November 2015 Pulmonary Case of the Month

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History of Present Illness

A 66 year-old woman was admitted to neurology with acute-onset dysarthria, right facial droop, and right-sided hemiparesis as a stroke alert. She also had a nonproductive cough and intermittent dyspnea for 4 months.

Past Medical History, Social History and Family History

- She has a history of hypertension and hyperlipidemia.
- She smoked 1-2 packs/day for 15 years but quit 35 years ago. She drinks two glasses of wine per day.
- There is a family history of bowel and breast cancer.

Physical Examination

- Vital signs: T 36.8, HR 81, BP 129/75, RR 18, O2 sat 93% RA
- General: No acute distress. Awake and alert.
- Heart, abdomen, and lungs: No significant abnormalities
- Neurological: Mild right-sided nasolabial fold flattening. Evidence of ptosis o the right eyelid. Hemiparesis on the right, the arm greater than leg. Sensation intact. Dysmetria on the right upper and lower extremities.

Laboratory Evaluation

- CBC: Hemoglobin 11.9 g/dL, white blood cells (WBC) 7,900 cells/mcL, platelets 290,000 cells/mcL
- Basic metabolic panel: Na+ 139 mEq/L, K+ 4 mEq/L, Cl- 100 mEq/L , bicarbonate 22 mEq/L, creatinine 0.7 mg/dL

Radiography

A head CT angiogram (CTA) was performed (Figure 1).

