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## June 2022 Pulmonary Case of the Month: A Hard Nut to Crack

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**History of Present Illness:** A 54-year-old man presented to clinic with chronic cough, dyspnea on exertion, unintentional weight loss, and night sweats. Seven months before, he developed dyspnea on exertion and symptoms did not improve with inhalers. Four months prior to presentation, he was treated for presumed community-acquired pneumonia of the right lower lobe. Neither symptoms nor chest radiograph improved with multiple courses of antibiotics. In the four weeks prior to presentation his symptoms progressed to the point that he was unable to walk in his house without significant dyspnea.

**Review of systems:** 10-pound unintentional weight loss and six weeks of night sweats.

**Past Medical History, Social History and**

**Family History:** The patient had a 15-pack-year smoking history and quit 15 years prior to presentation. He had no other past medical history, surgical history, family history, nor medications.

**Physical Examination:** Vital signs were normal on presentation. Physical exam showed faint wheezing and decreased breath sounds over the right posterior lung fields.

**Radiography:** Chest radiograph demonstrated dense opacification in the superior segment of the right lower lobe (Figure 1).

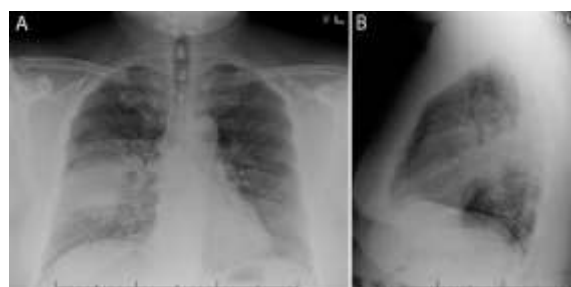


Figure 1. Initial chest radiography. A: PA view. B: Lateral view. ([Click here to view Figure 1 in an enlarged separate window](#))

What are ***diagnostic possibilities*** at this time?

1. Lung abscess
2. Lung cancer
3. Foreign body with post-obstructive pneumonia
4. Tuberculosis
5. 1 and 3
6. All the above

**Correct!**

**6. All of the above**

The night sweats and weight loss are not specific for distinguishing infection versus tumor. It is concerning that his symptoms haven't responded to antibiotics, making bacterial infection less likely.

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

1. Chest CT scan
2. PET scan
3. Bronchoscopy

4. Video assisted thorascopic (VATS) biopsy
5. 1 and 2
6. All the above

**Correct!**

**6. All the above**

Computed tomography (CT) of the chest shows extensive airspace consolidation in multiple segments of the right lower lobe with adjacent nodular groundglass opacification (Figure 2).

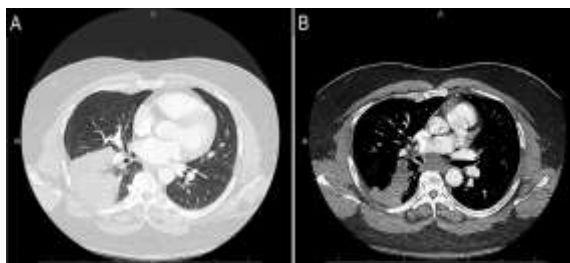


Figure 2. Representative images from thoracic CT in lung windows (A) and soft tissue windows (B). ([Click here to view Figure 2 in an enlarged separate window](#))

Consolidation extends from the right hilum to the pleural surface (Figure 2A). In addition, there is confluent subcarinal lymphadenopathy measuring 3.4 by 1.8 cm (Figure 2B).

Position emission tomography (PET) of the full body was obtained six weeks later (Figure 3).

