August 2012 Pulmonary Case of the Month:
All Eosinophilia Is Not Asthma

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History of Present Illness

A 73 year old man was seen with a one month history of shortness of breath. He dated this to an emergency room visit for an arm injury for which he had a DPT vaccination. Previously, he had been able to swim regularly, but he is now unable to swim due to worsening dyspnea. He also had some cough that was nonproductive.

PMH, SH and FH

He has a past medical history of coronary artery disease with prior stenting of his right and left anterior descending artery in 2010. He also has a history of hypertension, dyslipidemia, a carotid endarterectomy and a single seizure after a corneal transplant.

His present medications include:
- Atorvastatin
- Lisinopril
- Metoprolol
- Warfarin

He has a minimal smoking history and denied use of alcohol, drugs or unusual exposures

Physical Examination

His vitals signs were normal and he was afebrile but he was receiving supplemental oxygen at 3 lpm.
Chest examination revealed bilateral crackles but no wheezes.
Cardiovascular examination showed a regular rhythm with a Grade 2/6 systolic ejection murmur.
He had no clubbing or edema.
The remainder of the physical examination was either normal or noncontributory.

Chest X-ray

His admission chest x-ray is shown in Figure 1.
Figure 1. Admission chest x-ray showing the PA (Panel A) and lateral (Panel B).

Which of the following are possible causes of the patient’s clinical picture?
1. Coccidioidomycosis (Valley Fever)
2. Allergic reaction to the DPT vaccination
3. Pulmonary edema
4. A + C
5. All of the above
In the Southwest coccidioidomycosis is certainly a possibility. Although the presentation and chest x-ray are not classic, an atypical presentation of pulmonary edema is possible. There are no reports to our knowledge of a similar presentation 4 weeks after DPT vaccination.

His laboratory evaluation included a complete blood count showing a hemoglobin of 13.6 g/dL and a hematocrit of 40.9%. His white blood cell count was 10.3 X10⁶ cells/microliter. Differential showed no left shift but his eosinophils were slightly elevated at 5.2% or an absolute count of 530 cells/microliter. His N-terminal pro-brain naturetic peptide (NT-proBNP) was also slightly elevated 290. His INR was elevated at 2.53 compatible with his warfarin therapy. His cocci serology was negative.

To better define his thoracic lesions a CT scan of the chest was performed (Figure 2).

Which of the following should be done next?
1. PET scan
2. CT angiography
3. Bronchoscopy with bronchoalveolar lavage (BAL)
4. Bronchoscopy with transbronchial biopsy
5. Video-assisted thorascopic (VATS) biopsy
Correct!

3. Bronchoscopy with bronchoalveolar lavage

It is unclear how either a PET scan or a CT angiography would be helpful. Bronchoscopy with transbronchial biopsy is potentially dangerous because of the patient’s anticoagulant therapy. VATS biopsy seems over aggressive at this point.

Bronchoscopy with bronchoalveolar lavage (BAL) was performed and demonstrated normal anatomy and no endobronchial abnormalities. BAL showed 18% eosinophils cell differential. Smears, cultures and cytology were all negative.

Which of the following are associated with BAL eosinophilia?

1. Interstitial lung disease
2. Coccidioides infection
3. Drug-induced lung disease
4. Eosinophilic pneumonia
5. All of the above
Correct!
5. All of the above.

There was an increase in eosinophils noted in bronchoalveolar lavage fluid in this case; however, the percentage of eosinophils was nonspecific and some increase in lavage eosinophils can be seen in each of the listed disorders. Therefore, a VATS lung biopsy was performed to confirm a diagnosis (Figure 3).

Figure 3. VATS lung biopsy from upper lobe (Panels A & B) and lower lobe (Panels C & D). A high power view is shown from each (Panels B & D).

What should be done next?
1. Stop all the patient’s drugs
2. Begin amphotericin B
3. Begin ivermectin
4. Begin prednisone
5. Begin prednisone, azathioprine and N-acetylcysteine
The biopsy showed eosinophils and is consistent with eosinophilic pneumonia and possibly pulmonary fibrosis in the lower lobe biopsy. The collections of eosinophils are seen best in the lower power views (Figure 4).

![Figure 4. VATS lung biopsy showing collections of eosinophils in higher power views (arrows).](image)

Just as all that wheezes is not asthma, all eosinophilia is not asthma either. Causes of eosinophils in bronchoalveolar lavage fluid are listed in table 1.

Table 1. Causes of bronchoalveolar lavage eosinophilia

<table>
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<tr>
<th>Cause</th>
<th>Examples</th>
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<tr>
<td>Interstitial lung disease</td>
<td>Idiopathic pulmonary fibrosis, sarcoidosis, systemic lupus erythematosis</td>
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<tr>
<td>Drug-induced</td>
<td>Nitrofurantoin, phenytoin, L-trpytophan, ampicillin, minocycline, ranitidine</td>
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<td>Illicit drugs/toxins</td>
<td>Inhalation of heroin, crack cocaine, Scotchguard, dust (World Trade Center 9/11)</td>
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<tr>
<td>Infections</td>
<td>HIV, parasitic infections, fungal infections (coccid), Aspergillus, Stenotrophomonas maltophilia, paragonimiasis</td>
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Eosinophilic pneumonia is divided into acute eosinophilic pneumonia and chronic eosinophilic pneumonia. Acute eosinophilic pneumonia is usually associated with:

- Respiratory symptoms of < 2 weeks
- Hypoxemia often causing acute respiratory failure and mimicking ARDS
- BAL eosinophilia is usually above 25%
- No or mild blood eosinophilia (<1000)
- Lung biopsy evidence of eosinophilic infiltrates (acute and/or organizing diffuse alveolar damage with prominent eosinophils).

In contrast, chronic eosinophilic pneumonia is associated with

- Respiratory symptoms > 2 weeks
- Alveolar eosinophilia (≥ 40% eos on BAL)
- Blood eosinophilia (often ≥1000)
- Pulmonary infiltrates usually with a peripheral predominance
- Twice as frequent in women as men
- A third to half have a history of asthma
- Less than 10% are active smokers
- Although dyspnea and cough are common, respiratory failure is rare

Both are diagnosis of exclusion and the treatment is corticosteroids. However, if biopsy is planned, corticosteroid use should be avoided since as little as a day or two of corticosteroids can result a marked decrease in the number of eosinophils on biopsy making diagnosis more difficult. Relapse is frequent in chronic but not in acute eosinophilic pneumonia.

This patient had evidence of eosinophilic pneumonia with some underlying histologic features of UIP. Some cases of chronic eosinophilic pneumonia have been reported to lead to pulmonary fibrosis. This is possible in the current patient, although the clinical history did not suggest prior respiratory symptoms. He was treated with corticosteroids (prednisone 60 mg/day) with subsequent decrease in some of abnormalities on chest radiograph, although there was evidence of some persistent fibrotic changes, particularly in the lung bases.

References