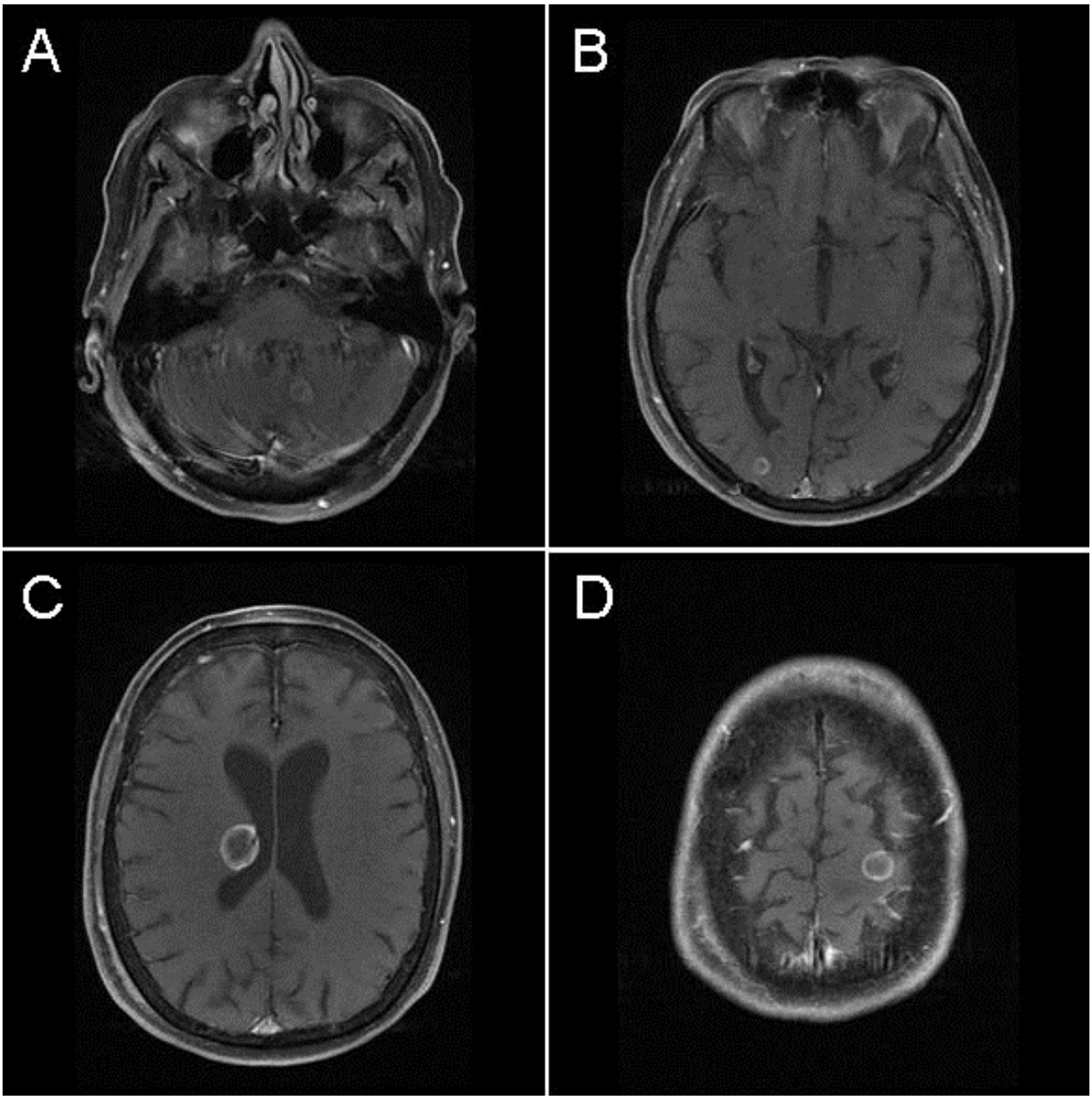

Figure 1. Representative images from CTA of the head.

Which of the following ***should be done next***?

1. Administer an intravenous injection of tissue plasminogen activator (TPA)
2. Administer detachable coils (coiling or endovascular embolization) or stereotactic radiosurgery
3. Begin an anti-convulsant and dexamethasone
4. 1 and 3
5. All of the above

Correct!
3. Begin an anticonvulsant and dexamethasone

Correct therapy relies upon correct interpretation of the CTA of the head. CTA did not show an acute intracranial hemorrhage, but there were ring-enhancing lesions in the right superior thalamus, right occipital, and left posterior frontal regions. This is most consistent with metastases to the brain. An anticonvulsant should be prescribed because of the high risk of seizures along with dexamethasone to improve symptoms by controlling cerebral edema.

Administration of TPA would be appropriate for a thrombotic stroke. However, administration of TPA in this patient's situation is potentially dangerous and could result in an intracranial hemorrhage. Coiling or stereotactic radiosurgery are appropriate for multiple arteriovenous malformations (AVMs). However, the ring-enhancing lesions in this patient's CTA are not consistent with AVMs.

What is the ***next step*** in the patient's evaluation?

1. Begin whole-brain radiation
2. Chest x-ray
3. CT scan of the abdomen to evaluate for renal or pancreatic cancer
4. Mammography to evaluate for metastatic breast carcinoma
5. All of the above

Correct!
2. Chest x-ray

None of the answers are totally inappropriate. Establishing a tissue diagnosis will help guide therapy. Whole-brain radiation would be appropriate if the patient was having uncontrolled seizures or other neurologic complications from the metastases. Of the possibilities for a primary source of her cancer, lung cancer seems likely based on her pulmonary symptoms. A chest x-ray was performed (Figure 2).

