

AMSER Case of the Month:

70-year-old female with chronic dry cough

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Patient Presentation

- **HPI:** 67-year-old female presenting for chronic intermittent nonproductive cough associated with post-nasal drip, rhinorrhea, and occasional shortness of breath ongoing for the last several years. Symptoms have progressed over the past month.
- **PMH:** Hypertension. Hyperlipidemia.
- **SHx:** Never smoker.

What Imaging Should We Order?

ACR Appropriateness Criteria

American College of Radiology
ACR Appropriateness Criteria®
Chronic Cough

Variant 1:

Chronic cough lasting more than 8 weeks. No known risk factors for lung cancer. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
Radiography chest	Usually Appropriate	☼
CT chest with IV contrast	May Be Appropriate	☼☼☼
CT chest without IV contrast	May Be Appropriate	☼☼☼
MRI chest without and with IV contrast	Usually Not Appropriate	○
MRI chest without IV Contrast	Usually Not Appropriate	○
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☼☼☼☼

Findings (Unlabeled)



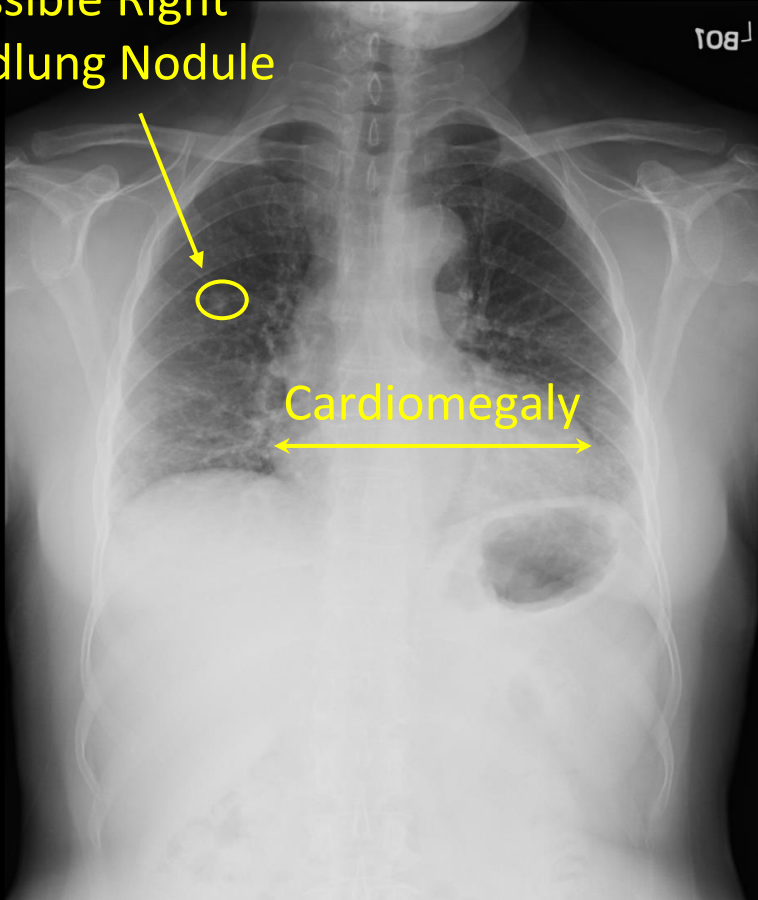
PA



Lateral

Findings (Labeled)

Possible Right
Midlung Nodule



Lower Lung
Interstitial
Prominence

Cardiomegaly

PA



No prior chest
radiographs
available for
comparison.

Chest CT
follow-up
recommended.

Lateral

ACR Appropriateness Criteria

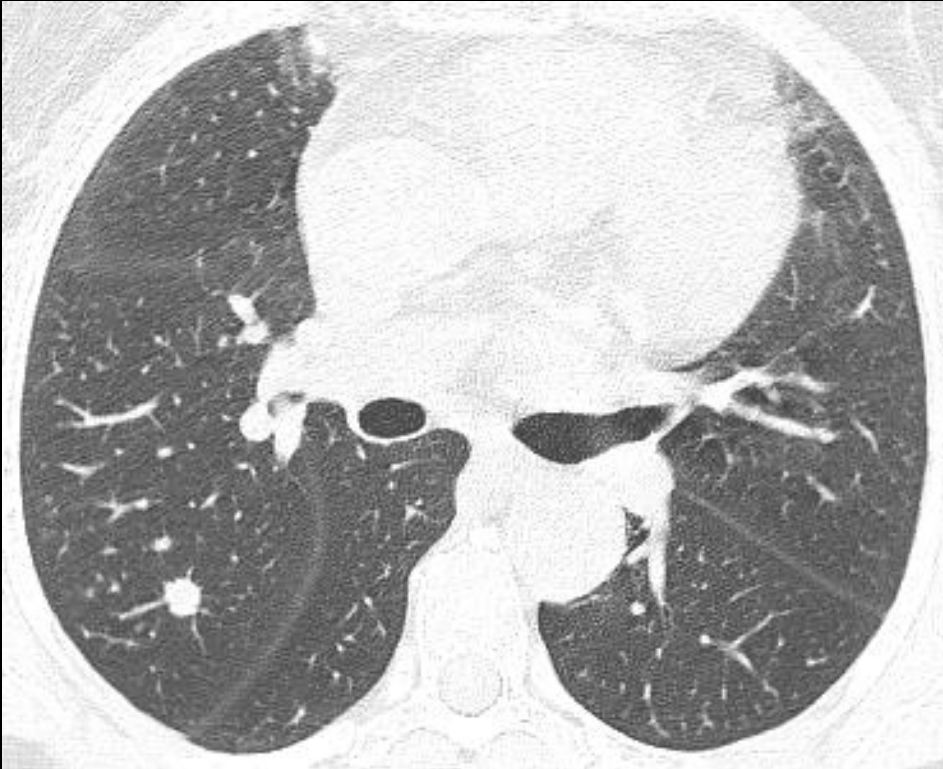
American College of Radiology
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Incidentally Detected Indeterminate Pulmonary Nodule

