diagnoses may also be encountered. This case also underscores the value of pathologic diagnosis in cases of indeterminate lung nodules.

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Introduction

Low dose CT is a widely accepted method of screening for lung cancer in high risk patients. While incidental findings commonly occur in this setting, the large number of patients screened also increases the probability of rare diagnoses and rare combinations of diagnoses. In this case a combination of a rare benign diagnosis and an uncommon incidental malignant diagnosis were made in the same patient.

Case report

A 61 year old asymptomatic male smoker presented for low dose lung CT lung cancer screening at the referral of his primary care physician. The initial study identified a suspicious 1.6 cm spiculated apical right upper lobe nodule and a small right lower lobe consolidation felt to represent infection and inflammation. A Lung-RADS category 4X was assigned due to the high risk apical nodule. PET/CT and pulmonary consultation were recommended in the original report.

* Corresponding author.

E-mail address: ajipa@metrohealth.org (A. Jipa).

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Fig. 1 – Contrast enhanced CT chest demonstrates spiculated nodule in the peripheral right upper lobe. CT characteristics are suspicious for primary lung malignancy.

The patient was referred to pulmonary medicine who recommended CT chest with contrast and whole body PET/CT. The apical nodule and a 1-2 cm right lower lobe consolidation (Figs. 1 and 2) were again noted on CT. PET/CT demonstrated increased FDG uptake in the basilar consolidation (Fig. 3A) but not in the apical nodule (Fig. 3B). There was no other significant abnormality on whole body PET/CT. Given the high risk location, history and morphologic features the nodule was deemed radiographically indeterminate and further consultation with thoracic surgery was initiated. At this point the basilar consolidation also displayed an indeterminate combination of radiologic and metabolic characteristics consistent with infectious, inflammatory, or neoplastic etiology.

Thoracic surgical consultant recommended tissue sampling of both the nodule and the consolidation. CT guided core needle biopsy was successfully performed by the hospital's radiology department for both lesions (Fig 4A and B). While the procedure was complicated by pneumothorax, the patient was immediately decompressed with a pleural catheter and had a rapid recovery, being discharged the next day.

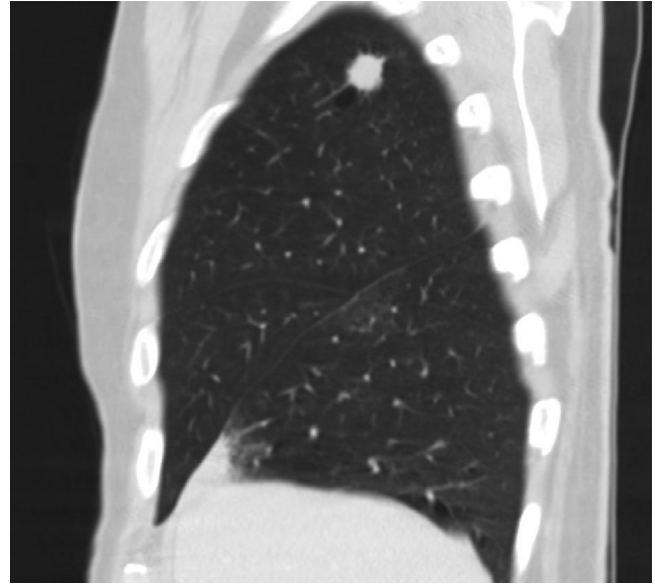


Fig. 2 – Contrast enhanced CT chest again demonstrates the right upper lobe nodule as well as a right lower lobe consolidation abutting the major fissure. Serendipitously, both abnormalities were visible on the same sagittal slice.

Biopsy yielded unexpected results for both nodules. The apical nodule contained amyloid with moderately cellular lymphoplasmacytic infiltrate. Amyloid was confirmed as congophilic material demonstrating classic apple-green birefringence on polarized microscopy (Fig. 5). A pathologic diagnosis of benign amyloid nodule or amyloidoma was made.