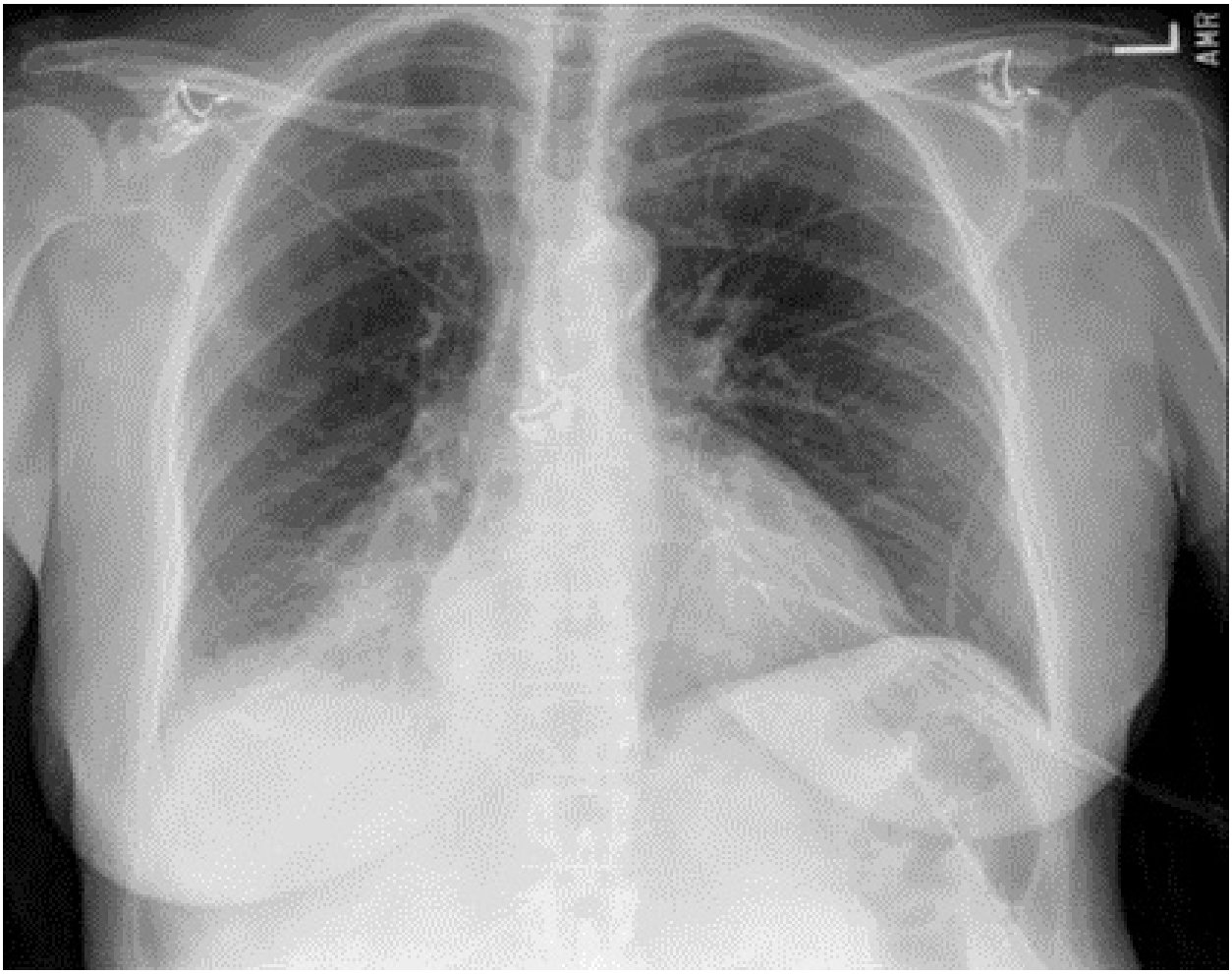

Figure 2. Chest radiograph.

Which of the following ***should be done next***?

1. Abdominal CT scan and mammogram
2. Chest CT scan
3. Colonoscopy for possible adenocarcinoma of the bowel
4. 1 and 3
5. All of the above

Correct!
2. Chest CT scan

The chest x-ray shows an abnormality along the right side of the heart partially silhouetting of the right hemidiaphragm. This is most consistent with atelectasis of the right lower lobe. Therefore, a thoracic CT scan was performed to better define the abnormality (Figure 3).