Variant 1:

Adult greater than or equal to 35 years of age. Incidentally detected indeterminate pulmonary nodule on chest radiograph. Next imaging study.

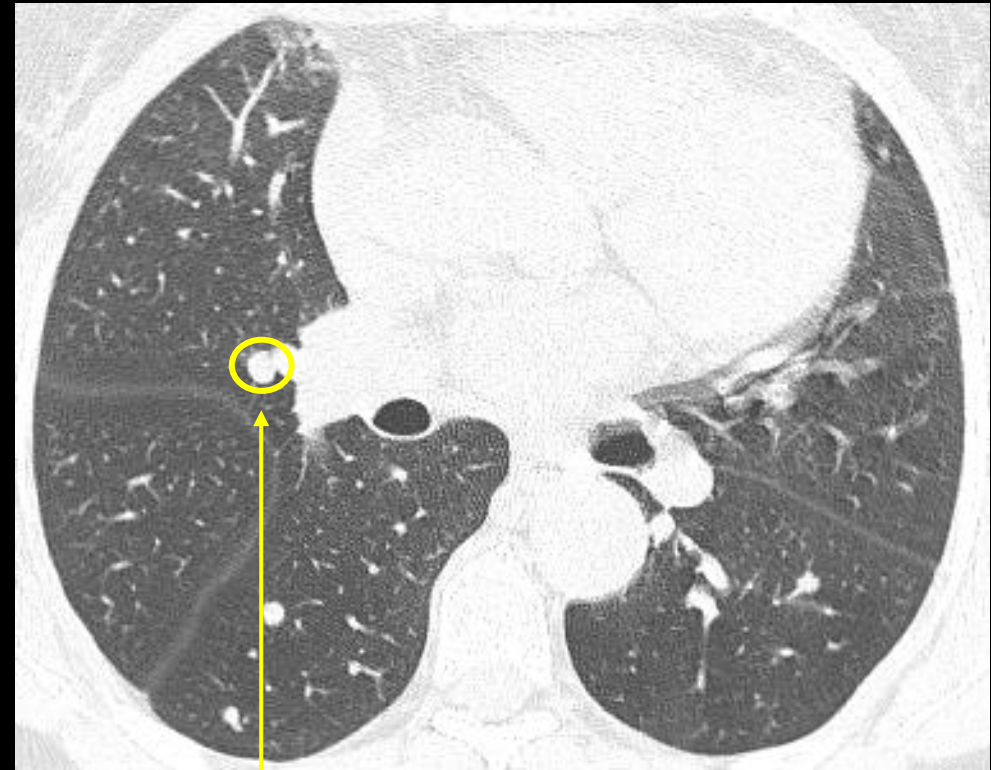
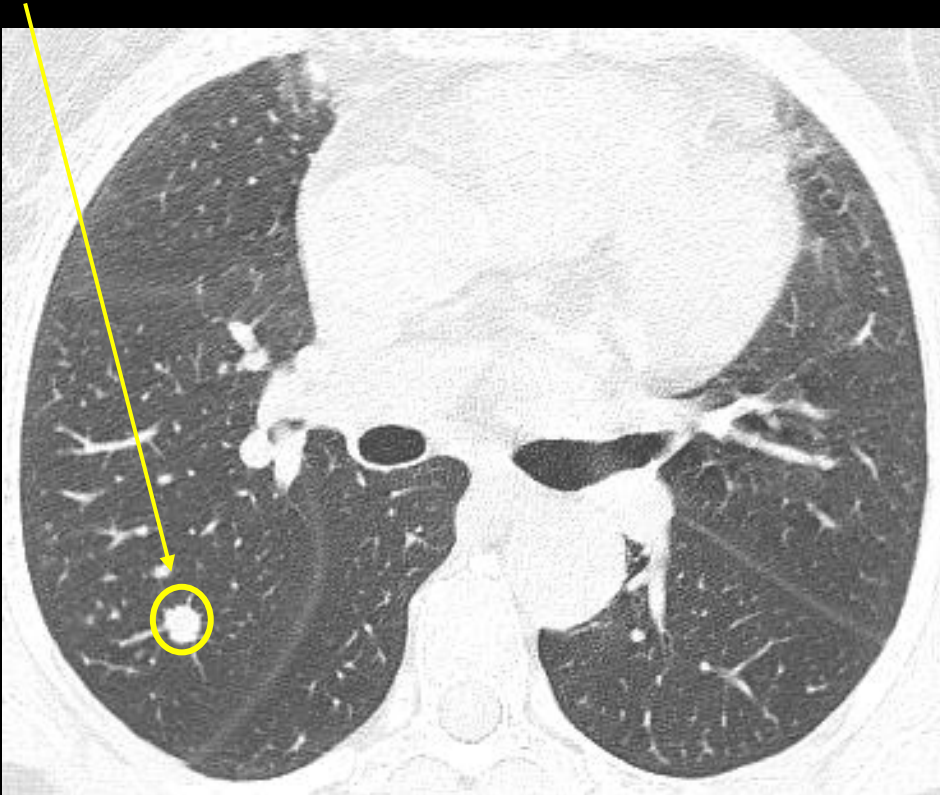
Procedure	Appropriateness Category	Relative Radiation Level
CT chest without IV contrast	Usually Appropriate	☼☼☼
Radiography chest	May Be Appropriate	☼
Image-guided transthoracic needle biopsy	Usually Not Appropriate	Varies
MRI chest without and with IV contrast	Usually Not Appropriate	○
MRI chest without IV contrast	Usually Not Appropriate	○
CT chest with IV contrast	Usually Not Appropriate	☼☼☼
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
FDG-PET/MRI whole body	Usually Not Appropriate	☼☼☼
FDG-PET/CT whole body	Usually Not Appropriate	☼☼☼☼

