# AMSER Rad Path Case of the Month:

62-year-old female with history of lung adenocarcinoma.

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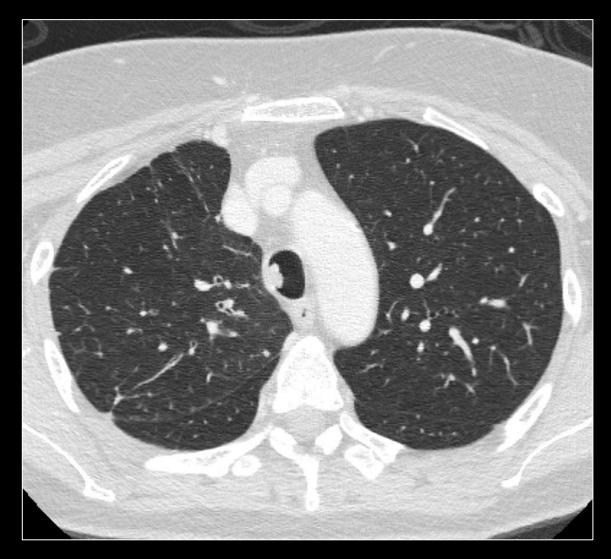
#### Patient Presentation

• 62 year-old female with advanced ALK + Non Small Cell Lung Cancer (NSCLC) on treatment with 1<sup>st</sup> line Alectinib with good response on last scans performed 12 weeks ago presents for restaging.

#### **Social History:**

Non-smoker

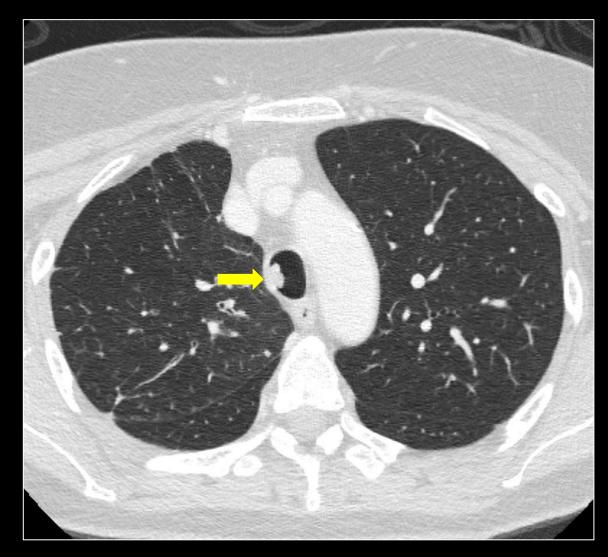
# CT Chest with IV Contrast (not labeled)





Axial Coronal

# CT Chest with IV Contrast (labeled)





Nondependent nodule along the right lateral tracheal wall measuring 1.0 cm (arrow). Patient referred to thoracic surgery for evaluation of the nodule.

#### Interval History

• The patient presented with a single episode of hemoptysis to an outside ED prior to scheduled thoracic surgery appointment.

#### Physical exam:

- Hemodynamically stable.
- BP 106/52
- HR 55
- Temp 97.9 °F

#### Pertinent Labs:

- Hgb 9.7
- D-dimer within normal limits

#### ACR Appropriateness Criteria

- The American College of Radiology (ACR) defines massive hemoptysis as "hemoptysis placing the patient at high risk for asphyxiation or exsanguination"
- hemodynamically stable following a single episode of hemoptysis, she underwent CT chest with IV contrast as appropriate initial imaging for non-massive hemoptysis