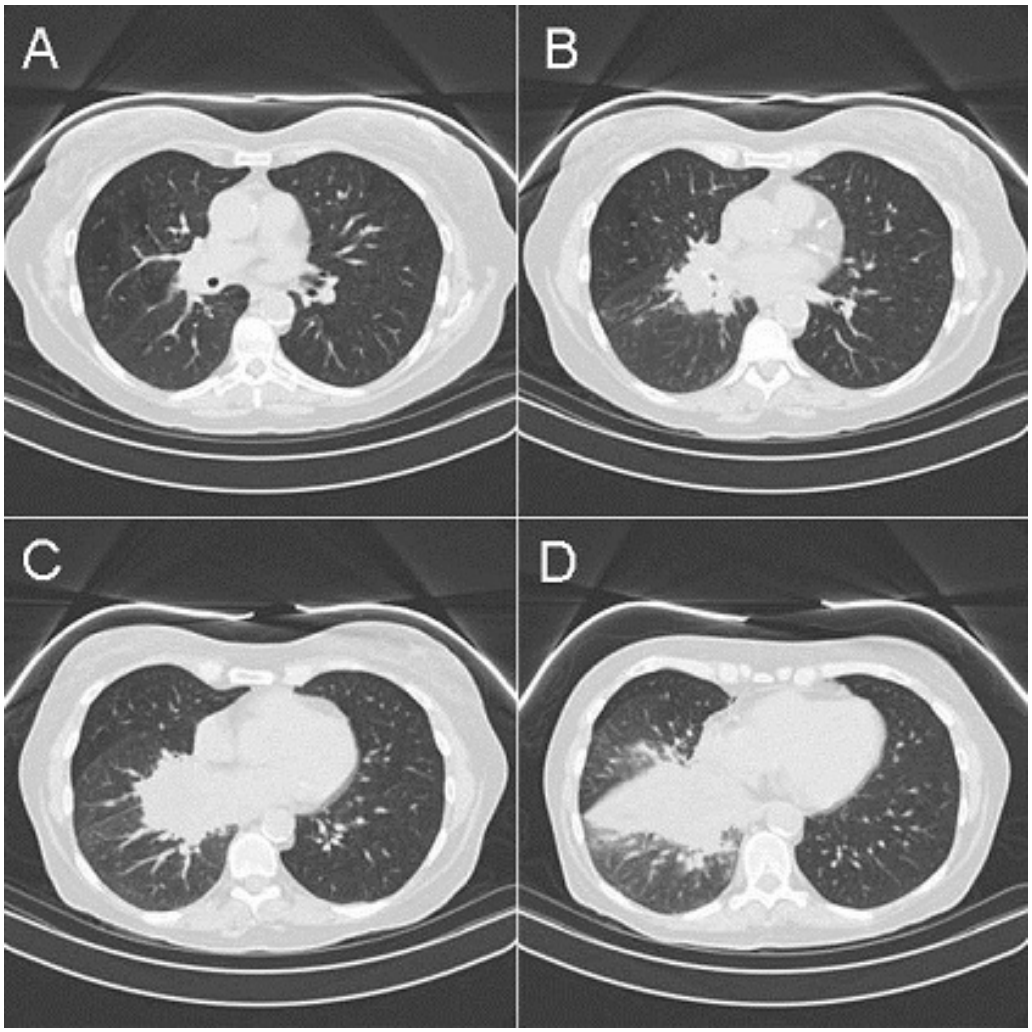

Figure 3. Representative images from the thoracic CT in lung windows confirming partial right lower lobe collapse.

What is the ***next appropriate step***?

1. Begin chemotherapy
2. Bronchoscopy
3. Needle biopsy of a brain lesion
4. Needle biopsy of lung mass
5. Video-assisted thorascopic (VATS) biopsy

Correct!
2. Bronchoscopy

The CT scan is most consistent with an endobronchial obstruction in the right lower lobe. Bronchoscopy would be the easiest procedure to make a diagnosis. Needle biopsy of the lung or brain or VATS are more invasive. Chemotherapy is not appropriate because no tissue diagnosis has been make. Bronchoscopy was performed along with endobronchial ultrasound (EBUS, Figure 4).