Findings (Unlabeled)



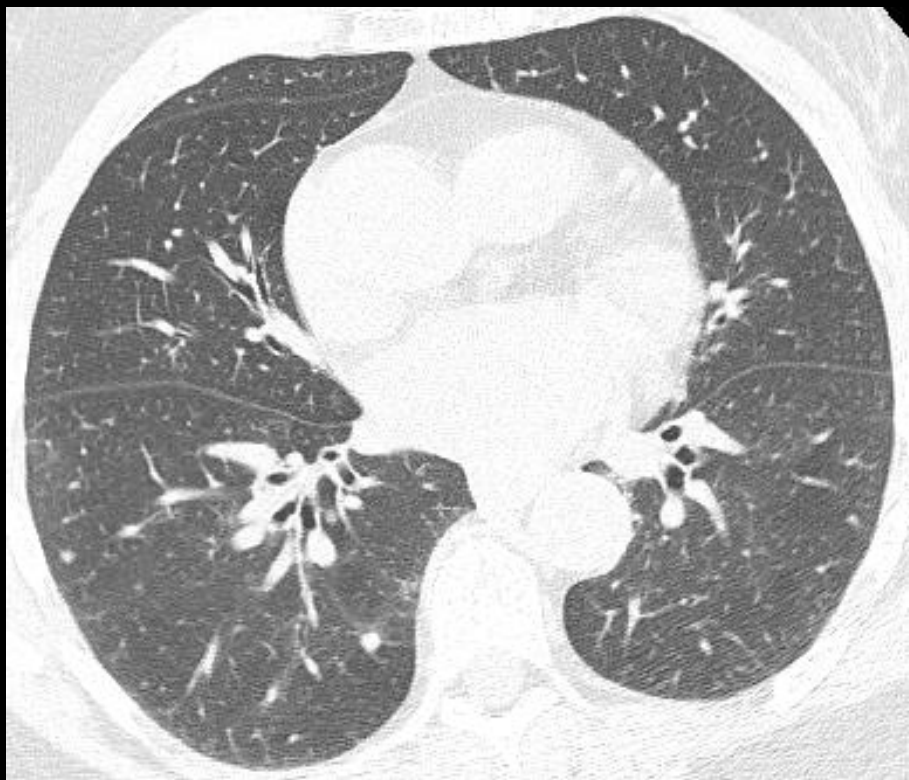
Solid, round 8 mm nodule
with smooth and well-
defined margins

Findings (Labeled)



6 mm Nodule

Findings (Unlabeled)

