AMSER Case of the Month: July 2023

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

Ateeya Hessami, MS4
Virginia Commonwealth University
School of Medicine

Mark S. Parker, MD, FACR
Peter Haar, MD, PHD
Raghavendra Pillappa, MD
VCU Health Systems
AMSER: Case of the Month May 2023

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
What Imaging Study Could be Performed to Address her Personal Concerns?
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.
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.
AMSER: Case of the Month May 2023
Findings (unlabeled)- Selected LDCT Images
AMSER: Case of the Month May 2023
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.
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.
## Differential Diagnosis: Endobronchial Nodules

<table>
<thead>
<tr>
<th>Non-Malignant Lesions</th>
<th>Primary Neoplasia</th>
<th>Secondary Neoplasia (Metastases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amyloidosis</td>
<td>Squamous cell cancer</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Small cell cancer</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Endobronchial M. tuberculosis</td>
<td>Carcinoid</td>
<td>Renal Cell Cancer</td>
</tr>
<tr>
<td>Fungi</td>
<td>Adenoid cystic Carcinoma</td>
<td>Colorectal Cancer</td>
</tr>
<tr>
<td>Hamartoma</td>
<td>Mucoepidermoid Carcinoma</td>
<td>Pancreatic Cancer</td>
</tr>
<tr>
<td>Hemangioma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leiomyoma Fibroma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Various Polyps (fibroepithelial)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foreign Body</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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
AMSER: Case of the Month May 2023
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)
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
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 SLCC 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
Lung neuroendocrine tumors account for about 1-2% of lung malignancies in adults, accounting for about 20-30% of all neuroendocrine tumors. Recent research reports suggest the 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.
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:
<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>5-year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical Carcinoid</td>
<td>88%</td>
</tr>
<tr>
<td>Large Cell Carcinoma</td>
<td>15-57%</td>
</tr>
<tr>
<td>Atypical Carcinoid</td>
<td>50%</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>
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
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
AMSER: Case of the Month May 2023

References


