September 2017 Pulmonary Case of the Month

*Lewis J. Wesselius, MD*

Department of Pulmonary Medicine
Mayo Clinic Arizona
Scottsdale, AZ USA

**History of Present Illness**

A 67-year-old woman with history of chronic lymphocytic leukemia (CLL) was referred due to a 6-week history of severe cough. Her CLL had recently relapsed and she was begun on ibrutinib (a small molecule drug that binds permanently to Bruton’s tyrosine kinase) in addition to acyclovir, sulfamethoxazole/trimethoprim and allopurinol.

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

Her CLL was initially diagnosed in 2009 and had responded to fludarabine, cyclophosphamide, and rituximab. She had no other chronic medical diseases. She smoked ½ pack per day but quit with the development of her cough. Family history was noncontributory.

**Physical Examination**

Her vital signs were unremarkable and she was afebrile but did cough frequently during the examination. There were shoddy small lymph nodes noted in both supraclavicular and axillary areas. Lungs were clear and the rest of the physical examination was unremarkable.

**Laboratory Evaluation**

Her complete blood count revealed her to be mildly anemic with a hemoglobin of 9.0 g/dL, an elevated white count of 33,700 cells/mcL with 88% lymphocytes, and a low platelet count of 60,000 cells/mcL. Her electrolytes were within normal limits and her blood urea nitrogen was 20 mg/dL, creatinine 1.1 mg/dL and uric acid 7.1 mg/dL.

**Chest Radiography**

A chest x-ray was performed (Figure 1).
Which of the following is true?

1. A pulmonary nodule is present in the left upper lobe (LUL)
2. Ibrutinib is well known to cause a chronic cough
3. Pneumonia is unlikely since she is afebrile
4. 1 and 3
5. All of the above
Correct!

1. A pulmonary nodule is present in the left upper lobe (LUL)

The chest x-ray shows a 3 cm LUL nodule (Figure 2).

![Chest x-ray showing 3 cm LUL nodule (circled).](image)

Figure 2. Chest x-ray showing 3 cm LUL nodule (circled).

Pneumonia is the most frequent pulmonary complication of CLL (1). Patients with pneumonia may occasionally be afebrile. To my knowledge, ibrutinib has not been associated with cough.

Which of the following should be **done at this time**?

1. Begin empiric antibiotics for presumptive community-acquired pneumonia
2. Needle biopsy the LUL nodule
3. Thoracic CT scan
4. 1 and 3
5. All of the above
The patient may well have pneumonia but the presentation with chronic nonproductive cough alone, lack of fever, and a LUL nodule is somewhat unusual. Since the patient was immunocompromised from her CLL, an infection other than community-acquired pneumonia is quite possible. Therefore, empiric antibiotics for community-acquired pneumonia alone are a poor choice unless begun while awaiting further diagnostic studies. Needle biopsy is probably premature, does not sample the airways and exposes the patient to a potential bleeding risk. Thoracic CT is indicated to better define the pulmonary nodule and because other abnormalities might be found (Figure 3).

Figure 3. Representative images from the thoracic CT scan in lung windows (A-E) and soft tissue windows (F).

Which of the following should be done next?

1. Bronchoscopy
2. Mediastinoscopy
3. Positron emission tomography/computed tomography (PET/CT)
4. 1 and 3
5. Any of the above are acceptable
Correct!

1. Bronchoscopy

The thoracic CT scan shows the LUL nodule seen on chest x-ray and several other subcentimeter nodules. The soft tissue window view in Figure 3F shows lymphadenopathy surrounding the trachea. It is unclear how PET/CT would be useful. The most likely diagnoses would all show increased glucose uptake. Mediastinoscopy could be used to sample the lymph nodes but is invasive and does not sample the lung. The best choice is bronchoscopy with bronchoalveolar lavage, bronchial biopsy and endobronchial ultrasound (EBUS) directed biopsy of the mediastinal masses. The bronchoalveolar lavage is done because of the possibility of infection and bronchial biopsy done for the possibility of a bronchial abnormality as the cause of her cough.

Bronchoscopy did not reveal any masses. However, the LUL bronchi were edematous and thickened. The stains and cultures for pathogens from the bronchoalveolar lavage were negative. EBUS biopsies of the mediastinal lymph nodes were consistent with CLL. The bronchial biopsies are shown in Figure 4.

![Figure 4](image)

Figure 4. A: low power view of bronchial biopsy. B: high power view of bronchial biopsy.

Which of the following is the most likely cause of her cough and lung nodules?

1. Aspergillus infection of the lung with submucosal bronchial spread
2. CLL infiltration of the bronchi and lung
3. Non-small cell cancer with lung and bronchial metastases
4. *Pneumocystis jirovecii* infection
5. Valley fever
Correct!

2. CLL infiltration of the bronchi and lung

The biopsy shows a lymphocytic infiltrate of the bronchi consistent with CLL infiltration. No pathogens were identified and the special staining of the cells was consistent with CLL. Although lung cancer is possible in this patient, the histology and special staining is inconsistent with non-small cell cancer.

CLL infiltration is an infrequent cause of pulmonary symptoms (1,2). However, CLL infiltration is seen in about 40% of patients at autopsy, a frequency about double that seen in chronic myelogenous leukemia (3). Usually these infiltrates occur in the pulmonary parenchyma but airway involvement has been rarely reported (3).

Our patient’s treatment with ibrutinib was continued and her cough resolved. She continues to do well as an outpatient.

References