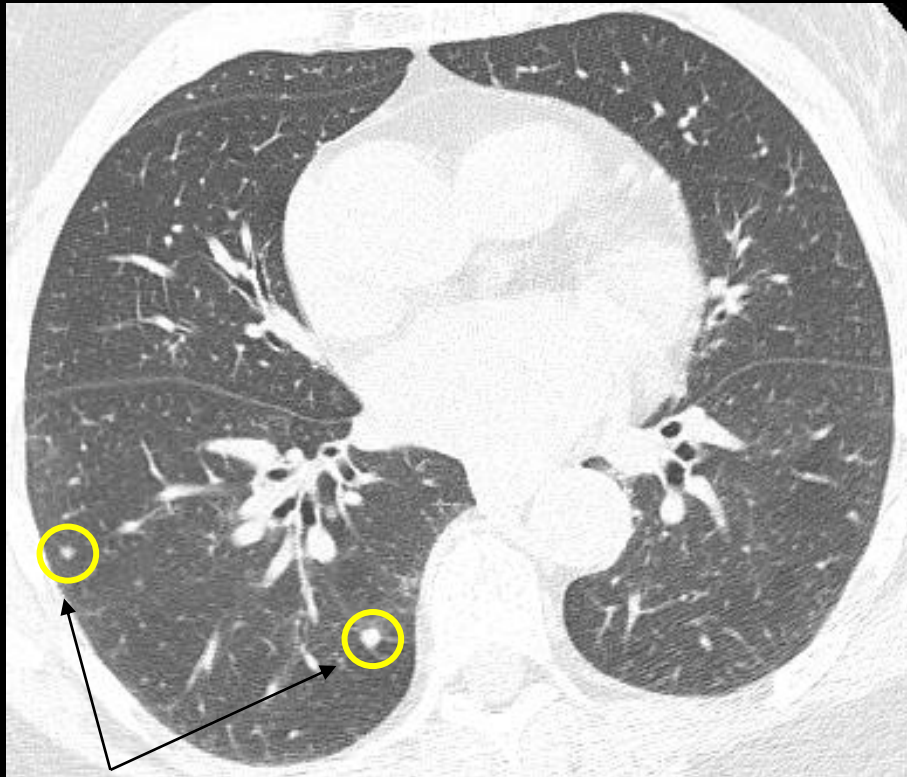


Inspiratory



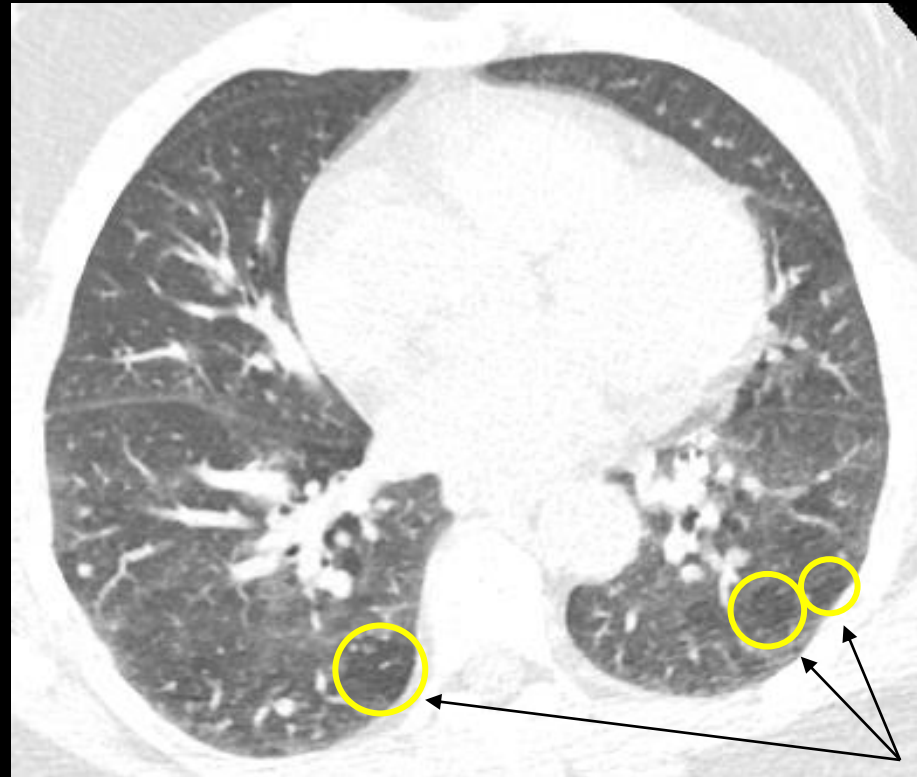
Expiratory

Findings (Labeled)



