February 2015 Critical Care Case of the Month: A Bloody Mess

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History of Presenting Illness:

A 23-year-old Ethiopian woman with a known history of systemic lupus erythematosus (SLE) but of unknown duration presented with the chief complaints of cough and generalised weakness for 1 week. She had a recent history of travelling to Ethiopia 3 months ago for 3 weeks. She complained of subjective fevers and one episode of blood tinged sputum. She also complained of fatigue and an episode of syncope which prompted her hospitalization.

PMH, SH and FH:

The patient has a past medical history of SLE diagnosed in Ethiopia of which no records were available. She is a student and denied alcohol, smoking or drug abuse. She denied any family history of autoimmune disorders. She did not take any medications at home.

Physical Examination:

Initial admission vital signs were temperature of 100.5 F, heart rate of 130, respiratory rate of 30 and blood pressure of 92/48. Oxygen saturation was 96% on 2 L/min via nasal cannula.

She appeared to be in moderate distress but was speaking in full sentences. Skin examination revealed a malar rash on her face. Her upper and lower extremities had excoriated plaques. Her anterior chest had flat non blanchable, macular rash. CVS examination revealed tachycardia without any murmurs. Respiratory exam was positive for bilaterally diffuse bronchial breath sounds. The remainder of her exam was within normal limits.

Laboratory and Radiology:

CBC: WBC 6.7 million cells/mcL, hemoglobin 7.1 g/dL, hematocrit 20.9, platelet 160,000 cells/mcL

Renal panel: within normal limits.

Troponin 0.01, creatine kinase 457 U/L, lactic acid 1.1 mm/L, HIV non-reactive

Liver function tests: AST 288 U/L, ALT 93 U/L alkaline phosphatase 136 IU/L, total bilirubin 0.9 mg/dL

Radiography:

Her initial chest x-ray is shown in figure 1. It was interpreted as showing diffuse pulmonary infiltrates, right lung greater than left. No pleural effusions. No pneumothorax.

Figure 1. Initial chest x-ray.

In a patient with these characteristics, which **other test(s)** would you order?

1. Arterial blood gases and lactic acid
2. Cardiac angiogram
3. Computed tomography (CT) of the chest without contrast
4. VATS lung biopsy
5. All of the above

Correct!

3. CT of the chest without contrast

This patient presents with cough, fatigue and an episode of blood tinged sputum in the setting of known autoimmune disease. Her initial chest x-ray shows bilateral infiltrates that can be secondary to many etiologies (e.g. ARDS or infection). Computed tomography (CT) scan of the chest is helpful in narrowing the differential diagnosis through the demonstration of ground glass opacities, consolidations or nodularity (1). Although an arterial blood gas is appropriate it will be less helpful in establishing the diagnosis and she already has had a lactic acid measured. Clinically she is not presenting with cardiac disease so a cardiac angiogram is not indicated at this time. VATS lung biopsy seems premature until other tests are performed.

In our patient, CT chest findings showed presence of ground glass or airspace-filling opacities that are diffuse and bilateral with greatest involvement in the right lower lobe and right middle lobe.

Figure 2. Representative lung window from the thoracic CT scan.

The patient was admitted to ICU and required intubation and mechanical ventilation, with high oxygen supplementation. With patient's blood pressure dropping, she was started on vasopressor support and empiric cefepime and vancomycin. However, even with aggressive resuscitation with fluids, vasopressors, broad spectrum antibiotics and mechanical ventilation, she did not improve. On serial hemoglobin measurements, it was noted that patient's hemoglobin was dropping consistently. Her initial blood and respiratory cultures were negative and lactic acid was within normal limits.

Which of the following would be **most useful** in making the diagnosis?

1. Bronchoscopy with sequential bronchoalveolar lavage
2. Lupus serology
3. Needle biopsy of the lung
4. Reculture pulmonary secretions and change antibiotics
5. VATS lung biopsy

Correct!