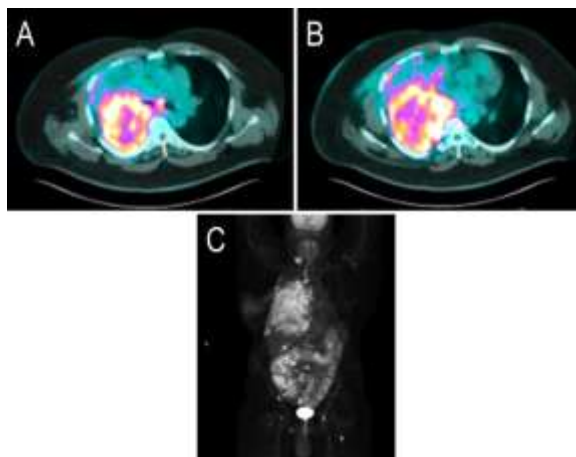


Figure 3. Representative images from the position emission tomography (PET) of the full body with transverse views through the chest (A,B) and coronal view of the whole body (C). ([Click here to view Figure 3 in an enlarged separate window](#))

PET demonstrates interval complete collapse of the right mainstem bronchus and right lung with diffuse fluorodeoxyglucose (FDG) uptake throughout the right lower lobe with FDG activity extending into the right middle and lower lobes. PET also shows FDG-avid supraclavicular and mediastinal lymphadenopathy and numerous FDG-avid osseous lesions throughout the axial and proximal appendicular skeleton. Right hemithorax video-assisted thorascopic surgery (VATS) was performed. Pleural studding was identified on both the parietal and visceral pleural surfaces with visible neoplastic implants on the surface of the right lower lobe (Figure 4).

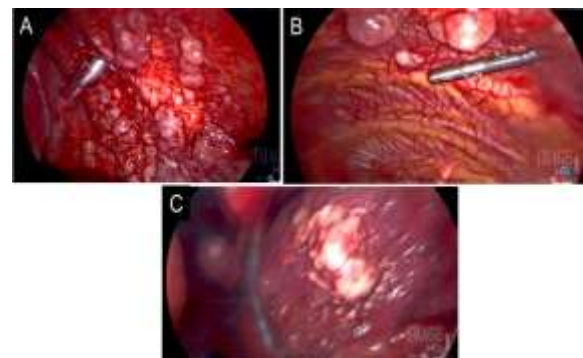


Figure 4. Images from VATS showing pleural studding. ([Click here to view Figure 4 in an enlarged separate window](#))

Bronchoscopy performed soon after VATS showed circumferential narrowing of the right mainstem bronchus and complete occlusion of the sub-segmental airways of the right upper lobe and bronchus intermedius by both endobronchial tumor and external compression (Figure 5).

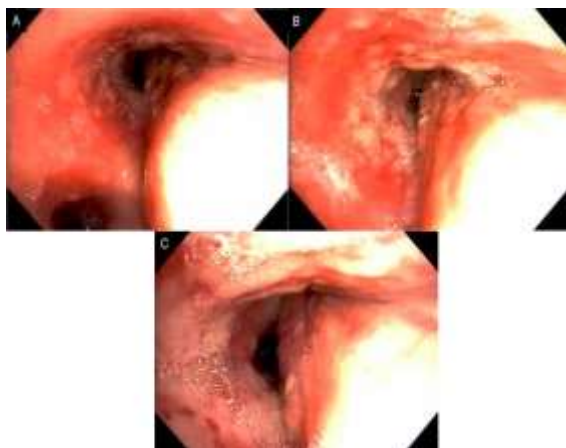


Figure 5. Images from bronchoscopy showing narrowing of the right mainstem bronchus. ([Click here to view Figure 5 in an enlarged separate window](#))

What is your *leading diagnosis* at this time?

1. Leiomyosarcoma
2. Military tuberculosis
3. Amelanotic melanoma
4. Squamous cell carcinoma
5. Coccidioidomycosis (Valley Fever)

**Correct!**

**4. Squamous cell carcinoma**

Biopsy specimens from the right pleural surface and right lower lobe showed sheets of monotonous small to medium-sized neoplastic cells with vesicular nuclei in a background of tumor necrosis and acute inflammation. Multiple areas demonstrated abrupt transition to well-differentiated squamous cell nests (Figure 6).

