Southwest Journal of Pulmonary, Critical Care & Sleep

Journal of the Arizona, New Mexico, Colorado and California Thoracic Societies
www.swjpcc.com

March 2024 Pulmonary Case of the Month: A Nodule of a Different Color

Lewis J. Wesselius MD
Pulmonary Department
Mayo Clinic Arizona
Scottsdale, AZ USA

History of Present Illness

The patient is a 73-year-old woman from Wisconsin seen in January 2024 for lung nodules. She had been followed by her physician in Wisconsin for lung nodules but had never had a biopsy or specific diagnosis. She reported that the nodules "waxed and waned." Her Wisconsin physician suggested she be evaluated in Arizona.
She has occasional cough attributed to paroxysmal nocturnal dyspnea, but denies sputum production, fever, chills or shortness of breath

Past Medical History, Family History and Social History

- Rheumatoid arthritis diagnosed in her 30s, although not currently on any treatment.
- Breast cancer 2006, treated with chemoradiation
- Osteoporosis
- Family history: negative for lung cancer or other lung disorders
- Social History: Lifelong nonsmoker

Medications

- None

Physical Examination

- Unremarkable

Laboratory

- Normal CBC
- Cocci serology: negative
- Rheumatoid factor: elevated 61 U/ml (normal < 15)
- Anti-cyclic citrullinated peptide antibody: negative
- Erythrocyte Sedimentation Rate: normal

Radiology

A thoracic CT of the chest done in Wisconsin in November 2023 showed an 18 mm nodule in medial right lower lobe (RLL, Figure 1A) and several other smaller nodules noted, largest other nodule in left lower lobe (LLL, Figure 1B, blue arrow).

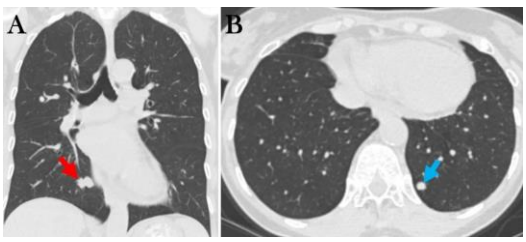

Figure 1. Selected images from thoracic CT done November 2023 showing RLL mass (A, red arrow) and LLL mass (B,

blue arrow). To view Figure 1 in a separate, enlarged window click here.

What is the ***next appropriate step*** in her evaluation?

1. Repeat the thoracic CT scan
2. Bronchoscopy
3. Positron emission tomography (PET) scan
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

A PET scan had been performed in Wisconsin at the time of her thoracic CT scan (Figure 2).

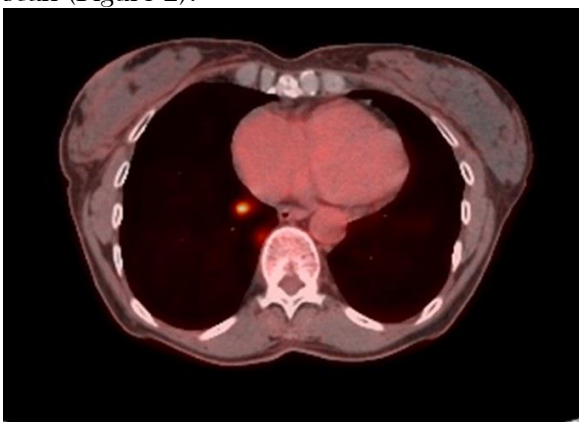

Figure 2. Image from PET scan done November 2023 showing increased fludeoxyglucose F18 (FDG) uptake in the RLL. To view figure 2 in a separate, enlarged window click here.

None of the other lesions had a detectable increase in FDG uptake.

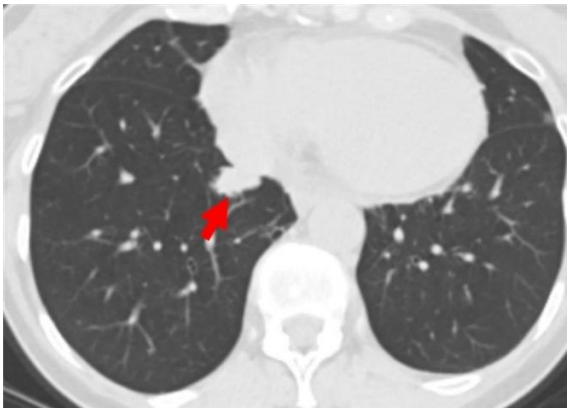

Figure 3. Repeat CT scan showed an increase in the size of the RLL nodule (red arrow). To view figure 3 in a separate, enlarged window click here.

What is the ***next appropriate step***?

1. Bronchoscopy
2. Follow-up thoracic CT scan in 3 months
3. Needle biopsy
4. 1 or 3
5. Any of the above

Correct!
4. 1 or 3

The lesion in the RLL is enlarging and has increased FDG uptake suggesting malignancy. Delaying 3 months to repeat the CT scan would accomplish nothing. Which technique for biopsy depends on many factors the size and location of the lesion and includes local resources and expertise. Robotic bronchoscopy seemed a better option than a CT- guided biopsy, particularly given the location deep in the pulmonary parenchyma which increases the chances of a pneumothorax (Figure 4).

