

## July 2016 Pulmonary Case of the Month

***Kashif Yaqub, MD  
Robert Viggiano, MD  
Imran S. Malik, MD  
Zayn A. Mian***

Department of Pulmonary Medicine  
Mayo Clinic Arizona  
Scottsdale, AZ USA

### ***History of Present Illness***

A 53 year-old woman presented to the emergency department with dyspnea over 3 weeks. There was no cough, wheezing or other complaints.

### ***Past Medical History, Social History and Family History***

She has no significant past medical history. She was a nonsmoker. Family history was unremarkable.

### ***Physical Examination***

Decreased breath sounds over the left lower chest but otherwise unremarkable.

### ***Laboratory Evaluation***

- Elevated white blood cell count with a left shift
- Na<sup>+</sup> 130 mEq/L
- 10-20 RBCs on urinalysis

### ***Radiographic Evaluation***

A CT angiogram of the chest was performed for possible pulmonary embolus (Figure 1).



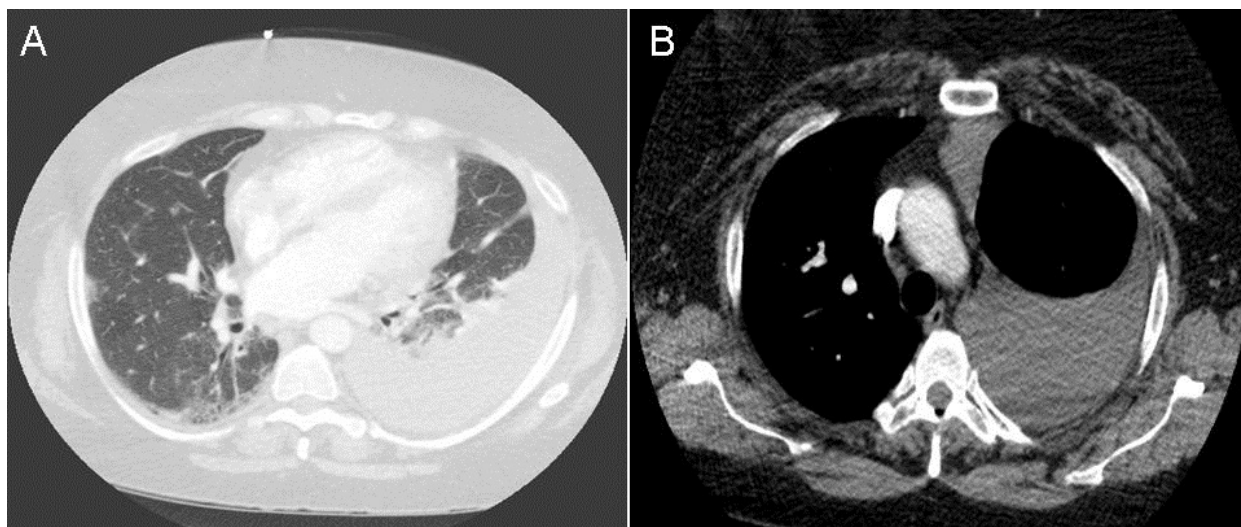


Figure 1. Representative images from the thoracic CT in lung windows (A) and soft tissue windows (B).

Which of the following is **appropriate at this time?**

1. Biopsy of left pleural mass
2. Bone marrow aspiration
3. Diuretics for congestive heart failure
4. Empiric antibiotics for empyema
5. Thoracentesis



**Correct!**  
**5. Thoracentesis**

The only abnormality seen on the CT scan is a large left pleural effusion. Although the white blood cell count is elevated with a left shift, this is nonspecific and does not necessarily indicate an infection such as empyema or a blood disorder where bone marrow aspiration might be helpful. Congestive heart failure is a consideration in a patient short of breath but a solitary left pleural effusion without a right pleural effusion would be unusual. There is no pleural mass. Unless contraindicated, the first step in evaluating a pleural effusion is thoracentesis.

A diagnostic thoracentesis was performed which was grossly bloody.

Which of the following is **true** regarding unilateral bloody pleural effusions?

