

AMSER Case of the Month: July 2023

63-year-old asymptomatic woman with history of
significant second-hand cigarette smoke exposure

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Patient Presentation

63-year-old asymptomatic woman

Past Medical History: Malignant melanoma of the neck skin
(excised 5-years earlier); migraines

Medications: Rizatriptan 10mg qD as needed; Prempro® 0.3-1.5mg qD

Allergies: No known drug allergies (NKDA)

Social History: Never smoker. Reports significant paternal second-hand
cigarette smoke exposure growing up (2-packs per day)

Family History: **Paternal** Esophageal cancer

Maternal Breast cancer, Stroke, Heart disease

Personal Concern: Increased personal risk of lung cancer

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What Imaging Study Could be Performed to
Address her Personal Concerns?

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ACR Appropriateness Criteria

Scenario	Scenario Id	Procedure	Adult RRL	Peds RRL	Appropriateness Category
Lung cancer screening, <20 pack yrs smoking history, no family hx of lung cancer, initial imaging	3196020	Radiography chest	<0.1 mSv ⊕	<0.03 mSv [ped]..	Usually not appropriate
		MRI chest without IV contrast	0 mSv ○	0 mSv [ped] ○	Usually not appropriate
		CT chest with IV contrast	1-10 mSv ⊕⊕⊕	3-10 mSv [ped]..	Usually not appropriate
		MRI chest without and with IV contrast	0 mSv ○	0 mSv [ped] ○	Usually not appropriate
		CT chest without IV contrast screening	1-10 mSv ⊕⊕⊕	Not Assigned	Usually not appropriate
		CT chest without and with IV contrast	1-10 mSv ⊕⊕⊕	3-10 mSv [ped]..	Usually not appropriate
		FDG-PET/CT skull base to mid-thigh	10-30 mSv ⊕⊕⊕⊕	3-10 mSv [ped]..	Usually not appropriate
Lung cancer screening, <20 pack yrs smoking history, no hx of COPD, initial imaging	3196021	Radiography chest	<0.1 mSv ⊕	<0.03 mSv [ped]..	Usually not appropriate
		MRI chest without IV contrast	0 mSv ○	0 mSv [ped] ○	Usually not appropriate
		CT chest with IV contrast	1-10 mSv ⊕⊕⊕	3-10 mSv [ped]..	Usually not appropriate
		MRI chest without and with IV contrast	0 mSv ○	0 mSv [ped] ○	Usually not appropriate

Unenhanced low-dose chest CT (LDCT) was ordered by their PCP per patient request. Patient paid out of pocket for screening as she did not meet United States Preventive Services (USPSTF) or Centers for Medicare and Medicaid Services (CMS) eligibility requirements for screening.

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ACR Appropriateness Criteria