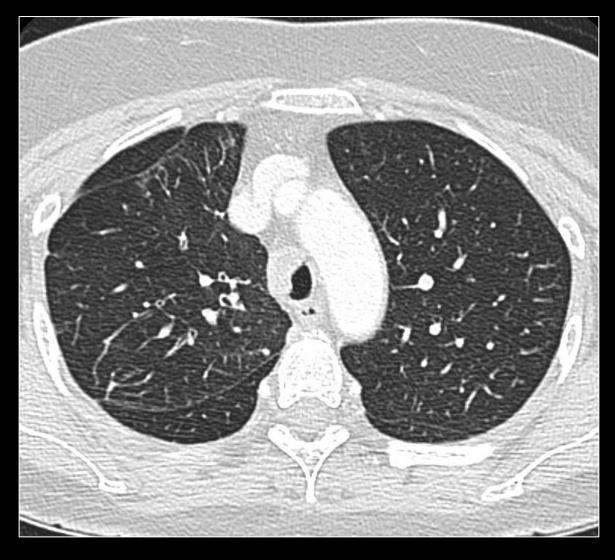
Variant 1:	Massive (	life-threatening)	hemoptysis.	Initial imaging.
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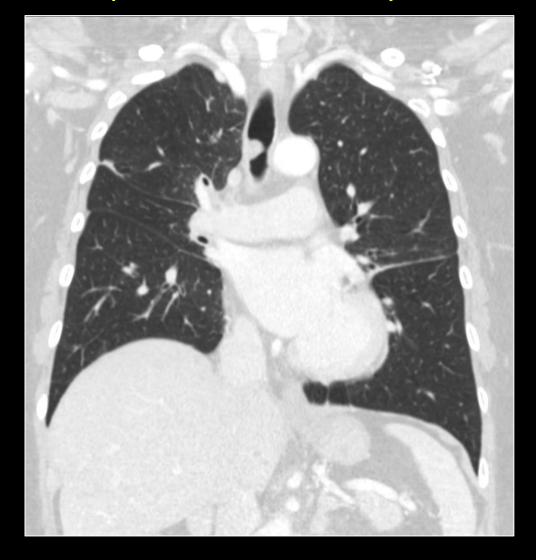
Procedure	Appropriateness Category	Relative Radiation Level
Arteriography bronchial with embolization	Usually Appropriate	***
CTA chest with IV contrast	Usually Appropriate	���
Radiography chest	Usually Appropriate	•
CT chest with IV contrast	Usually Appropriate	���
CT chest without IV contrast	May Be Appropriate	<b>⊕⊕⊕</b>
CT chest without and with IV contrast	Usually Not Appropriate	<b>⊕⊕⊕</b>

#### Variant 2: Nonmassive (non-life-threatening) hemoptysis. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
CT chest with IV contrast	Usually Appropriate	<b>⊕⊕⊕</b>
CTA chest with IV contrast	Usually Appropriate	<b>₩</b>
Radiography chest	Usually Appropriate	<b>⊕</b>
Arteriography bronchial with embolization	May Be Appropriate	<b>∞∞∞</b>
CT chest without IV contrast	May Be Appropriate	<b>₩₩</b>
CT chest without and with IV contrast	Usually Not Appropriate	<b>₩</b>

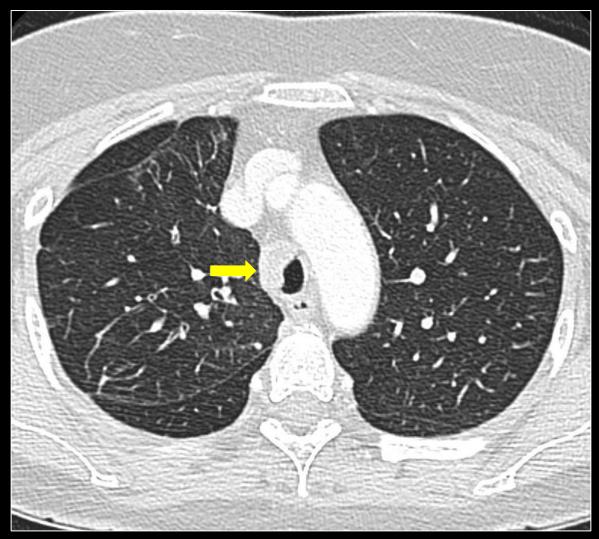
# CT Chest with IV Contrast (not labeled)





Axial Coronal

# CT Chest with IV Contrast (labeled)



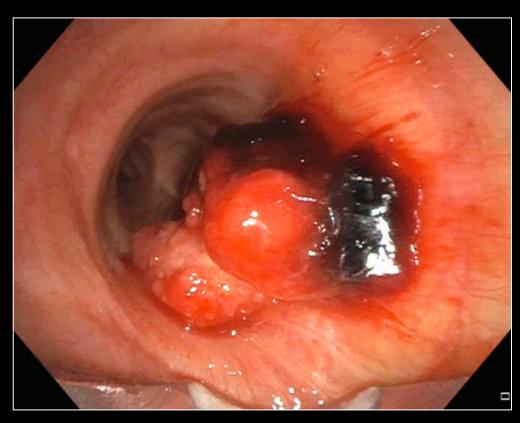


Increase in size of endotracheal lesion along the right lateral wall now extending anteriorly and to the left of midline measuring 2.0 cm (arrow) with associated narrowing of the tracheal lumen.