Scattered
Nodules

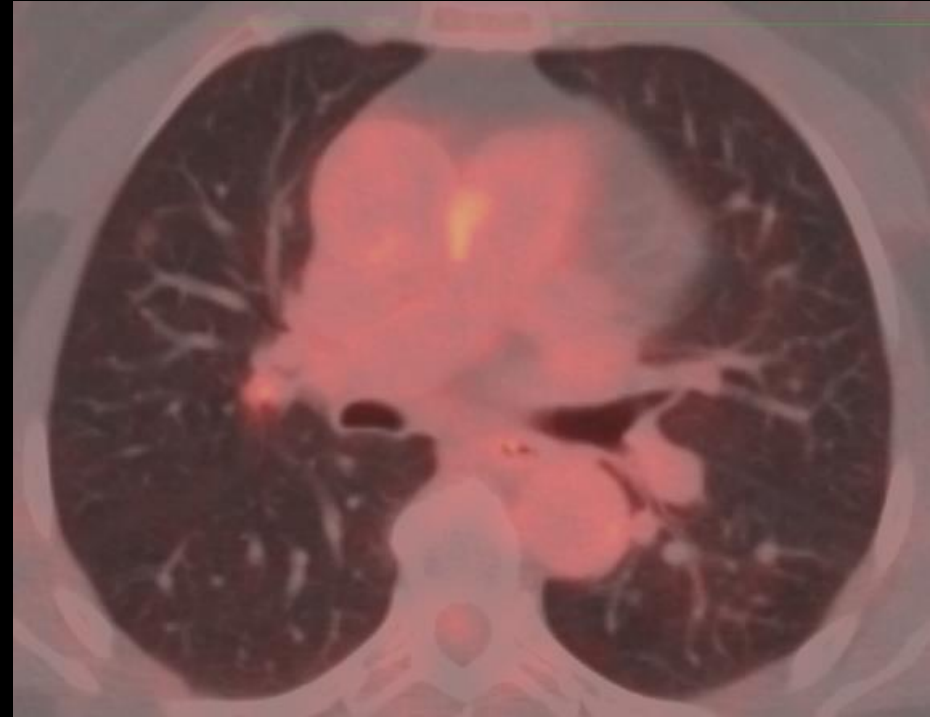
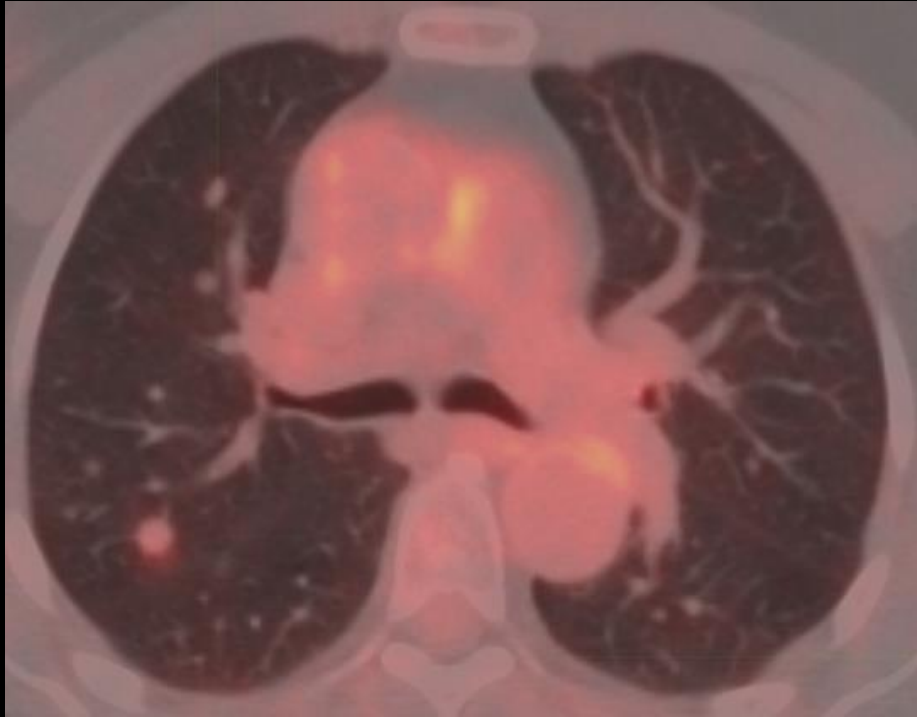
Inspiratory