The basilar nodule contained dense lymphoid tissue with characteristics of lymphoma (Fig. 6). Immunostaining was positive for CD20, BCL-2 but negative for CD5, CD10 and CD42 suggesting an extranodal marginal zone lymphoma, also known as a lymphoma of the mucosa-associated lymphoid tissue (MALT) (Fig. 7A-D). The patient was referred to medical and radiation oncology. Given the lack of other suspicious

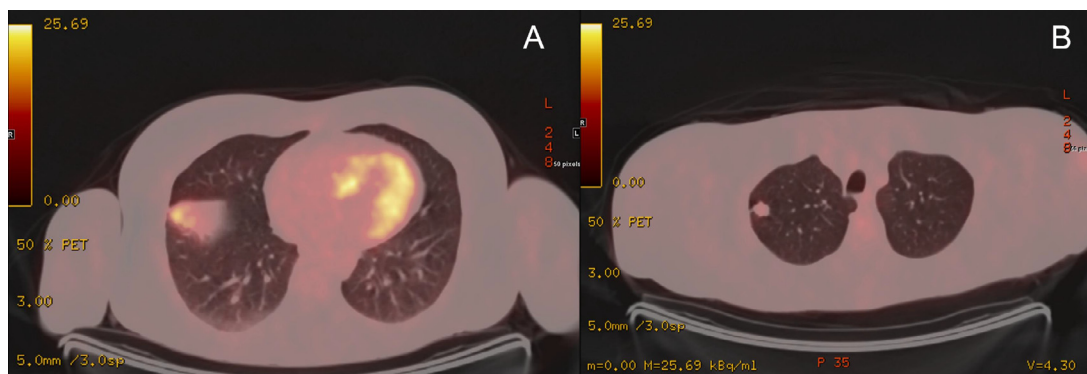


Fig. 3 – A (right) FDG PET/CT demonstrates increased FDG uptake in the right lower lobe consolidation. This radiographic and metabolic appearance is nonspecific to infectious, inflammatory, or neoplastic lesions. Image 3B (left) FDG PET/CT does not demonstrate increased FDG uptake in the right upper lobe nodule.

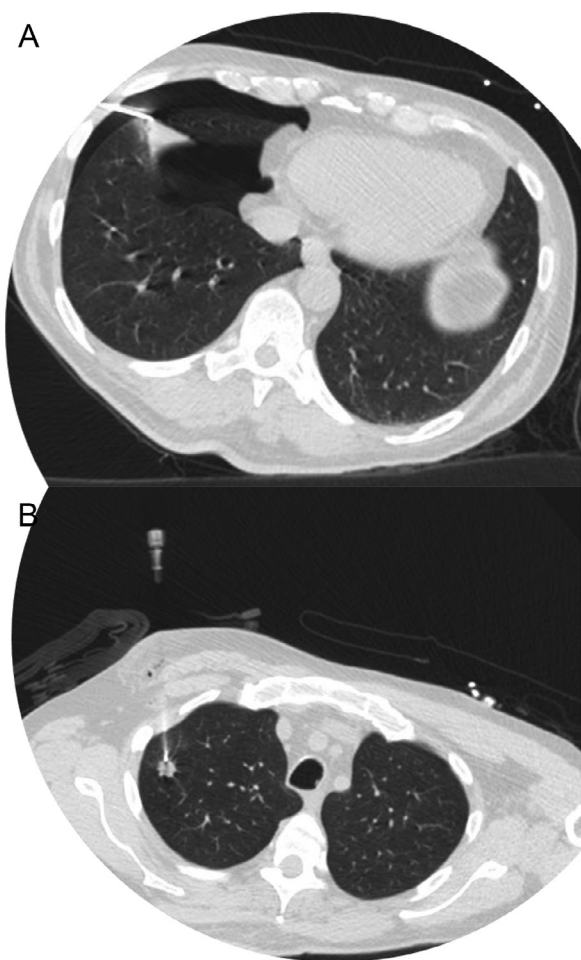


Fig. 4 – A (top) Noncontrast CT performed during biopsy demonstrates needle tip in the right lower lobe consolidation and developing pneumothorax. Image 4B (bottom) noncontrast CT performed during biopsy demonstrates needle tip in the right upper lobe nodule.

areas on PET/CT, this was determined to be local disease and the patient was offered definitive treatment with radiotherapy alone.

The patient underwent radiotherapy with a total dose to 36 Gray delivered in 10 fractions. Radiotherapy was well tolerated and follow up CT 8 weeks post treatment demonstrated significant decrease in size of the basilar consolidation (Fig. 8A and B).

Discussion

Amyloid nodules are rare benign lung lesions representing a focal deposit of amyloid material; they have been alternatively been called amyloidomas or focal amyloidosis. Importantly, amyloid nodules are not associated with and are distinct from the pulmonary manifestations of systemic forms of amyloidosis. These are rare lesions of uncertain prevalence, without

clear risk factors or associations although most have been reported in adults [1]. The highest prevalence has been reported in the sixth decade of life [1]; however this may be biased due to increased imaging of older adults.