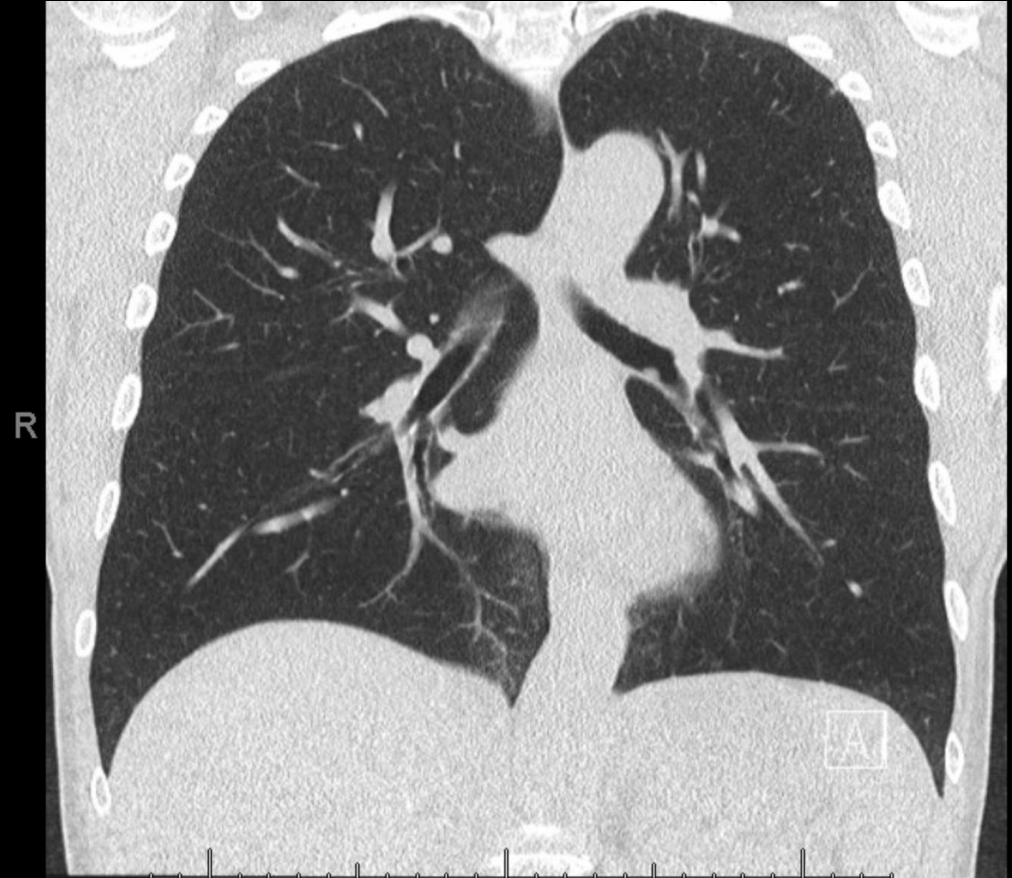
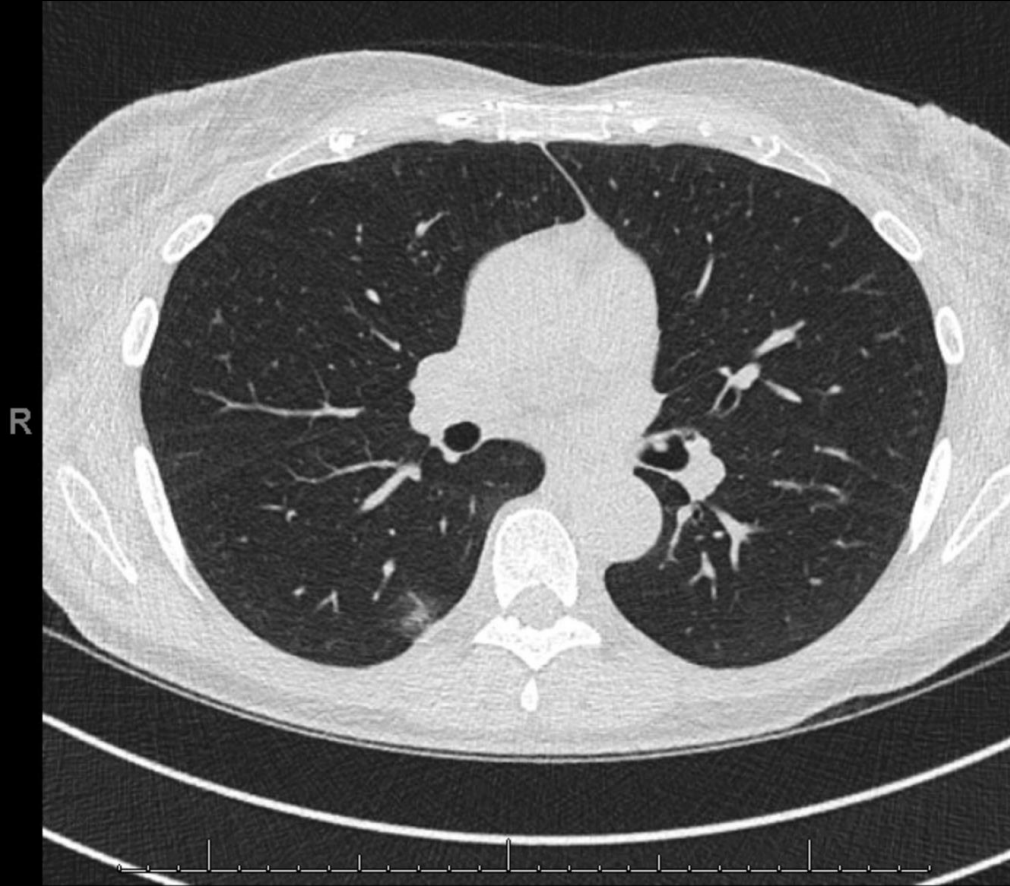
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		MRI chest without IV contrast	0 mSv ○	0 mSv [ped] ○	Usually not appropriate	●
		CT chest with IV contrast	1-10 mSv ☼☼☼	3-10 mSv [ped]..	Usually not appropriate	●
		MRI chest without and with IV contrast	0 mSv ○	0 mSv [ped] ○	Usually not appropriate	●