1. About half are secondary to malignancy
2. Are often associated with traumatic thoracentesis
3. Can be seen with pulmonary embolism
4. 1 and 3
5. All of the above



**Correct!**  
**4. 1 and 3**

Bloody pleural effusions are often due to malignancy (1). They can also be seen with pulmonary embolism with infarction (1). These are uncommon and are usually large pulmonary emboli. Traumatic thoracentesis can result in blood-tinged fluid but would be very unlikely to result in a grossly bloody aspiration.

Which of the following would be the **next diagnostic step(s)**?

1. Blind pleural biopsy
2. Coccidioidomycosis serology
3. Video-assisted thorascopic surgery (VATS)
4. 1 and 3
5. All of the above



**Correct!**

### **3. Video-assisted thorascopic surgery (VATS)**

Neither a blind pleural biopsy or coccidioidomycosis serology is necessarily wrong. However, in a series of pleural effusions secondary to coccidioidomycosis none were grossly bloody (2). In metastatic malignancy to the pleura, the surface is studded with areas of cancer. If the biopsy is done through one of the abnormal areas a diagnosis can be made, but if it is done between the studs of cancer, the biopsy will be nondiagnostic (1). In the case of mesothelioma, a histologic diagnosis is often difficult and often requires the confirmation of the surgeon.

A VATS was performed. There was extensive fibrinous, bloody adhesions in the chest. In excess of one liter dark bloody pleural fluid was obtained. There were no obvious areas of malignancy that could be seen. Random biopsies were obtained from the parietal pleura in two separate locations.

The biopsy is shown in Figure 2.

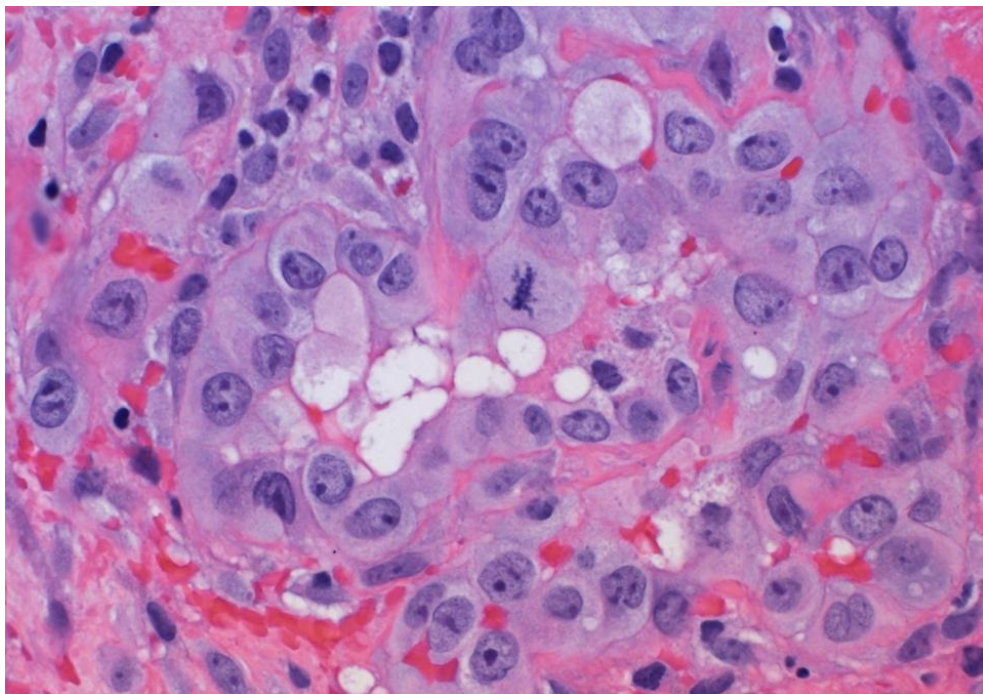


Figure 2. High power view of pleural biopsy (H&E).

Which of the following is **true regarding the pleural biopsy?**

1. The biopsy is normal
2. There are numerous granuloma with caseous necrosis
3. There are numerous granuloma without necrosis
4. There are numerous mitotic figures suggesting malignancy
5. There are numerous spherules within the biopsy suggesting Coccidioidomycosis



**Correct!**

**4. There are numerous mitotic figures suggesting malignancy**

There are numerous mitotic figures and red blood cells in the biopsy (Figure 3).