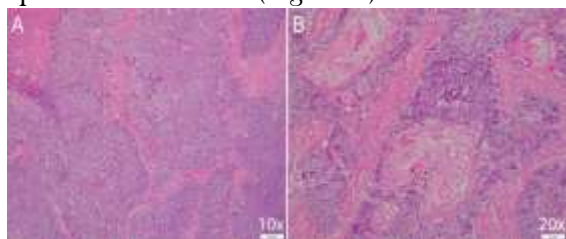


Figure 6. Histology showing well-differentiated squamous cell nests. ([Click here to view Figure 6 in an enlarged separate window](#))

Tumor cells were diffusely and strongly positive for p40 (squamous differential marker) and NUT (nuclear protein in testis) marker. Genetic testing confirmed a fusion event between the BRD4 and NUTM1 genes.

What is the *diagnosis*?

1. Adeno/Squamous Carcinoma
2. Large Cell Carcinoma
3. Lymphoepithelial carcinoma
4. NUT Carcinoma
5. Poorly differentiated squamous cell carcinoma

**Correct!**

**4. NUT Carcinoma**

*Clinical discussion*

Nuclear protein in testis (NUT) carcinoma is a rare genetically defined subtype of squamous cell carcinoma notable for rapid growth and dismal prognosis (1). Median age at diagnosis of primary pulmonary NUT carcinoma is 30 years. Median survival following diagnosis is 2.2 months (2). The typical patient with primary pulmonary NUT carcinoma is previously healthy, a non-smoker, and presents with chronic cough and dyspnea (2). Males and females are affected equally. The differential diagnosis for NUT carcinoma includes other poorly differentiated and aggressive tumors, including poorly differentiated carcinoma, non-small cell lung cancer, small cell lung cancer, and high-grade neuroendocrine carcinoma.

Approximately half of NUT carcinomas occur in the thorax. NUT carcinoma has a characteristic histologic appearance and is diagnosed via immunohistochemistry and molecular genetic testing.

*Radiology Discussion*

Fifty percent of NUT carcinomas occur in the thorax (3). From a case series of nine patients with primary pulmonary NUT

carcinomas, all tumors were centrally located, all tumors were greater than five centimeters in diameter at time of diagnosis, and 62% occurred in the right lung. In each case the primary tumor caused post-obstructive atelectasis and was accompanied by an ipsilateral pleural effusion. Notably, the contralateral lung was not involved in any case. Mediastinal adenopathy is always present. The bones are the most common site of extra-thoracic spread. In reported cases, the tumor is intensely FDG-avid (2).

### *Pathology Discussion*

Pathology demonstrates sheets of undifferentiated cells, often with foci of abrupt keratinization (1). Tumor cells are typically p40 or p63 positive. NUT carcinoma is diagnosed via immunohistochemistry with a commercially available assay (100% specificity, 87% sensitivity) (3). In 70% of cases, NUT carcinoma is caused by a reciprocal translocation between the NUTM1 gene on chromosome 15 and the BRD4 gene on chromosome 19 (1). If available, genetic testing can be utilized to identify the BRD4-NUT oncogene.

After diagnosis, the patient was referred to the oncology service. He has since received his first round of chemotherapy, consisting of methotrexate, doxorubicin, cisplatin, and vinblastine.

### *References*

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2. Sholl LM, Nishino M, Pokharel S, Mino-Kenudson M, French CA, Janne PA, Lathan C. Primary Pulmonary NUT Midline Carcinoma: Clinical, Radiographic, and Pathologic Characterizations. *J Thorac Oncol.* 2015 Jun;10(6):951-9. [\[CrossRef\]](#) [\[PubMed\]](#)
3. French CA. NUT Carcinoma: Clinicopathologic features, pathogenesis, and treatment. *Pathol Int.* 2018 Nov;68(11):583-595. [\[CrossRef\]](#) [\[PubMed\]](#)