April 2012 Pulmonary Case of the Month: Could Have Fooled Me!

Bridgett A. Ronan, MD
Robert Viggiano, MD
Lewis J. Wesselius, MD

Pulmonary Medicine
Mayo Clinic Arizona
Scottsdale, AZ

History of Present Illness
A 60 year old man was seen by his primary care physician with cough for 2 weeks which was dry and worse with deep breathing. He had been exposed to smoke from industrial storage fire just prior to the onset of his cough. He had developed fever for the past 3 days.

PMH, SH and FH
He has a history of osteopenia and was found to have a +PPD in high school for which he was never treated with isoniazid. Originally from New York he has lived in Arizona for 14 years. He was a former smoker having a 45 pack-year history having quit in 2007. He drives a delivery truck. His sister had tuberculosis which was treated and his father has emphysema.

Physical Examination
He had mild rhonchi in the right upper lung field. Otherwise, the physical exam was unremarkable.

Laboratory and Chest X-ray
A CBC was performed which revealed a hemoglobin of 11.7 g/dL, white blood cell (WBC) count of 11.9 X 1000 cells/ml with 79% neutrophils, and a platelet count of 337 X 1000/mL. Coccidioidomycosis serologies were drawn. A chest x-ray was taken (Figure 1).
Considerations at this point include:
1. Community acquired pneumonia
2. Coccidioidomycosis
3. Tuberculosis
4. Pneumonitis from smoke inhalation
5. Pulmonary embolism
6. All of the above
Community acquired pneumonia remains a consideration in a 60 year old previously healthy man although the presentation and the chest x-ray are unusual. Coccidioidomycosis is common in the Southwest and remains in most differentials of chest disease. Tuberculosis is possible especially with his previous history of a +PPD and a + family history. However, the patient’s subacute course and chest x-ray with lower lobe predominance would be unusual. Pneumonitis from smoke inhalation this long after exposure would be extremely unusual. His presentation would also be very unusual for pulmonary embolism.

The patient was treated with Levaquin and Tessalon Perles and scheduled for follow up in 2 weeks. His fever and cough improved although the later remained unproductive.

However, 7 days after being seen he went to the emergency room with new onset of pleuritic pain and right shoulder and flank pain. His chest X-ray was repeated (Figure 2).

Figure 2. Repeat chest x-ray showing increasing size of several nodules and the development of new nodules.
He was admitted to the hospital and treated with ceftriaxone and azithromycin. Repeat of his CBC revealed his hemoglobin and WBC to be minimally changed at 11.3 and 13.8 respectively. Urinanalysis revealed microscopic hematuria. Coccidioidomycosis enzyme-linked assays revealed a negative IgM but a positive IgG at 1.1 IV (normal <1.0). CT abdomen was done for flank pain but was interpreted as being unremarkable. CT of the chest was performed (Figure 3).

Figure 3. Representative images from the thoracic CT scan proceeding caudally A-C.

Which of the following would be indicated?
  1. Coccidioidomycosis testing by complement fixation
  2. Quantiferon for tuberculosis
  3. Bronchoscopy
  4. Rheumatologic testing
  5. All of the above
The diagnosis at this point is unclear. Since the elevated IgG antibodies to coccidioidomycosis are equivocal, the more specific complement fixation test is indicated (1). Quantiferon is indicated to rapidly evaluate for tuberculosis. Bronchoscopy is indicated to evaluate for cancer as well as to assure adequate cultures. Rheumatologic testing is indicated because of the lung nodules as well as the microscopic hematuria.

On bronchoscopy blood was noted in both mainstem bronchi. A bronchoalveolar lavage (BAL) was performed of the right middle lobe. The return became sequentially bloodier with each aliquot. The coccidioidomycosis complement fixation test was 1:2 (normal < 1:4). Quantiferon was negative. Erythrocyte sedimentation rate was >100 mm/hr (normal < 20), C-reactive protein was elevated 141 mg/dL (normal <6), perinuclear anti-neutrophil cytoplasmic antibody (pANAC) and myeloperoxidase (MPO) antibody were both positive. Creatinine was normal although there was moderate hemoglobin present on repeat UA. Extractable nuclear antibody (ENA), anti-nuclear antibody (ANA), cytoplasmic ANCA (anti-PR3, cANCA), and anti-glomerular basement membrane (GBM) were all negative.