Typically, amyloid nodules present as solitary solid lung nodules, often with chest radiographic and CT characteristics indistinguishable from nonmetastatic primary lung tumors [1,2]. In this case, an amyloid nodule presented with a suspicious spiculated morphology. Due to the inability to distinguish amyloid nodules from primary lung cancers, they have traditionally been diagnosed by surgical pathology following lung resection [3].

While amyloid nodules have been incidentally detected using amyloid-specific nuclear medicine tracers [4], their FDG-PET characteristics have yet to be systematically described. The lack of increased metabolism observed in this case, however is consistent with the pathophysiologic process of amyloid deposition.

Given their rarity and similar CT features to primary lung cancer, diagnosis of amyloid nodule is exceeding difficult without biopsy and this diagnostic consideration should not change standard management of high-risk lung nodules. While radiologic diagnosis is difficult; the pathologic findings are both classic and distinctive; once a pathologic diagnosis can be reached the patient can be safely spared surgical treatment or radiotherapy.

Compared to amyloid nodule, pulmonary MALT lymphoma is a more common entity. The most common primary lung lymphoma, these are indolent malignancies that tend that demonstrate slow lymphangitic and peribronchial spread. In late stages distant metastases are possible. They are primarily tumors of adulthood with a maximum incidence during the sixth decade of life [5–7]. Pathogenesis may involve a bacterial infectious agent, specifically *Chlamydia psittaci* or *Achromobacter xylosoxidans* and active research is being undertaken in this direction [7]. There is an increased risk of development in patients with autoimmune disease (especially Sjogren syndrome), HIV, systemic amyloidosis, or lymphoid interstitial pneumonia [5,6]. Tumors either tend to be diagnosed in 2 clinical scenarios: cough or dyspnea associated with extensive lymphomatous involvement of the lung or an incidental finding of CT performed for other reasons [5–7].

Pulmonary MALT lymphomas have a protean appearance on CT. The most common presenting abnormality reported is pulmonary consolidation, although the disease can also present as pulmonary nodules or ground glass opacities. Air bronchograms may be present in larger consolidations [5,6,8,9]. Disease can be unifocal or multifocal, unilateral or bilateral on presentation [6,9]. A retrospective study of 53 cases reported 44% as presenting with consolidations with 66% with bilateral lesions [8], although a smaller retrospective series of 24 cases [9] reported consolidations in most cases and bilateral abnormalities in most cases on presentation. Pulmonary MALT lymphomas, like most lymphomas, demonstrate increased FDG uptake [5,6]. In our case, the patient presented with a single FDG avid pulmonary consolidation.

Given their varied radiologic appearance, pulmonary MALT lymphoma may be considered a differential diagnosis for many different imaging patterns on lung CT, but should be especially suspected in cases of persistent pulmonary con-

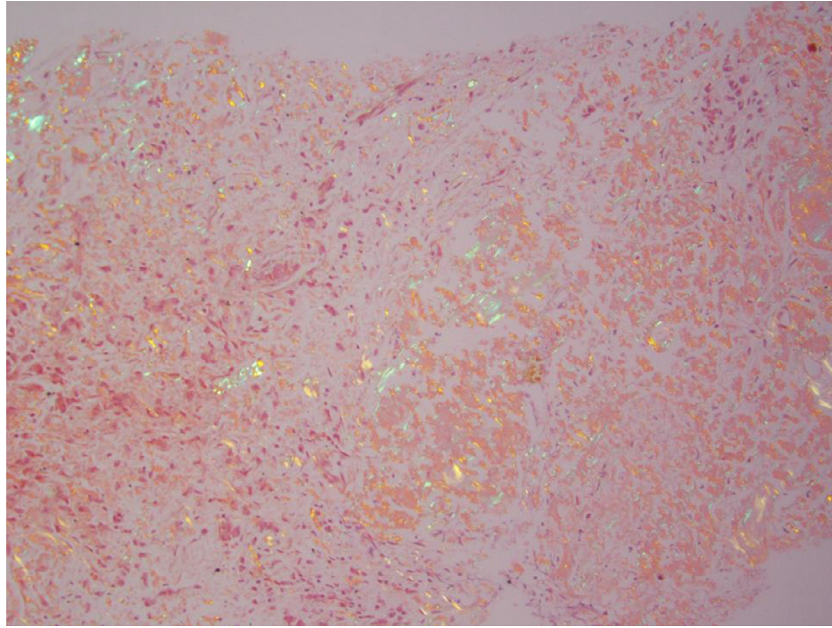


Fig. 5 – Congo Red Stain, polarized microscopy under 20x magnification demonstrates congophilic material with apple-green birefringence consistent with amyloid.