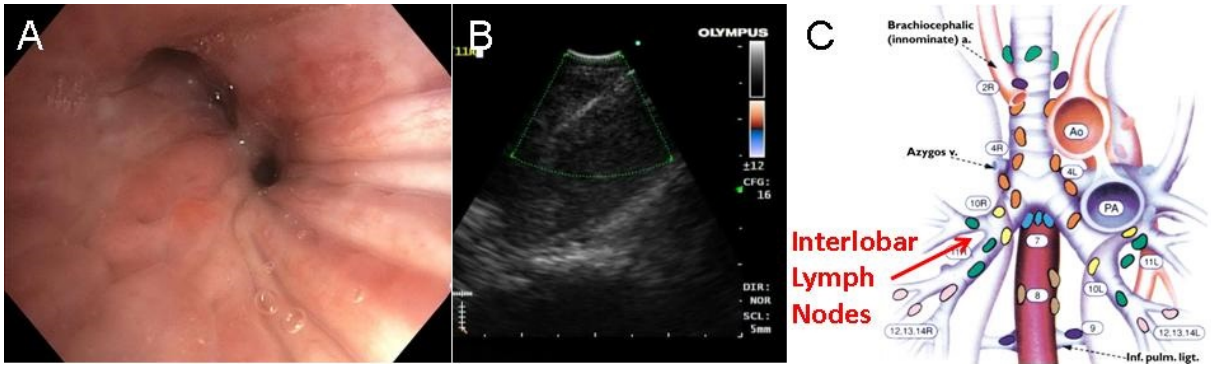

Figure 4. Panel A: bronchoscopic view of RLL bronchus showing narrowing and mucosal abnormality. Panel B: EBUS showing enlarged interlobar lymph nodes. Panel C: location of lymph nodes.

Biopsy of the bronchial mucosa was nondiagnostic but the EBUS-directed lymph node aspiration was consistent with adenocarcinoma or non-small cell lung cancer (NSCLC, Figure 5).

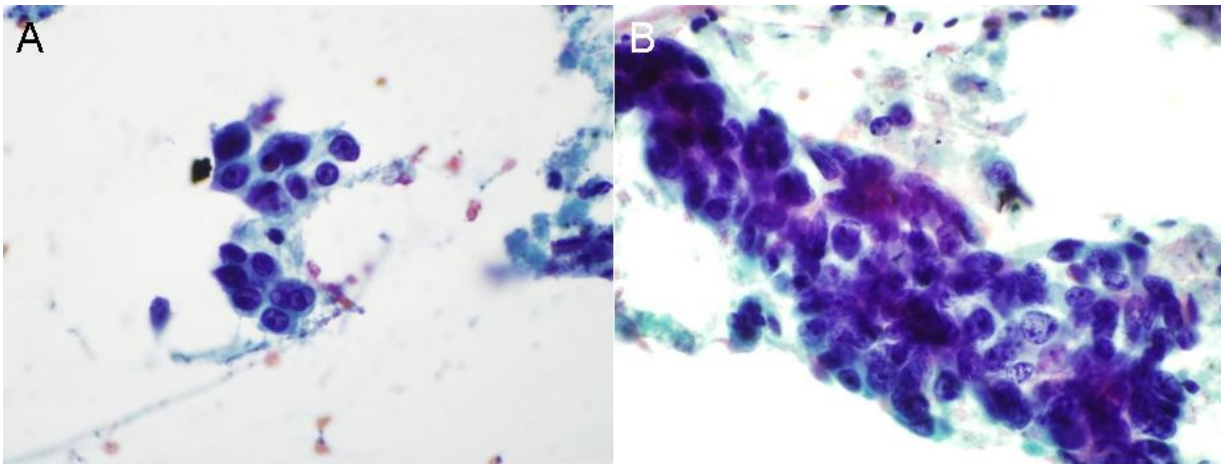

Figure 5. Papanicolaou smear of lymph node aspirate consistent with adenocarcinoma or NSCC.