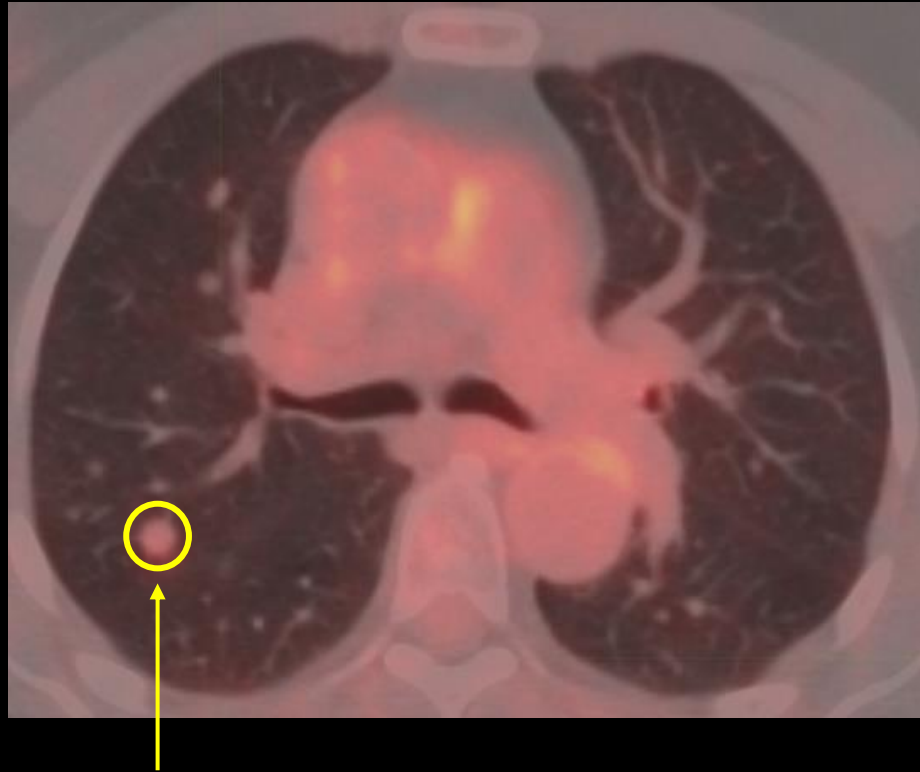
Expiratory

Moderate Air Trapping

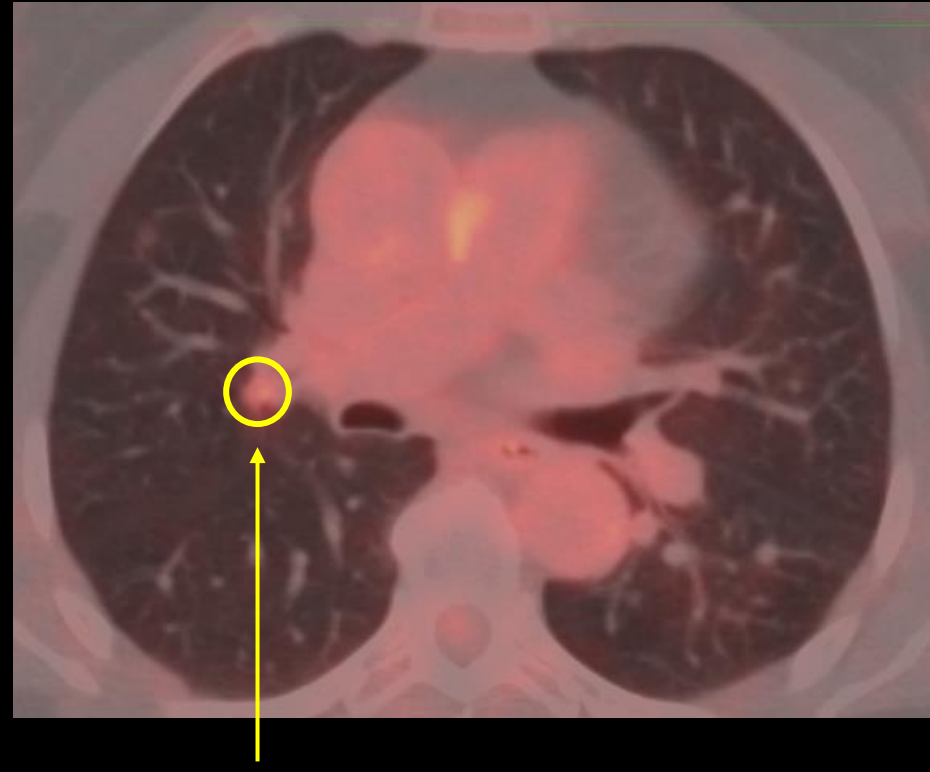
Findings (Unlabeled)



Findings (Labeled)



FDG-Avid Lesion corresponding with 8 mm Lung Nodule on CT



FDG-Avid Lesion corresponding with 6 mm Lung Nodule on CT

Differential Diagnosis

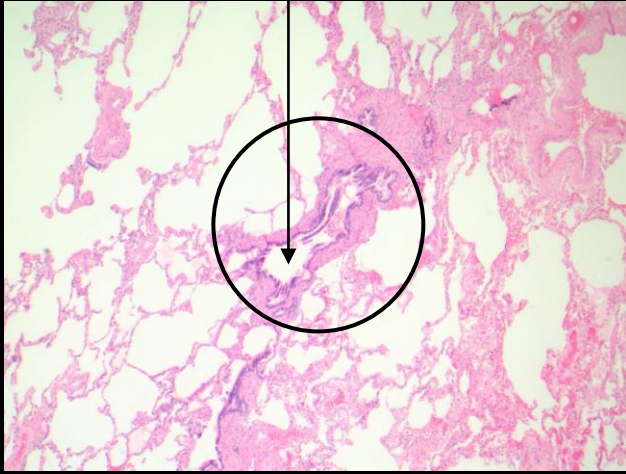
- Metastatic Cancer
- Pulmonary Adenocarcinoma
- Follicular Bronchiolitis
 - Sjogren Syndrome
 - Rheumatoid Arthritis
- Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia