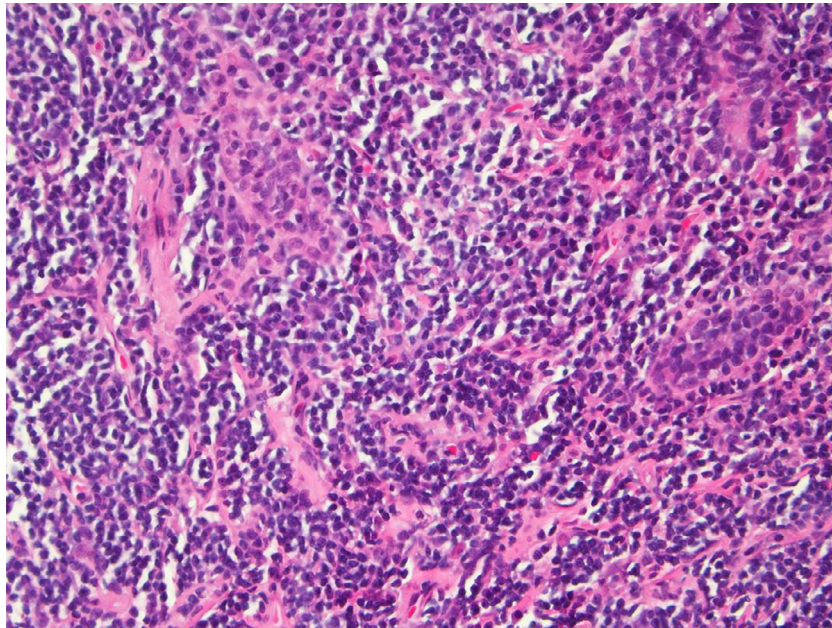


Fig. 6 – Standard H&E stain under 40x magnification demonstrates dense lymphocytic infiltrate.

solidations. Consolidations detected during screening such as this case are technically not nodules and therefore not triaged using Lung-RADS. PET/CT is a valuable tool in diagnosis. A lack of FDG avidity would make lymphoma very unlikely but increased FDG uptake is seen in both benign and malignant processes.

The prognosis for pulmonary MALT lymphomas, and indeed for MALT lymphomas in general is excellent. Treatment with radiotherapy alone for local disease or radiotherapy with rituximab for advanced disease is effective. There is a risk of late transformation to histologically and clinically aggressive forms of lymphoma; unfortunately this risk is unpredictable.