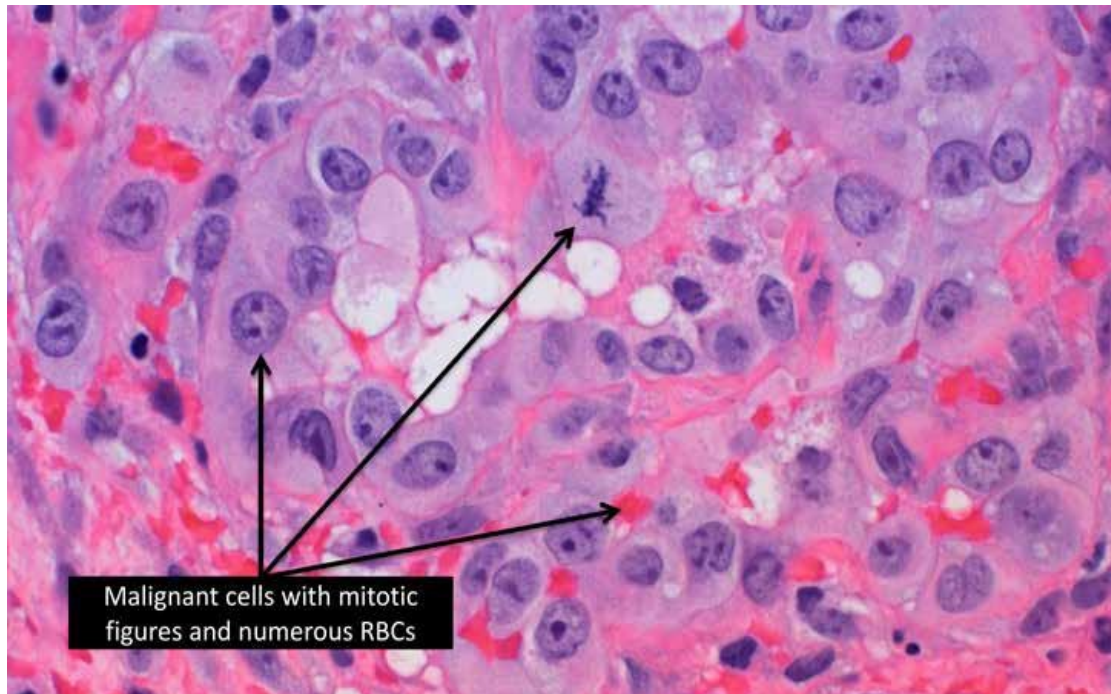


Figure 3. Pleural biopsy showing mitotic figures and red blood cells (RBSs).

A lower power view of the biopsy showing tumor infiltrating the chest wall and stained positive for CD31 (Figure 4).