Which of the following is the most likely diagnosis?
1. ANCA-positive vasculitis
2. Systemic lupus erythematosi (SLE)
3. Rheumatoid arthritis
4. Goodpasture’s syndrome
5. Leukocytoclastic vasculitis
Correct!

1. ANCA-positive vasculitis

There are multiple clinical findings that suggest vasculitis. Some are listed below:

- Diffuse alveolar hemorrhage
- Acute glomerulonephritis
- Pulmonary-renal syndrome
- Upper airway disease
- Otitis, sinusitis, epistaxis
- Nodular or cavitary chest disease
- Palpable purpura
- Mononeuritis multiplex
- Multisystem disease not easily explained

In a patient suspected of rheumatologic vasculitis some of the laboratory tests that are useful in separating the disorders include:

- General inflammatory markers: ESR, CRP
- Secondary vasculitis: ANA, ENA, rheumatoid factor (RF), Cyclic citrullinated peptide antibody (CCP), cryoglobulins
- Immune Complex-mediated: Anti GBM
- Idiopathic vasculitis: ANCA’s

The patient has ANCA-positive vasculitis (APV) which is usually separated from the other vasculitis by ANCA positivity. APV is subdivided into three diseases (2):

1. Necrotizing granulomatous vasculitis (NGV, formerly known as Wegener’s Granulomatosis)
2. Churg-Strauss Syndrome (CSS)
3. Microscopic Polyangiitis (MPA)

These are distinguished by clinical findings, ANCA test positivity, and biopsy. The different diseases have different prevalences of ANCA positivity listed below (Table 1).

<table>
<thead>
<tr>
<th>Disease</th>
<th>cANCA positive (anti-PR3)</th>
<th>pANCA positive (anti-MPO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized NGV</td>
<td>70-95</td>
<td>0-10</td>
</tr>
<tr>
<td>Localized NGV</td>
<td>40-50</td>
<td>0-10</td>
</tr>
<tr>
<td>MPA</td>
<td>10-20</td>
<td>30-80</td>
</tr>
<tr>
<td>CSS</td>
<td>0-10</td>
<td>30-75</td>
</tr>
</tbody>
</table>

Necrotizing granulomatous vasculitis (NGV, formerly known as Wegener’s granulomatosis) is the most common ANCA-positive vasculitis that presents with respiratory tract disease. It can present in a generalized form involving lungs,
kidneys and other organs or a localized form involving a single organ system. Most have glomerulonephritis (90%). Abnormal chest imaging can consist of alveolar, interstitial, nodular, and/or cavitary patterns. Biopsy shows necrotizing vasculitis and granulomas.

In microscopic polyangitis the patients invariably have glomerulonephritis but pulmonary disease is present in 30%. Joints, skin, and nerves may also be involved. Biopsy shows necrotizing vasculitis without granulomas.

Churg-Strauss syndrome (CSS) is the rarest of the ANCA-positive disorders. Asthma and eosinophilia usually accompany CSS. In addition to the lungs the vasculitis often involves the skin, nerves, sinuses, or heart. Biopsy shows a necrotizing vasculitis and granulomas with eosinophils.

Which of the following are therapies for the ANCA-positive vasculitides?
1. High dose corticosteroids
2. Cyclophosphamide
3. Rituximab
4. Plasma exchange
5. All of the above
Correct!

5. All of the above

All have been used for therapy. High dose methylprednisolone is often given at 1 gram daily for 3 days, then prednisone at 1 mg/kg. Cyclophosphamide is usually given at 2 mg/kg daily up to 200 mg. Rituximab is given weekly for 4 weeks. Plasma exchange can be used in patients critically ill. The corticosteroids are usually tapered with azathioprine or methotrexate usually given for maintenance therapy. None has been shown to be superior therapy (3).

The patient was given 1 gram solumedrol initially for 3 days and a rituximab infusion. He showed marked improvement. He was discharged taking 60 mg of prednisone daily and scheduled for Rituximab infusions. His pleuritic chest pain resolved and his follow up chest X-ray showed marked improvement (Figure 4).

Figure 4. Follow up chest x-ray taken at the time of discharge from the hospital.

References