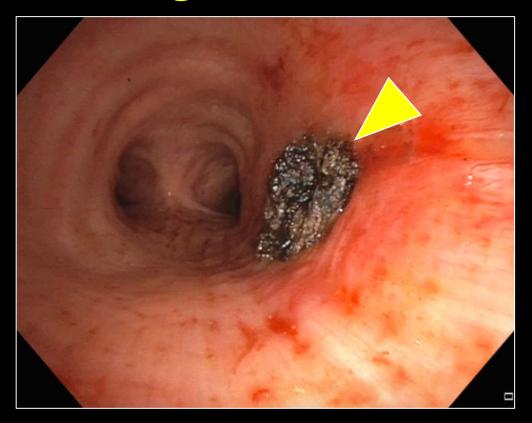
### Imaging DDx for Focal Tracheal Mass

- Primary Tracheal Malignancies
  - Squamous cell carcinoma
  - Adenoid cystic carcinoma
- Bronchial carcinoid tumor
- Metastasis
  - Direct invasion from lung, thyroid, esophagus, larynx
  - Hematologic or lymphangitic spread from breast, kidney, colon, skin (melanoma)
- Mucous secretions or tracheal debris
- Foreign Body

# Bronchoscopic Findings

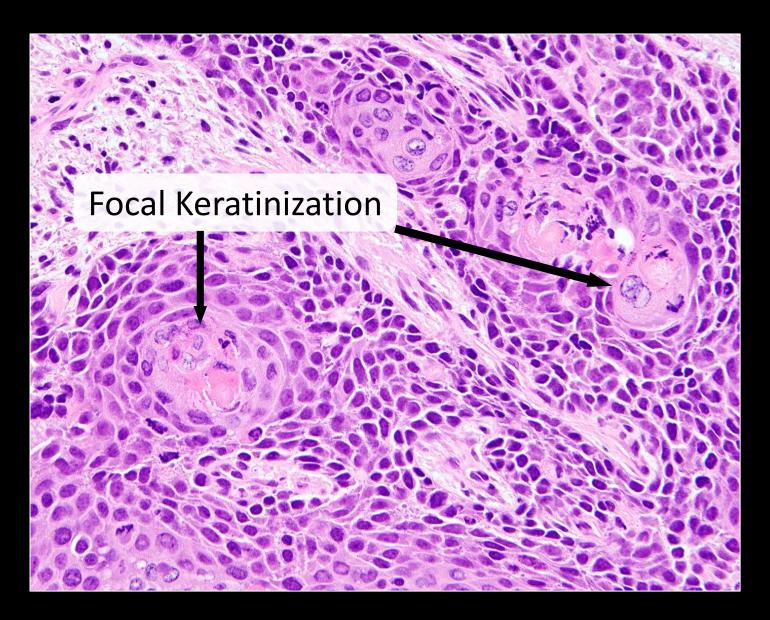


Tracheal tumor was located along the right lateral tracheal wall 2 cm above the carina. Tumor was cored out by the rigid forceps, followed by argon plasma coagulation (APC) and cryoablation therapy.



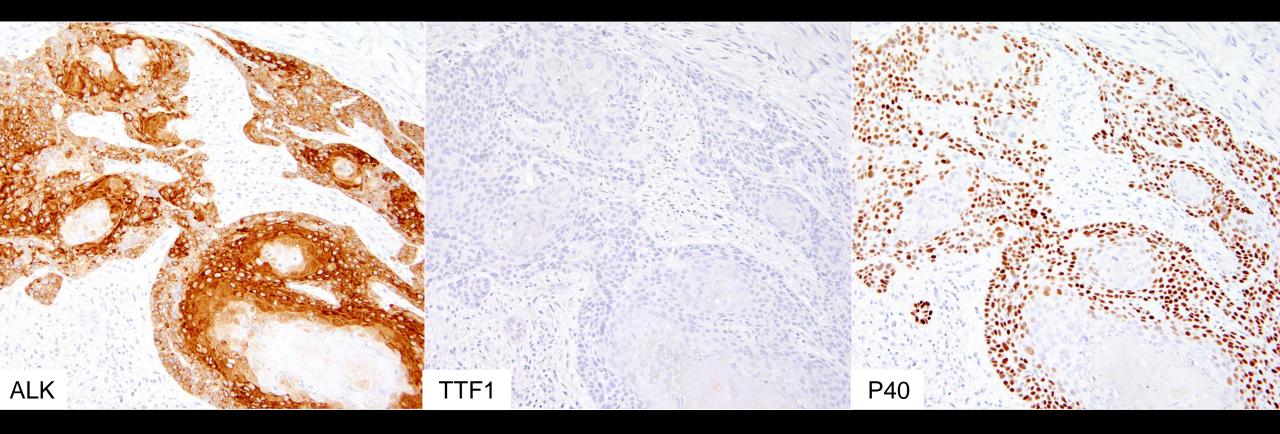
Tumor bed was ablated by cryoablation and APC (arrowhead).