1. Bronchoscopy with sequential bronchoalveolar lavage

Bronchoalveolar inspection and sequential bronchoalveolar lavage (BAL) is the test of choice. Bronchoscopy with BAL will be useful to rule out infections, inflammatory processes, and diffuse alveolar hemorrhage (DAH). Although indicated, lupus serology would most likely only confirm the diagnosis. Cultures would be unlikely to change her clinical course. Needle biopsy and VATS lung biopsy are overly aggressive and not indicated at this time.

The bronchoscopy was done at bedside following the American Thoracic Society guidelines (2). It showed a bloody fluid throughout the airways. After wedging the bronchoscope in the right middle lobe, a lavage with normal saline was performed with return of bloody secretions. Subsequent aliquots of lavage fluid returned with progressively bloody characteristics which was diagnostic of DAH (2). Additionally, a neutrophil predominance was found in the cellular component and is common in cases of DAH (2). For patients who can complete pulmonary function testing, another sensitive marker for DAH is a sequential increase in diffusing capacity for carbon monoxide (DLCO).

It is important to distinguish DAH from other pulmonary manifestations of SLE such as lupus pneumonitis, lupus pleuritis, pulmonary embolism secondary to circulating lupus anticoagulant, pulmonary hypertension. To rule out the above mentioned causes and evaluate the presence of other collagen vascular disease, several lab tests were ordered which are below:

Positive:

- ANA titer 1:2560, speckled pattern
- Anti-ribonucleoprotein >8
- Anti-Smith >8
- Anti-SSA 32.
- Complement C3-26 mg/dL
- Complement C4-5.8 mg/dL

Negative:

- Anti-glomerulo-basement-membrane
- Anti-neutrophil cytoplasmic antibody
- Anti-double-stranded DNA
- Blood cultures
- Respiratory cultures
- Acid fast bacilli culture
- β -D glucan assay
- HIV
- CT angiogram of chest: negative for PE
- Echocardiogram: Negative for pulmonary hypertension with normal EF

Is diffuse alveolar hemorrhage a **frequent** pathology in SLE?

1. True
2. False

Correct!
2. False

Diffuse alveolar hemorrhage (DAH) is a rare but catastrophic complication of SLE. It is characterized by bleeding into the alveolar space due to disruption of alveolar-capillary basement membrane (3). Its incidence ranges from 2 to 5.4 % in patients with SLE (4,5). The classic triad of hemoptysis, new pulmonary alveolar infiltrates and fall in hemoglobin is seen 25 to 75 % of patients (6). Temperature elevation $>38^{\circ}\text{C}$ is also another inconsistent systemic finding. Most commonly involved are women with a median age of 27 years.

As DAH is a rare complication of SLE, pathologic mechanisms are not well understood. Previous reports from tissue biopsy suggest damage of small blood vessels and alveoli from immune complexes. The most common histological findings seen are pulmonary capillaritis, bland pulmonary hemorrhage and diffuse alveolar damage. The most common extra pulmonary complication is lupus nephritis 64-90% (6). The short term mortality rates vary from 25% to 50% in a patient with SLE complicated by DAH (3).

Which of the following is **effective treatment** for SLE induced DAH?

1. Corticosteroids
2. Cyclophosphamide
3. Plasmapheresis
4. Rituximab
5. All of the above

Correct!
5. All of the above

DAH associated with SLE is rare but with very high mortality. Initial treatment is generally with high dose corticosteroids as our patient received (1). Other cytotoxic drugs such as cyclophosphamide can be added if there is poor response to steroids, as also in our case. She also received 5 days of plasmapheresis, which is another option for difficult cases but has not been demonstrated to improve mortality rates. Other case reports exist with a good response to mycophenolate mofetil, rituximab or even extracorporeal membrane oxygenation (ECMO) (7-9). Concomitant infections are an important co-factor that has been shown to increase mortality (10).

In summary, DAH is a rare but serious complication of SLE. It should be considered in the differential diagnosis in SLE patient presenting with pulmonary complaints and decreasing hemoglobin. Early bronchoscopy should be considered to establish the diagnosis and evaluate for concomitant infection. Immunosuppressive therapy should be started in a timely manner to improve patient outcomes.

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