September 2012 Pulmonary Case of the Month: The War on Drugs

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History of Present Illness
A 69 year old woman was seen with a three day history of nonproductive cough and shortness of breath.

PMH, SH and FH
She has a past history of atrial fibrillation and hypothyroidism. Her present medications include:
- Diltiazem
- Amiodarone
- Aspirin
- Levothyroxine
- Multi vitamins
There is a 20 pack-year smoking history but she quit in 1998. She is employed as a law school professor.

Physical Examination
Her physical examination is normal.

Chest X-ray
Her admission chest x-ray is shown in Figure 1.

Figure 1. Chest x-ray showing the PA (Panel A) and lateral (Panel B) views.
An electrocardiogram showed normal sinus rhythm.

Which of the following is the most likely cause of the patient’s clinical picture?

1. Viral bronchitis
2. Exacerbation of COPD
3. Pneumonia
4. Congestive heart failure
5. Drug reaction
Correct!

1. Viral bronchitis

Both the physical examination and chest x-ray are normal. This makes pneumonia and congestive heart failure unlikely. There is no history of COPD which would be unlikely with a 20 pack-year history of smoking. Drug reaction is possible with amiodarone being the most likely cause but is much less common than a respiratory tract infection.

She was asked to return for follow up a week later. She returns with worsening symptoms and was admitted to the hospital.

Laboratory evaluation shows a slightly low hemoglobin 11.6 g/dL and an elevated white blood cell count of 11,100 cells/μL and an elevated neutrophil count (90% neutrophils).

Repeat chest x-ray is show in figure 2.

![Figure 2](image)

Figure 2. Repeat chest x-ray on week after the x-ray show in figure 1 showing the PA (Panel A) and lateral (Panel B) views.

A CT scan was performed (Figure 3).
The patient was started on piperacillin-tazobactam, levofloxacin, and doxycycline. Worsening of cough and pleuritic chest pain were noted. Sputum cultures and smears were negative.

Which of the following is the next step in her evaluation?
1. PET scan
2. CT angiography
3. Bronchoscopy with bronchoalveolar lavage (BAL)
4. Needle biopsy
5. Video-assisted thorascopic (VATS) biopsy
2. Bronchoscopy with bronchoalveolar lavage

A PET scan is usually for assessing the metabolic activity of a pulmonary nodule and a CT angiogram is usually to evaluate for abnormal pulmonary vasculature. There is no evidence of a nodule or pulmonary vascular abnormality. Several potential diagnoses may be identified with bronchoscopy with bronchoalveolar lavage, potentially saving the patient an open lung biopsy.

The bronchoscopy with bronchoalveolar lavage had a negative cytology and smears. A cell differential was requested on the fluid, but was not performed due to a laboratory problem with specimen processing.

She was empirically begun on fluconazole. However, the patient continued to deteriorate and was transferred to the ICU. A trial of BiPAP failed and she was intubated on day 5 of hospitalization due to worsening hypoxia and respiratory distress. A video-assisted thorascopic (VATS) lung biopsy was performed (Figure 4).

![Figure 4. Representative images from the VATS lung biopsy (Panels A-C) including a high power image of Panel B (Panel D).](image-url)
Which of the following should be done next?
1. Stop the patient’s amiodarone
2. Begin amphotericin B
3. Begin corticosteroids
4. A + C
5. All of the above
The lung biopsy (Figure 5) shows acute lung injury, with organizing pneumonia, with scattered eosinophils (arrows) within the interstitium and occasionally alveoli.

Figure 5. Representative images from open lung biopsy with arrows indicating collections of eosinophils.

Some of the alveolar spaces show the presence of numerous macrophages and occasional neutrophils. The presence of eosinophils with or without macrophages, lymphocytes, neutrophils in the lung biopsy is considered diagnostic of pulmonary eosinophilia.

As we mentioned last month there are numerous causes of pulmonary eosinophilia in addition to eosinophilic pneumonia including interstitial diseases, infections, toxins and drugs (1). Larsen et al. (2) recently reported four cases of eosinophilic pneumonia associated with amiodarone. Two of the cases were classified as acute eosinophilic pneumonia and two were classified as chronic eosinophilic pneumonia.

Our patient was started on high dose corticosteroids (methylprednisolone 125 mg q 6 hr) and antibiotics were stopped after a 14 day course with exception of
fluconazole. She has very slowly improved on tapering doses of corticosteroids. Although patients with idiopathic acute eosinophilic pneumonia often dramatically improve with corticosteroids (3), this patient might have shown slow improvement because of the very long half-life of amiodarone in the lung.

References

1. Wesselius LJ. August 2012 pulmonary case of the month: all eosinophilia is not asthma. Southwest J Pulm Crit Care 2012;5:58-64.