#### Micro Path - Keratin



Frozen Section Analysis from bronchoscopy procedure revealed extensive squamous differentiation and focal keratinization in the center of the tumor islands.

# Immunohistochemistry



ALK IHC stains tumors with ALK rearrangements. (stained brown).

TTF1 IHC stains lung adenocarcinoma (lack of stain indicates absence of TTF1).

P40 IHC stains squamous cell carcinoma (stained brown).

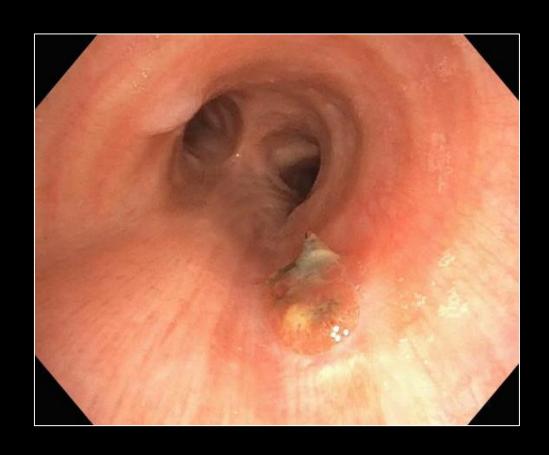
## Summary of Pathologic Findings

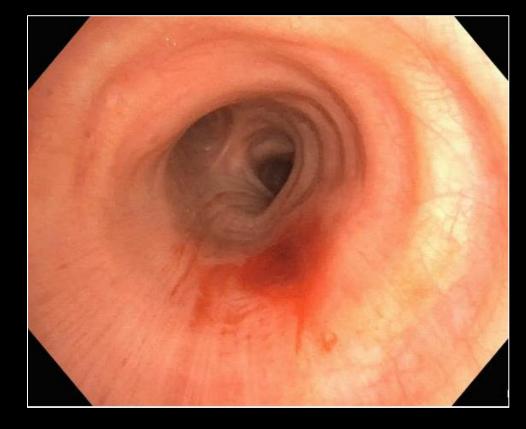
- Patient has a history of ALK+, TTF1+ right upper lobe adenocarcinoma with mucinous and signet ring cell features with a new tracheal lesion.
- The new tracheal tumor is morphologically different, consisting of an ALK+, P40+, TTF1- carcinoma with extensive squamous differentiation including focal keratinization.
- Because of the strong ALK positivity (despite the difference in morphology), the current tumor likely represents a transformation of the patient's known ALK+ adenocarcinoma to squamous differentiation.

#### Final Dx:

ALK+ Tumor with Extensive Squamous Cell Transformation

# Follow up Bronchoscopy



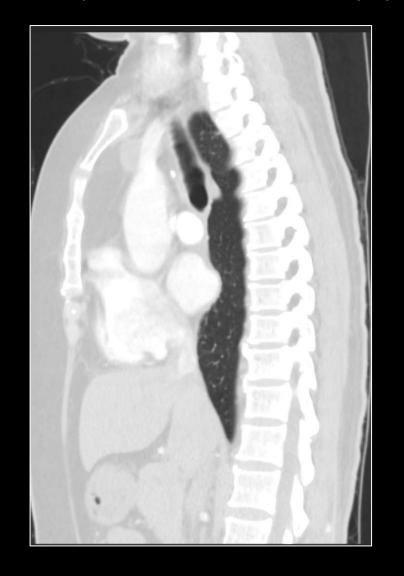


Post APC mucosal bulging in the core out area. Endobronchial biopsy samples were taken from this area and tumor bed area underwent cryoablation.

Normal ice saline instilled to tracheobronchial tree to confirm no active bleed from the biopsy sites.

#### Follow-up imaging at time of follow up bronchoscopy





No tracheal abnormality.

#### Case Discussion

- Tracheal metastasis from primary lung cancer is an extremely rare occurrence with a reported incidence of 0.44%.
  - A single-institution retrospective analysis of 1372 patients who underwent surgical resection of primary lung cancer found only 6 cases of tracheal metastasis, 0.77% (5/647) in squamous cell carcinoma and 0.18% (1/552) in adenocarcinoma<sup>[3]</sup>.
- Tracheal metastasis from other primary cancers is also rare, but has been reported in the literature arising from the following primary cancers: breast, kidney, colon, connective tissue, cervix, or skin.