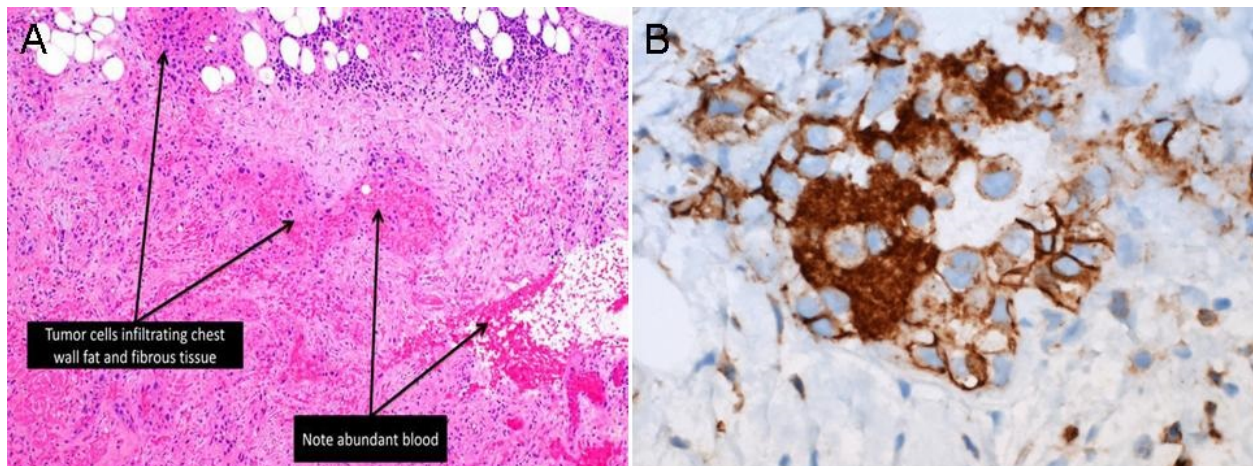


Figure 4. Panel A: Lower power view showing infiltration of the chest wall by tumor cells. Panel B: Immunohistochemistry showing CD31+ cells.



A diagnosis of pleural epithelial angiosarcoma was made.

Which of the following is/are **risk factors** for pleural epithelial angiosarcoma?

1. Asbestos exposure
2. Cigarette smoking
3. History of tuberculosis complications (chronic pyothorax or pleuritis)
4. Radiotherapy for ovarian cancer
5. All of the above



Correct!  
5. All of the above

There are only about 50 published case reports of pleural epithelial angiosarcoma in the English literature with an incidence of approximately 1% of all soft tissue tumors (3,4). The mean age of diagnosis is 58 years and the male to female ratio is 6:1. Risk factors can include occupational exposure to asbestos, prior radiation therapy, cigarette smoking and prior history of tuberculous complications. The most common presenting symptoms can include chest pain, dyspnea, hemoptysis, cough and weight loss. Radiological findings on chest x-ray can include pleural thickening in early stages or diffuse opacification of the hemithorax. On chest CT, a lobulated mass with irregular margins can be seen. Positron emission tomographic (PET) scan shows non-specific diffuse and homogeneous fluorodeoxyglucose (FDG) uptake indistinguishable from malignant mesothelioma.

Our case is unique because our patient had no identifiable risk factors and imaging did not show typical radiographic findings of angiosarcoma. In addition, inspection of the pleural at the time of surgery was grossly unremarkable.

Although localized angiosarcomas may have a relatively good prognosis after resection, diffuse disease has a poor prognosis. Chemotherapy and radiotherapy are often used. Bevacizumab and paclitaxel may have some beneficial effect (5,6). There is an ongoing trial of regorafenib, an oral multi-kinase inhibitor.

### **References**

1. Hooper C, Lee YC, Maskell N; BTS Pleural Guideline Group. Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. *Thorax*. 2010 Aug;65 Suppl 2:ii4-17. [\[CrossRef\]](#) [\[PubMed\]](#)
2. Merchant M, Romero AO, Libke RD, Joseph J. Pleural effusion in hospitalized patients with Coccidioidomycosis. *Respir Med*. 2008 Apr;102(4):537-40. [\[CrossRef\]](#) [\[PubMed\]](#)
3. Dainese E, Pozzi B, Milani M, Rossi G, Pezzotta MG, Vertemati G, Tricomi P, Sessa F. Primary pleural epithelioid angiosarcoma. A case report and review of the literature. *Pathol Res Pract*. 2010 Jun 15;206(6):415-9. [\[CrossRef\]](#) [\[PubMed\]](#)
4. Kao YC, Chow JM, Wang KM, Fang CL, Chu JS, Chen CL. Primary pleural angiosarcoma as a mimicker of mesothelioma: a case report \*\*VS\*\*. *Diagn Pathol*. 2011 Dec 30;6:130. [\[CrossRef\]](#) [\[PubMed\]](#)
5. Agulnik M, Yarber JL, Okuno SH, von Mehren M, Jovanovic BD, Brockstein BE, Evens AM, Benjamin RS. An open-label, multicenter, phase II study of bevacizumab for the treatment of angiosarcoma and epithelioid hemangioendotheliomas. *Ann Oncol*. 2013 Jan;24(1):257-63. [\[CrossRef\]](#) [\[PubMed\]](#)
6. Penel N, Bui BN, Bay JO, et al. Phase II trial of weekly paclitaxel for unresectable angiosarcoma: the ANGIOTAX Study. *J Clin Oncol*. 2008 Nov 10;26(32):5269-74. [\[CrossRef\]](#) [\[PubMed\]](#)