Surgical Intervention

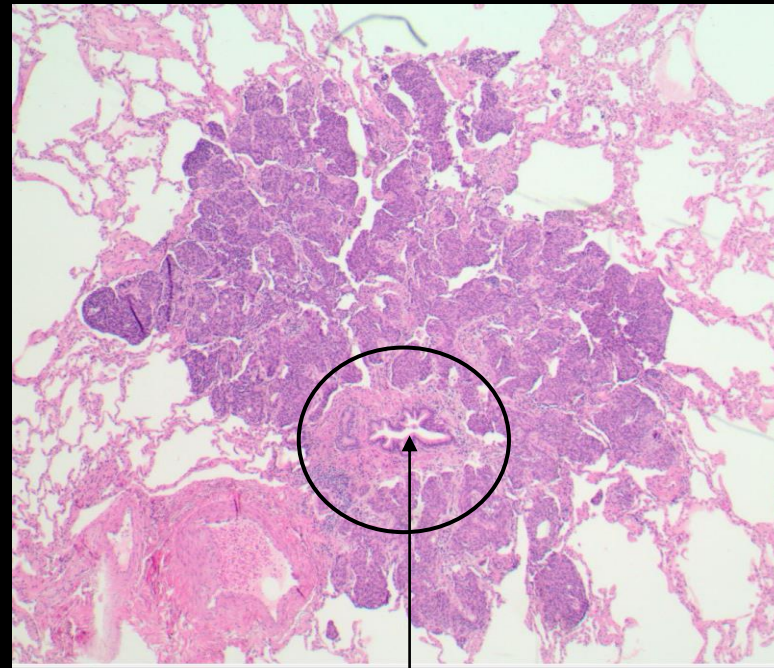
- Bronchoscopy with Transbronchial Biopsy and EBUS TBNA: Nondiagnostic
- Right Thoracoscopy with RUL and RLL Wedge Resection pursued

Histopathology

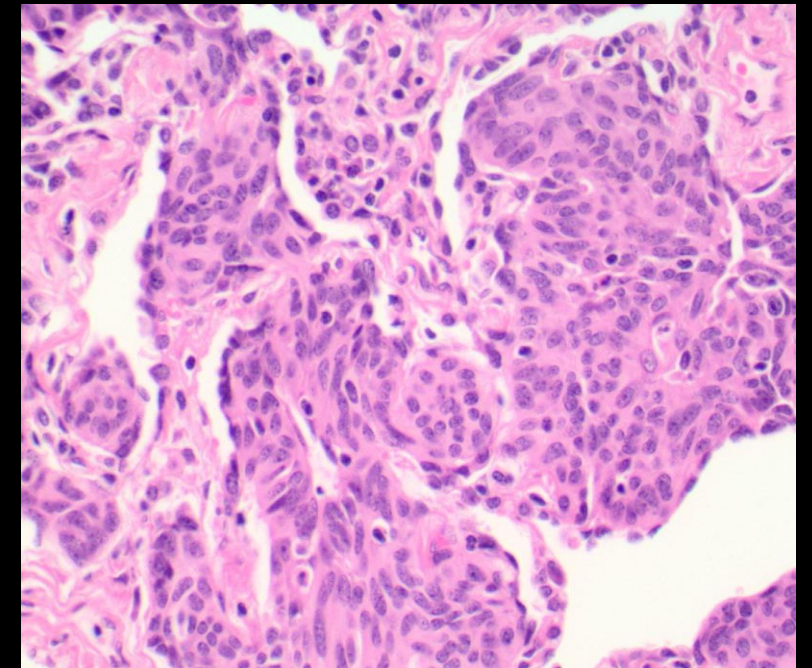
Dilated Bronchiolar Lumen



Peribronchiolar, Mildly Atypical Epithelial Cells forming Pseudorosettes
Tumorlet presenting as a nodule on left. Higher magnification on right.



Bronchiolar Lumen (Arrow) with Cellular Proliferation Surrounding Bronchiole (Circle)



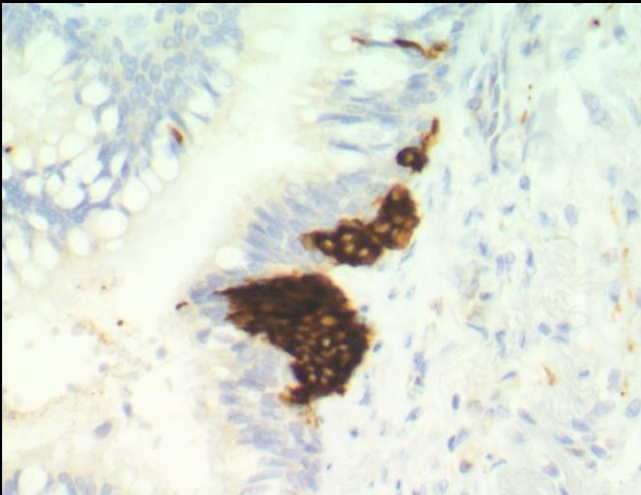
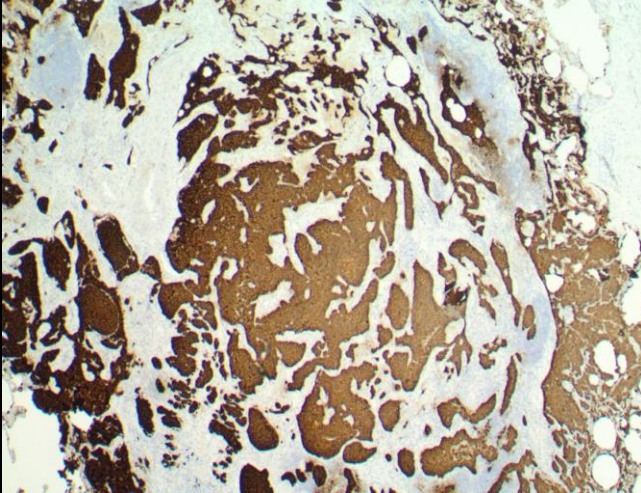
Spindle Cells of Relatively the Same Size and Shape