#### Case Discussion

- Patients with tracheal lesions most commonly present with hemoptysis and coughing
- Tracheal metastases are often discovered in asymptomatic patients<sup>[3]</sup>
- There have been case reports of sudden death from airway obstruction secondary to endobronchial / tracheal metastasis<sup>[3]</sup>
- Treatment considerations:
  - Given the risk for hemoptysis and airway obstruction, initial management includes determining whether the patient requires emergent intubation or tracheostomy placement.
  - Most patients with a tracheal mass will undergo bronchoscopic biopsy.
  - Treatment options include chemotherapy, radiation therapy, bronchoscopic ablation, and surgical resection with tracheal anastomosis.

#### Case Discussion

- Anaplastic lymphoma kinase (ALK) is a tyrosine kinase used as a molecular/histologic marker in several tumor types, including nonsmall cell lung cancers, predominantly adenocarcinomas.
- There has been a case report of ALK positive adenocarcinoma with high PD-L1 expression transforming to squamous cell carcinoma following treatment with Alectinib
  - The evolving literature suggests Alectinib may impose selective pressures predisposing to phenotypic transformation (to squamous cell carcinoma) in certain tumor subtypes<sup>[9]</sup>.

#### References:

- 1. Bedayat A, Yang E, Ghandili S, Galera P, Chalian H, Ansari-Gilani K, Guo HH. Tracheobronchial Tumors: Radiologic-Pathologic Correlation of Tumors and Mimics. Curr Probl Diagn Radiol. 2020 Jul-Aug;49(4):275-284. doi: 10.1067/j.cpradiol.2019.04.003. Epub 2019 Apr 8. PMID: 31076268; PMCID: PMC7115773.
- 2. Byard RW. Endobronchial/tracheal metastasis and sudden death. J Forensic Sci. 2014 Jul;59(4):1139-41. doi: 10.1111/1556-4029.12431. Epub 2014 Feb 6. PMID: 24502794.
- 3. Chong S, Kim TS, and Han J. Tracheal Metastasis of Lung Cancer: CT Findings in Six Patients. American Journal of Roentgenology 2006;186:1, 220-224
- 4. Feng SH, Yang ST. The new 8th TNM staging system of lung cancer and its potential imaging interpretation pitfalls and limitations with CT image demonstrations. Diagn Interv Radiol. 2019 Jul;25(4):270-279. doi: 10.5152/dir.2019.18458. PMID: 31295144; PMCID: PMC6622436.
- 5. Hong SR, Lee YJ, Hong YJ, Hur J, Kim YJ, Choi BW, Lee HJ. Differentiation between mucus secretion and endoluminal tumors in the airway: analysis and comparison of CT findings. AJR Am J Roentgenol. 2014 May;202(5):982-8. doi: 10.2214/AJR.13.11392. PMID: 24758650.
- 6. Shin JY, Yoon JK, Marwaha G. External Validation of the New International Association for the Study of Lung Cancer Tumor, Node, and Metastasis 8th Edition Staging System and Updated T Descriptors in Determining Prognosis for Patients With Non-Small Cell Lung Cancer Patients With N3 Disease. Clin Lung Cancer. 2017 Nov;18(6):e481-e489. doi: 10.1016/j.cllc.2017.05.009. Epub 2017 May 10. PMID: 28559200.
- 7. Solomon B, Lovly CM. 2021 Anaplastic lymphoma kinase (ALK) fusion oncogene positive non-small cell lung cancer. In Vora S (Ed.), UptoDate. Available from https://www.uptodate.com/contents/anaplastic-lymphoma-kinase-alk-fusion-oncogene-positive-non-small-cell-lung-cancer#H12
- 8. Yano Y, Fujiwara T, Mizuta M. Endotracheal Metastasis Causing Airway Obstruction. Clin Pract Cases Emerg Med. 2019 Jan 21;4(1):96-98. doi: 10.5811/cpcem.2019.10.44964. PMID: 32064440; PMCID: PMC7012555
- 9. Zhang Y, Qin Y, Xu H, Yao Q, Gao Y, Feng Y, Ren J. Case Report: A Case Report of a Histological Transformation of ALK-Rearranged Adenocarcinoma With High Expression of PD-L1 to Squamous Cell Carcinoma After Treatment With Alectinib. Pathology and Oncology Research. 2021;27. doi:10.3389/pore.2021.637745