Radiographic Study	Dose (mSv)	Equivalent #CXR
Chest PA	0.013	1
L-spine AP	0.44	30
Mammogram (4 view)	0.2	15
Dental Panorama	0.012	1
BE	5	350
CT L-spine	7	550
CT Abdomen	10	750
CT Chest	10	750
LDCT Chest	1.5	113

Listed as “usually not appropriate,” but screening was performed at the patient’s request due to a high level of personal anxiety, personal concerns of having an occult lung cancer due to significant childhood second-hand smoke exposure and a strong family history of cancers in both parents.

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Findings (unlabeled)- Selected LDCT Images



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Findings (labeled)- Selected LDCT Images

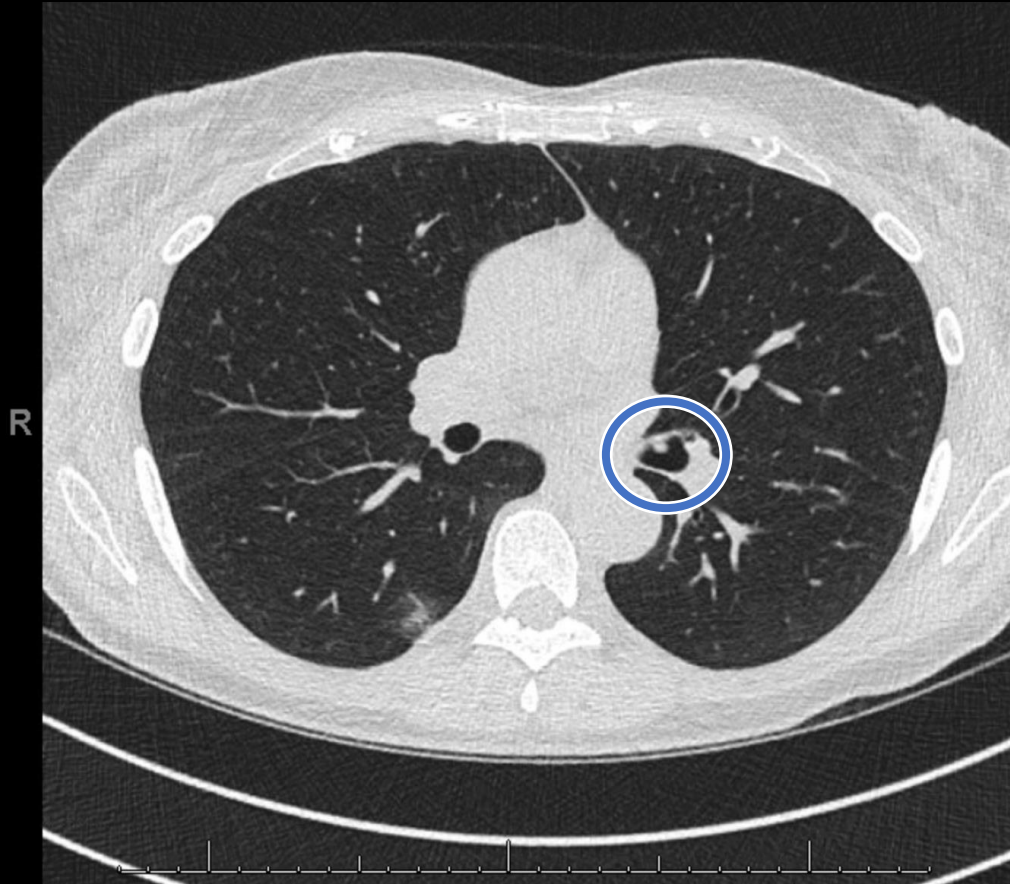


Figure 1A: Unenhanced axial image (lung windows) at the lingular bronchus level shows a solid, ovoid, non-calcified endoluminal LungRADS category 4A nodule.

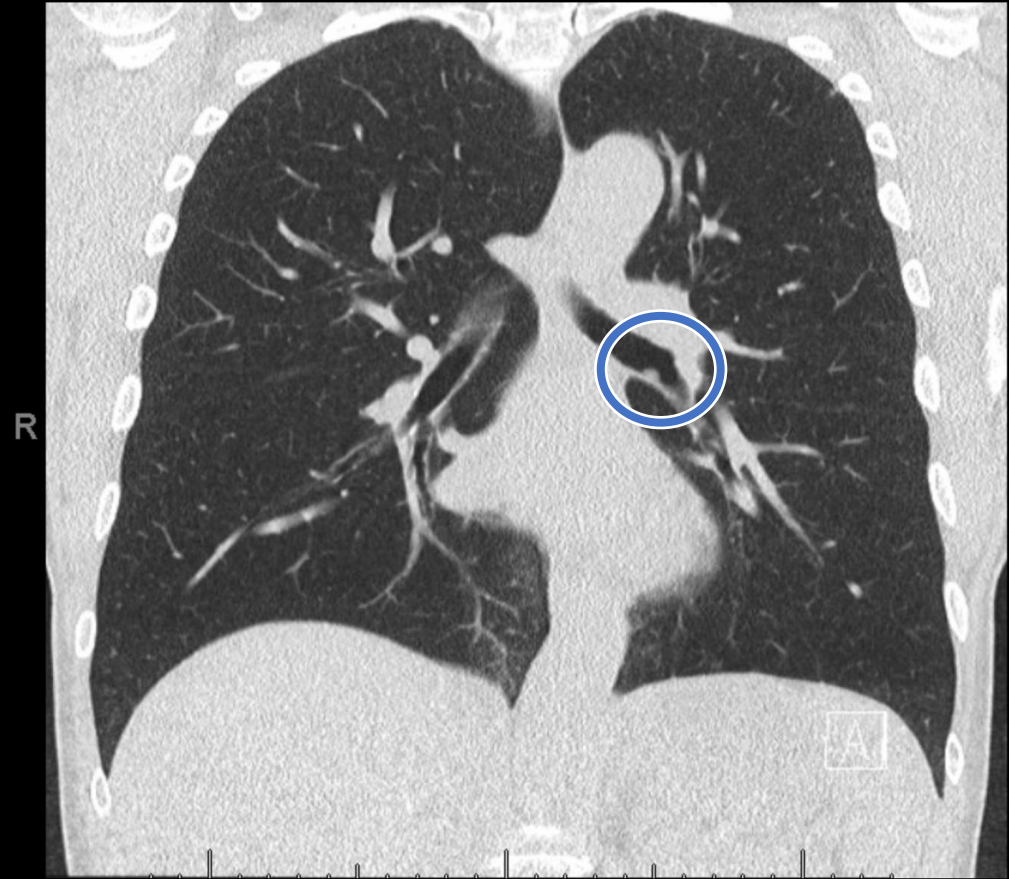


Figure 1B: Unenhanced coronal image (lung windows) at the lingular bronchus level confirms the presence of a solid, ovoid, non-calcified endoluminal LungRADS category 4A nodule.