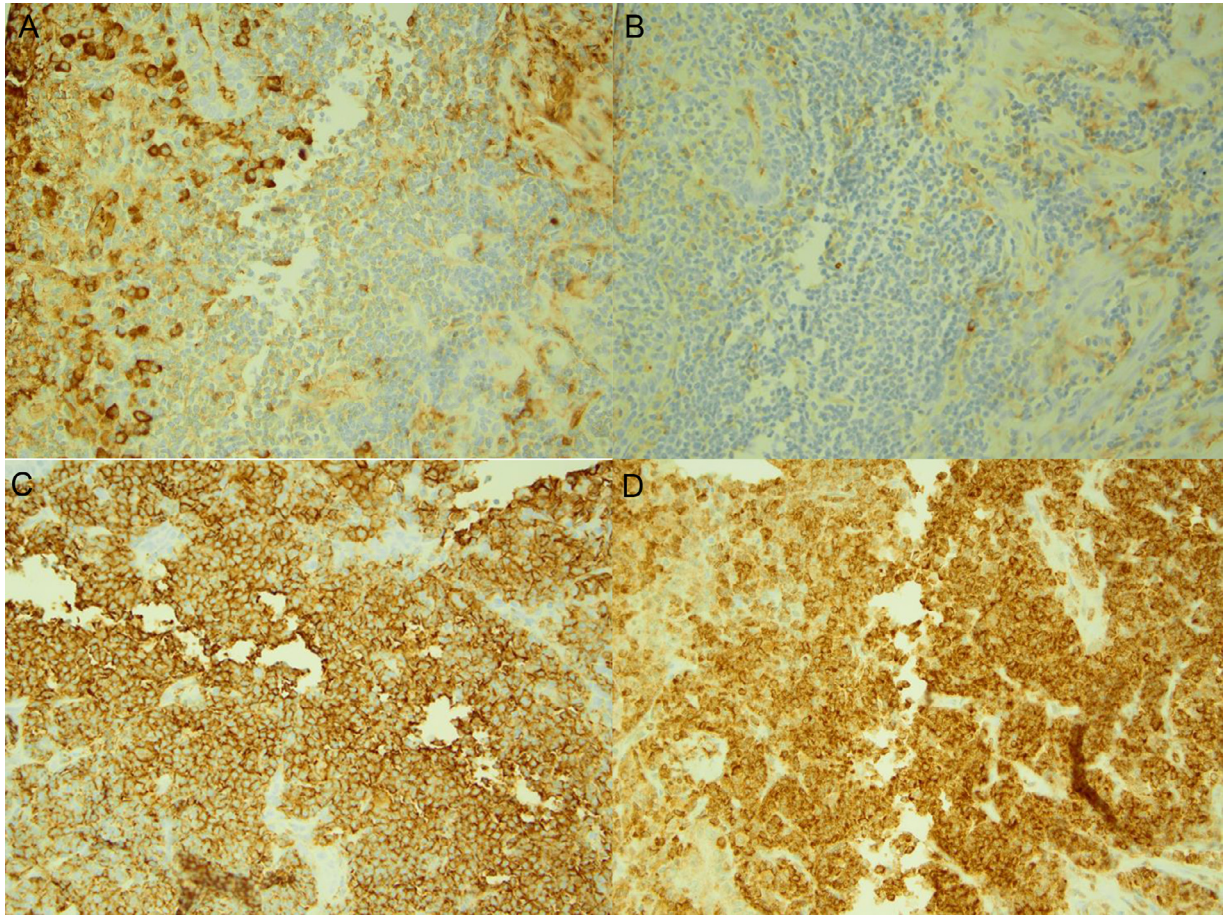


Fig. 7 – Figure 7A (top left) and figure 7B (top right). Immunostaining demonstrates significantly more cells positive for kappa light chain (7A) than lambda light chain (7B) suggesting a clonal lymphocyte population consistent with lymphoma. Figure 7C (bottom left). The cells stain positive for CD20, indicating B cell lineage Figure 7D (bottom right). The cells stain positive for BCL-2, consistent with marginal zone lymphoma.

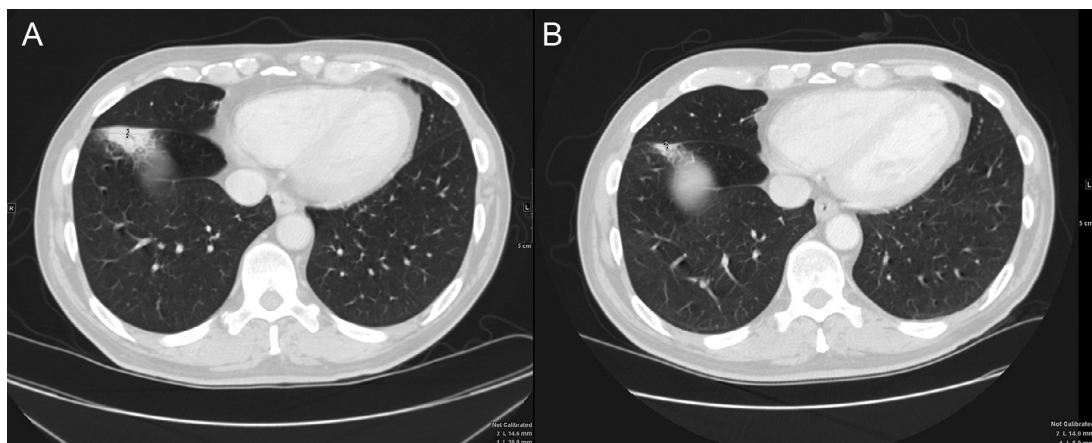


Fig. 8 – A (Right) Initial contrast-enhanced CT demonstrates pulmonary MALT lymphoma presenting as right lower lobe consolidation. Figure 8B (Left). Follow up study performed 4 weeks after completion of radiotherapy demonstrates significantly decreased size of the right lower lobe consolidation consistent with treatment response.

Conclusion

While incidental findings are a common occurrence with lung cancer screening CT, the combination of a rare benign lesion and an uncommon lymphoma is exceedingly rare and has not been reported before. The case underscores the value of biopsy where imaging findings are indeterminate and the value of radiology-pathologic correlation.

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