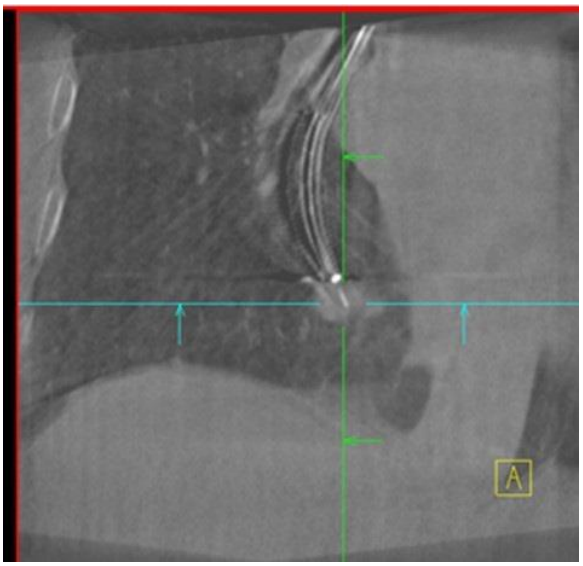

Figure 4. Robotic bronchoscopy showing the biopsy forceps in the lesion. To view figure 4 in a separate, enlarged window click here.

The biopsy results are shown in Figure 5 with positive staining for Congo red.

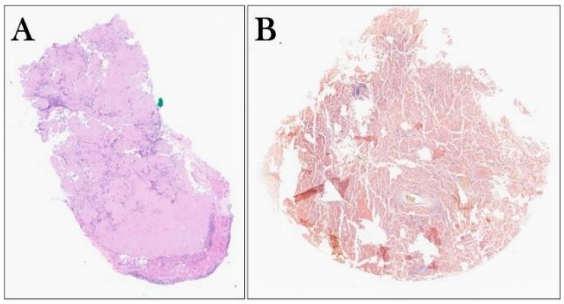

Figure 5. Histology of lung biopsy showing hematoxylin and eosin (H&E) staining (A) and Congo red staining (B). To view figure 5 in a separate, enlarged window click here.

The positive staining in this clinical situation for ***Congo red indicates***?

1. Amyloidosis
2. Asbestosis
3. Idiopathic non-specific interstitial fibrosis (NSIP)
4. Lung carcinoma
5. Usual idiopathic pulmonary fibrosis

Correct!
1. Amyloidosis

The "brick red" staining on the Congo red stain indicates the presence of amyloid. In situ hybridization showed the presence of lambda chain plasma cells (Figure 6).

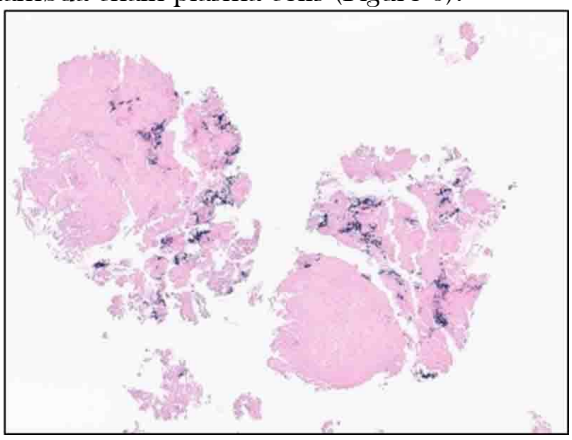

Figure 6. In situ hybridization for lambda chain positive cells. To view figure 6 in a separate, enlarged window click here.

What should be ***done next***?

1. Daratumumab in combination with bortezomib, cyclophosphamide, and dexamethasone
2. Begin mycophenolate
3. Begin prednisone 30 mg daily
4. Observation with follow-up
5. Total body MRI to search for underlying malignancy

Correct!
4. Observation with follow-up

There are 3 types of pulmonary amyloidosis (1,2):

- Nodular pulmonary amyloidosis;
- Diffuse alveolar-septal amyloidosis;
- Tracheobronchial amyloidosis.

Nodular pulmonary amyloidosis is often an incidental finding on chest imaging and usually represents localized immunoglobulin light chain or mixed immunoglobulin light chain/heavy chain amyloidosis. The mean age of patients is 67 with a male/female ratio of 3:2. Nodular amyloidosis usually presents at peripheral subpleural locations of variable size and can be bilateral. Usually the nodules

are small, but cases up to 15 cm have been reported.

Which of the following disease(s) have been ***associated with nodular pulmonary amyloidosis***?

1. Lymphoma
2. Adenocarcinoma of the lung
3. Sjogren's syndrome
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

Some studies suggest an association with underlying lymphoproliferative disorder in the spectrum of extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (MALT lymphoma) (3). There also may be an association with Sjogren's syndrome. In general, nodular amyloidosis is managed conservatively, with excision performed in some cases. Some patients will progress and develop systemic amyloidosis requiring chemotherapy. Unless systemic disease develops, the prognosis of nodular pulmonary amyloidosis is very good.

References

1. Milani P, Basset M, Russo F, Foli A, Palladini G, Merlini G. The lung in amyloidosis. Eur Respir Rev. 2017 Sep 6;26(145):170046. [CrossRef] [PubMed]
2. Khan NA, Bhandari BS, Jyothula S, Ocazionez D, Buryanek J, Jani PP. Pulmonary manifestations of amyloidosis. Respir Med. 2023 Nov-Dec;219:107426. [CrossRef] [PubMed]
3. Grogg KL, Aubry MC, Vrana JA, Theis JD, Dogan A. Nodular pulmonary amyloidosis is characterized by localized immunoglobulin deposition and is frequently associated with an indolent B-cell lymphoproliferative disorder. Am J Surg Pathol. 2013 Mar;37(3):406-12. [CrossRef] [PubMed]