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LungRADS v2.0



Lung-RADS® 2022

Release Date: November 2022

4A	Suspicious Estimated Population Prevalence: 4%	Solid nodule: <ul style="list-style-type: none"> • ≥ 8 to < 15 mm (≥ 268 to $< 1,767$ mm³) at baseline OR • Growing < 8 mm (< 268 mm³) OR • New 6 to < 8 mm (113 to < 268 mm³) 	3-month LDCT; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm ³) solid nodule or solid component
		Part-solid nodule: <ul style="list-style-type: none"> • ≥ 6 mm total mean diameter (≥ 113 mm³) with solid component ≥ 6 mm to < 8 mm (≥ 113 to < 268 mm³) at baseline OR • New or growing < 4 mm (< 34 mm³) solid component 	
		Airway nodule , segmental or more proximal at baseline or new (see note 11)	
		Atypical pulmonary cyst: (see note 12) <ul style="list-style-type: none"> • Thick-walled cyst OR • Multilocular cyst at baseline OR • Thin- or thick-walled cyst that becomes multilocular 	
4B	Very Suspicious Estimated Population Prevalence: 2%	Airway nodule , segmental or more proximal, and stable or growing (see note 11)	Referral for further clinical evaluation
		Solid nodule: <ul style="list-style-type: none"> • ≥ 15 mm (≥ 1767 mm³) at baseline OR • New or growing ≥ 8 mm (≥ 268 mm³) 	Diagnostic chest CT with or without contrast; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm ³) solid nodule or solid component; tissue sampling; and/or referral for further clinical evaluation Management depends on clinical evaluation, patient preference, and the probability of malignancy (see note 13)
		Part-solid nodule: <ul style="list-style-type: none"> • Solid component ≥ 8 mm (≥ 268 mm³) at baseline OR • New or growing ≥ 4 mm (≥ 34 mm³) solid component 	
		Atypical pulmonary cyst: (see note 12) <ul style="list-style-type: none"> • Thick-walled cyst with growing wall thickness/nodularity OR • Growing multilocular cyst (mean diameter) OR • Multilocular cyst with increased loculation or new/increased opacity (nodular, ground glass, or consolidation) 	
Slow-growing-solid or part-solid nodule that demonstrates growth over multiple screening exams (see note 8)			
4X	Estimated Population Prevalence: $< 1\%$	Category 3 or 4 nodules with additional features or imaging findings that increase suspicion for lung cancer (see note 14)	

LungRADS 4A:

Includes Airway Nodule
- **Footnote 11:** Endotracheal or endobronchial abnormalities that are segmental or more proximal.

Recommendations:

3-month follow-up LDCT. Segmental or more proximal airway nodules that persist on the 3-month follow-up LDCT are upgraded to **LungRADS 4B** with recommendations for further clinical investigation with **bronchoscopy**.

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Differential Diagnosis: Endobronchial Nodules

Non-Malignant Lesions	Primary Neoplasia	Secondary Neoplasia (Metastases)
Amyloidosis	Squamous cell cancer	Breast Cancer
Sarcoidosis	Small cell cancer	Melanoma
Endobronchial <i>M. tuberculosis</i>	Carcinoid	Renal Cell Cancer
Fungi	Adenoid cystic Carcinoma	Colorectal Cancer
Hamartoma	Mucoepidermoid Carcinoma	Pancreatic Cancer
Hemangioma		
Leiomyoma Fibroma		
Various Polyps (fibroepithelial)		
Foreign Body		

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Clinical Steps Following Imaging Results

Patient was seen in the **Pulmonology Clinic**

Subsequently referred to **Interventional Pulmonology**

Fiberoptic bronchoscopy was performed:

During the procedure labs obtained included:

Acid-fast bacilli culture: No Acid-fast Bacilli isolated

Fungal culture: No growth to date

Respiratory culture: Mixed Respiratory Flora

Surgical Pathology of Lesion Biopsy: Confirmed final diagnosis

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Pathology Findings

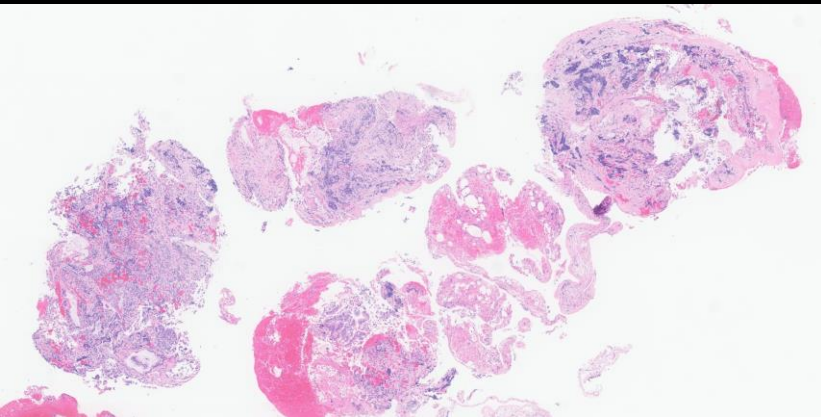


Figure 2A:
Fragments from the bronchoscopic biopsy

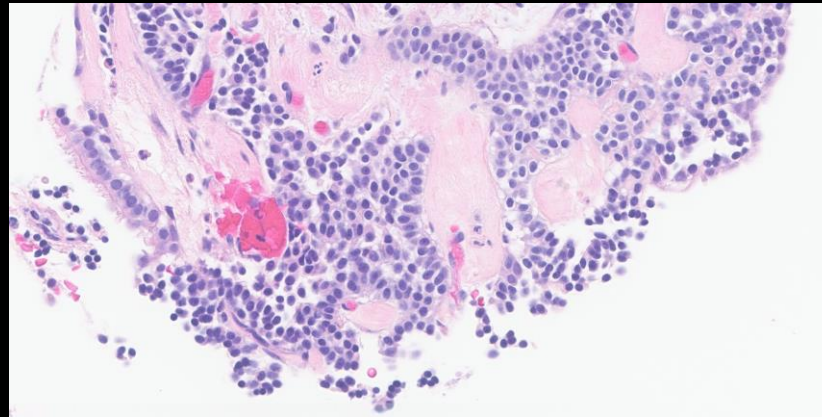


Figure 2B:
Tumor cells exhibiting **organoid pattern**

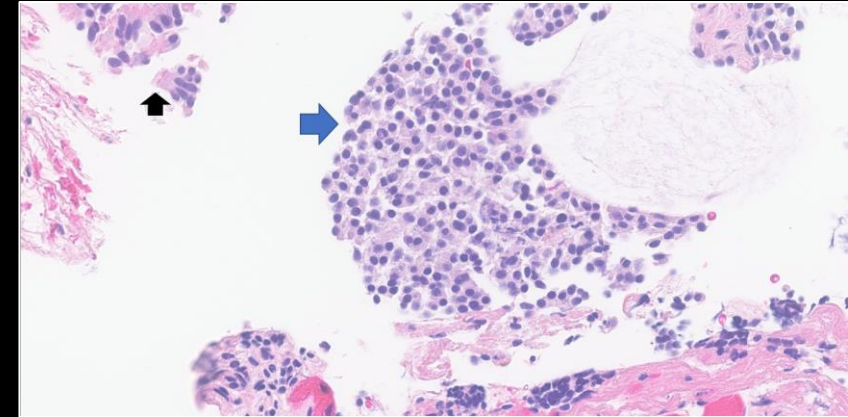


Figure 2C:
Normal ciliated columnar cells (**black arrow**), tumor cells with round nuclei and moderate amounts of cytoplasm (**blue arrow**)

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Pathology Findings

Immunohistochemical workup: The tumor cells are pan-keratin, **neuroendocrine marker** (such as synaptophysin) **positive**, and show a low proliferation rate of 1-2% on Ki-67, supporting the interpretation of a well differentiated neuroendocrine tumor.