Which of the following therapies is ***not true*** regarding NSCLC brain metastasis?

1. Metastatic brain tumors that are epidermal growth factor receptor (EGFR) positive will respond to EGFR tyrosine kinase inhibitors such as gefitinib or erlotinib
2. Metastatic brain tumors that have 4-anaplastic lymphoma kinase (ALK) translocations will respond to crizotinib
3. Prophylactic brain radiation has not been shown to be beneficial in NSCLC
4. Stereotactic radiosurgery should be considered in those with 1-4 brain metastases
5. Surgical resection should be considered in those with solitary brain metastasis

Correct!
2. Metastatic brain tumors that have 4-anaplastic lymphoma kinase (ALK) translocations will respond to crizotinib

Among patients with lung cancer, 50% have brain metastases. Prophylactic cranial irradiation has been shown to be beneficial in small cell lung cancer, but there is not enough data for NSCLC. Surgical resection should be considered in those with solitary brain metastasis and good prognosis characteristics. Whole brain radiotherapy (WBRT) should be considered after surgical resection to reduce local recurrence and the risk of developing additional brain metastases. However, WBRT does not offer substantial benefit to NSCLC patients with a poorer prognosis based on prognostic scores.

Stereotactic radiosurgery is a technique of radiation delivery that allows for a greater single-dose fractionation of radiation-thereby reducing radiation dose to surrounding brain tissue and theoretically causing fewer neurocognitive side effects that WBRT. It should be used in patients who are not surgical candidates and have 1-4 brain metastases. Stereotactic radiosurgery can be considered as an alternative to surgical resection. Systemic agents (i.e., radiosensitizing medications and cytotoxic drugs) do not improve meaningful outcomes.

Recently, chemotherapy has been shown to benefit two molecular defined populations of NSCLC patients. EGFR mutations can be treated with EGFR tyrosine kinase inhibitors (TKIs) such as gefitinib or erlotinib. EGFR inhibitors have an intracranial response approaching 80%.

Tumors with 4-anaplastic lymphoma kinase (ALK, echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase) translocations respond to crizotinib. Unfortunately, brain metastasis do not respond well to crizotinib despite an excellent effect on extracranial disease. This may due to the poor penetration of crizotinib through the blood-brain barrier in some patients.

Our patient was started on levetiracetam (Keppra) and dexamethasone. Radiation oncology was consulted and the underwent mapping for whole-brain radiation. She was discharged with follow-up with oncology to consider chemotherapy.

References

1. Ko JP, Drucker EA, Shepard JA, Mountain CF, Dresler C, Sabloff B, McLoud TC. CT depiction of regional nodal stations for lung cancer staging. AJR Am J Roentgenol. 2000;174(3):775-82. [CrossRef] [PubMed]
2. Yu JQ, Yang ZG, Austin JH, Guo YK, Zhang SF. Adenosquamous carcinoma of the lung: CT-pathological correlation. Clin Radiol. 2005;60(3):364-9. [CrossRef] [PubMed]
3. Dawe DE, Greenspoon JN, Ellis PM. Brain metastases in non-small-cell lung cancer. Clin Lung Cancer. 2014;15(4):249-57. [CrossRef] [PubMed]

4. Okamoto I, Nakagawa K. Echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase-targeted therapy for advanced non-small cell lung cancer: molecular and clinical aspects. Cancer Sci. 2012;103(8):1391-6. [CrossRef] [PubMed]
5. Morabito A, Carillio G, Daniele G, et al. Treatment of small cell lung cancer. Crit Rev Oncol Hematol. 2014;91(3):257-70. [CrossRef] [PubMed]
6. Paumier A, Le Péchoux C. Post-operative radiation therapy. Transl Lung Cancer Res. 2013;2(5):423-32. [CrossRef] [PubMed]