Mild Traction Bronchiolectasis



Granular Chromatin
"Salt and Pepper"

Histopathology



Final Pathological Report

- Right upper lobe, Wedge Resection
 - Typical carcinoid tumor, 0.6 cm, Negative margin
 - Carcinoid tumorlets (x3)
- Right lower lobe, Wedge Resection
 - Typical carcinoid tumor, 0.6 cm, Negative margin
 - Carcinoid tumorlets and neuroendocrine hyperplasia, multifocal (x20)
 - One lymph node, negative for metastasis (0/1)

Positive Staining for Synaptophysin

Final Dx:

**Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia
(DIPNECH)**

Case Discussion

DIPNECH is a rare pre-neoplastic pulmonary disorder that is characterized by hyperplasia of pulmonary neuroendocrine cells

- Pulmonary neuroendocrine cells are distributed throughout the pulmonary tract from the bronchi to the alveolar ducts
 - Neuroendocrine cells (NECs) play a role in lung development in fetal life and decrease in density as we age
 - In adults, NECs play a role as airway chemoreceptors and can cause airway vasoconstriction through release of serotonin

Epidemiology

- Lung neuroendocrine tumors (NETs) account for about 1-2% of all lung malignancies
- Hayes et al. 2022 performed a cohort study of 311 patients and found that 20% of those diagnosed with Lung NETs had DIPNECH
- Baseline demographics for those with DIPNECH were 95% female, 59% never smokers, and had a mean BMI of 34.4

Case Discussion

Etiology

- Idiopathic

Clinical Presentation

- Long history of cough, breathlessness, dyspnea, and wheezing
- Most patients will also show evidence of obstructive lung disease on pulmonary function testing

Differential Diagnosis

- Reactive airway disease (asthma), obstructive bronchial neoplasm, endobronchial metastasis, granulomas, pneumoconiosis

Diagnosis

- Surgical biopsy is the gold standard
- CT chest can aid in diagnosis (see following slide for typical radiological findings)

Case Discussion

Imaging

- DIPNECH is characterized by cellular proliferation of the bronchial wall
- Typical CT findings include
 - Bronchial wall thickening
 - Mild bronchiectasis, lobular or regional air trapping
 - Mosaic pattern of attenuation
 - Lung nodules in a centrilobular distribution
 - Lower lung zone predominance in the craniocaudal plane

Treatment

- Al-Toubah et al. treated patients with presumed or confirmed DIPNECH with somatostatin analogs. 79% showed symptomatic improvement, and 14/15 showed improvement in FEV1 after treatment.

Prognosis

- Hayes et al. 2022 cohort study found that the DIPNECH cohort had a 15-year survival rate of 86%.

References:

1. Almquist DR, Ernani V, Sonbol MB. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia: DIPNECH. *Curr Opin Pulm Med*. 2021 Jul 1;27(4):255-261. doi: 10.1097/MCP.0000000000000776. PMID: 33927131.
2. Al-Toubah T, Strosberg J, Halfdanarson TR, Oleinikov K, Gross DJ, Haider M, Sonbol MB, Almquist D, Grozinsky-Glasberg S. Somatostatin Analogs Improve Respiratory Symptoms in Patients With Diffuse Idiopathic Neuroendocrine Cell Hyperplasia. *Chest*. 2020 Jul;158(1):401-405. doi: 10.1016/j.chest.2020.01.031. Epub 2020 Feb 12. PMID: 32059961.
3. Chassagnon G, Favelle O, Marchand-Adam S, De Muret A, Revel MP. DIPNECH: when to suggest this diagnosis on CT. *Clin Radiol*. 2015 Mar;70(3):317-25. doi: 10.1016/j.crad.2014.10.012. Epub 2014 Nov 22. PMID: 25465294.
4. Hayes AR, Luong TV, Banks J, Shah H, Watkins J, Lim E, Patel A, Grossman AB, Navalkissoor S, Krell D, Caplin ME. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH): Prevalence, clinicopathological characteristics and survival outcome in a cohort of 311 patients with well-differentiated lung neuroendocrine tumours. *J Neuroendocrinol*. 2022 Oct;34(10):e13184. doi: 10.1111/jne.13184. Epub 2022 Sep 19. PMID: 36121922.
5. Little BP, Junn JC, Zheng KS, Sanchez FW, Henry TS, Veeraraghavan S, Berkowitz EA. Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia: Imaging and Clinical Features of a Frequently Delayed Diagnosis. *AJR Am J Roentgenol*. 2020 Dec;215(6):1312-1320. doi: 10.2214/AJR.19.22628. Epub 2020 Oct 6. PMID: 33021835.
6. Wirtschafter E, Walts AE, Liu ST, Marchevsky AM. Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia of the Lung (DIPNECH): Current Best Evidence. *Lung*. 2015 Oct;193(5):659-67. doi: 10.1007/s00408-015-9755-1. Epub 2015 Jun 24. PMID: 26104490.