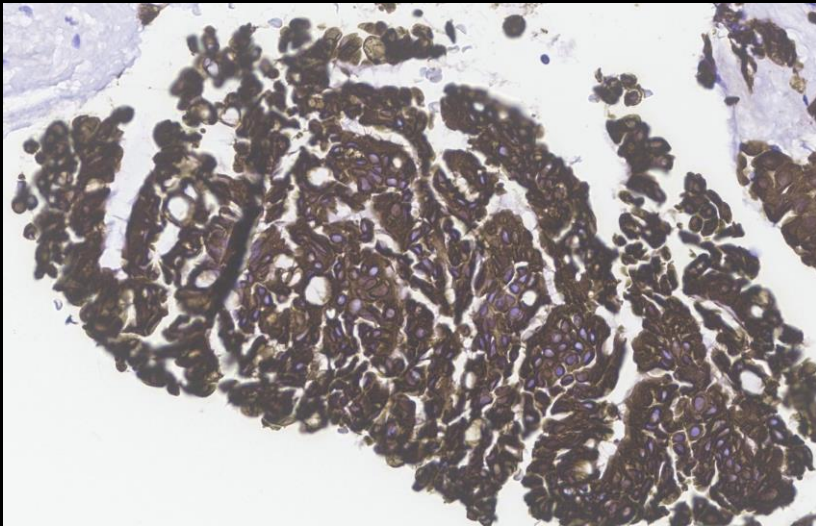


Figure 3A:
Pan-keratin positive

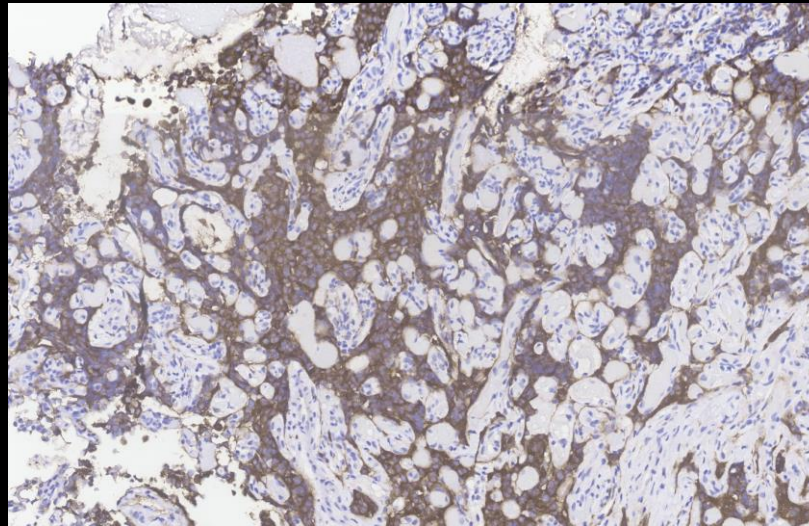


Figure 3B:
Synaptophysin positive

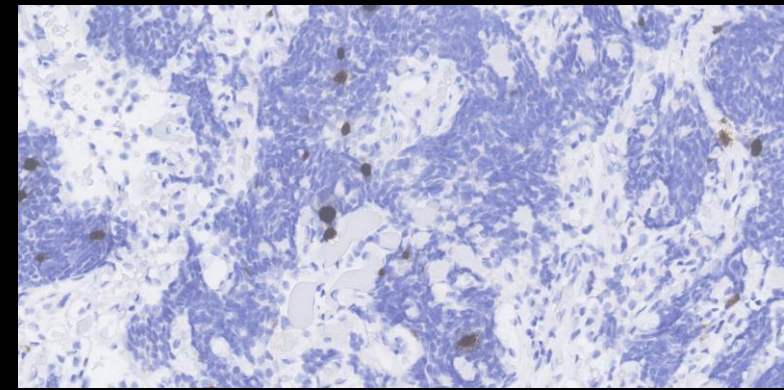


Figure 3C:
Low Ki-67 proliferation rate

Final Diagnosis:

Well-differentiated Neuroendocrine Carcinoid Tumor

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Lung Neuroendocrine Tumors

Neuroendocrine Tumors may be found throughout various organ systems including the GI tract, lung, thymus, and ovaries:

GI tract (Most common site)

Lungs (2nd most common site)

Types of Bronchopulmonary Neuroendocrine Tumors:

Typical carcinoid tumor (low-grade)

Atypical carcinoid tumor (intermediate grade)

Large-cell neuroendocrine carcinoma (LCNEC)

Small-cell lung carcinoma (SCLC)

(Note: Both LCNEC and SCLC are high grade; rapidly grow, often metastasize, poor prognosis)

Relationship to Cigarette Smoking

LCNEC and SCLC are strongly correlated to tobacco usage, but the relationship between carcinoid tumors and cigarette smoking is **uncertain**

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Lung Neuroendocrine Tumor Incidence

- Lung neuroendocrine tumors**- account for about 1-2% of lung malignancies in adults
 - account for about 20-30% of all neuroendocrine tumors

Recent research reports suggest **incidence of lung neuroendocrine tumors is increasing**

- Likely partially due to advanced medical imaging techniques being used for earlier detection of asymptomatic tumors

Bronchial carcinoid tumors are most commonly found as endobronchial lesions

- Around 75% arise in the lobar bronchi, and 10% from the mainstem bronchi
- Around 15% can be found in the periphery, as peripheral pulmonary nodules

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Lung Neuroendocrine Tumors

Clinical Presentation:

Often initially **asymptomatic** until a size threshold is reached

Airway obstruction- cough, atelectasis, recurrent pneumonia

Hemoptysis- adjacent airway or vascular erosion

Treatment:

Typical Carcinoid: Localized- initially conservative resection (endobronchial laser resection surgical sleeve/wedge/segmental resection)

Nuclear scintigraphy (Gallium-68-DOTATATE / Octreotide)

Bronchoscopy surveillance

Atypical Carcinoid: Often require extensive resection (lobectomy/ pneumonectomy) and chemotherapy

Prognosis:

Typical Carcinoid	88% 5-year survival	Large Cell Carcinoma	15-57% 5-year survival
Atypical Carcinoid	50% 5-year survival	Small cell carcinoma	<5% 5-year survival

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Patient's Treatment Plan

Thoracic Surgery consultation presented her 2 options:

Endobronchial therapy laser and coring

Surgical resection of the left mainstem bronchus

Possible need to also remove one of the lobar bronchi/lobes depending on the distal margin

Due to lesion proximity to the left minor carina, discussed potential need for lobectomy/sleeve resection

Patient elected to undergo endobronchial therapy with follow-up cross-sectional imaging surveillance

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Lung Cancer Diagnoses in Never Smokers

Lung cancer is the leading cancer killer worldwide

10-20% of annual lung cancer diagnoses occur in never smokers:

(Defined as either never smoked or smoked <100 cigarettes in their lifetime)

Research suggests other risk factors such as **second-hand smoke exposure**, radon gas, asbestos, air pollution, and a family history of lung cancer could contribute

Lung cancer in never smokers **occurs more frequently in women**, and often at an earlier age

Worldwide, lung cancer in never smokers is increasing- particularly in Asia

Percentage of lung cancer patients who never smoked:

China: 39.7%; South Korea: 38%

Compared to Europe and North America, which are around 10-20%

Research suggests clinicians should consider other risk factors for never-smokers when making clinical decisions regarding screening

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