March 2014 Critical Care Case of the Month: Interstitial Lung Disease

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History of Present Illness

An 80 year-old man with a history of chronic obstructive pulmonary disease, asbestosis and interstitial lung disease, presented to the outpatient clinic with cough, sinus congestion and mild sputum. He was sent home with amoxicillin for the treatment of a sinus infection. However, he came back to emergency department with worsening respiratory symptoms including shortness of breath and persistent cough. He required 8-10 L/min of oxygen to maintain an oxygen saturation above 90 %.

PMH

- COPD
- Asbestosis
- Interstitial lung disease
- Diabetes mellitus, type II
- Hypertension
- Aortic valve replacement

Medications

- Fluticasone-salmeterol 250-50 mcg inhaler
- Mometasone 50 mcg/actuation nasal spray
- Furosemide 40 mg PO daily
- Felodipine 5 mg PO BID
- Warfarin 3 mg PO daily
- Insulin aspart 5 units SC injection before meals
- Insulin glargine 15 units SC injection night time

Social History

- 50 pack-year prior smoking history
- No ethanol or recreational drugs
- No recent travel history
- Significant history of asbestos exposure.

Physical Examination

Vital signs: temperature 37.2 °C, pulse 116 beats/min, respiratory rate 32-34 breaths/min, blood pressure 179/77 mmHg, SpO₂ 90 % on 10 L/ min non-rebreathing mask (NRB).

General: Alert and oriented but appearing distressed, tachypneic and dyspneic

Skin: Diaphoretic, no rash or lesions noted.

HEENT: Unremarkable.

Respiratory: Diffuse rales but no wheezing or stridor.

CVS: Tachycardic, regular rhythm, soft systolic murmur.

Abdomen: Soft, non-tender, no tenderness, no guarding, no hepato-splenomegaly

Lymph: No cervical lymphadenopathy

Extremities: No peripheral edema, normal tone, normal range of movement

Laboratory

CBC: WBC $20.2 \times 10^3 /\mu\text{L}$, hemoglobin 9.3 g/dL, hematocrit 29.8 %, platelets 272,000/ μL .

Chemistries: Na⁺ 134 meq/L, K⁺ 4.8 meq/L, Cl⁻ 108 meq/L, CO₂ 19 mmol/L, blood urea nitrogen (BUN) 58 mg/dL, creatinine 1.7 mg/dL, glucose 272 mg/dL, calcium 9.7 mg/dL, albumin 2.2 g/dL, liver function test-within normal limits.

Prothrombin time (PT) 28.0 sec, international normalized ratio (INR) 2.5, partial thromboplastin time (PTT) 44.5 sec

An old chest x-ray and CT scan were reviewed (Figure 1).

Figure 1. Old PA (panel A) and lateral (Panel B) and representative image from an old CT scan (panel C).

Which of the followings are the **findings of asbestos related disease** on chest x-ray? (click on correct answer to move to next panel)

1. Reticular or patchy opacity
2. Calcified pleural plaque
3. Bilateral consolidation
4. Pulmonary edema
5. 1 + 2
6. 3 + 4

Correct!
5. 1 + 2

Asbestos fiber inhalation can lead to diverse pulmonary disorders including asbestosis, pleural disease and malignancy. Asbestosis represents diffuse pulmonary fibrosis, and peripheral reticular opacities with lower lung field predilection are the characteristic chest x-ray findings. CT scan helps diagnosis of early stage asbestosis with normal chest x-ray finding, and subpleural curvilinear lines, pleural thickening, lobular septal thickening, and honeycombing change are commonly found on CT image (1).

Later on the same day, patient developed severe hypoxemia requiring intubation and ICU transfer. The arterial blood gases (ABG) before intubation were as follows:

ABG: pH 7.37, pCO₂ 36.0 mmHg, pO₂ 68.0 mmHg HCO₃⁻ 20.8 meq/L, SaO₂ 90.8 % while receiving 10 L O₂ NRB

Broad spectrum coverage for bacterial and fungal disease was begun with vancomycin, azithromycin, meropenem and fluconazole. However, testing for mycoplasma, coccidioidomycosis, legionella, respiratory viral panel, sputum, and blood cultures were all negative. Subsequent bronchoalveolar lavage showed a cell count of 0.46 X 10⁶ and a differential of 83% neutrophils, 3% lymphocytes, 13% macrophages, and 1% eosinophils with no evidence of infection.

A chest x-ray and chest CT were performed after intubation (Figure 2).

Figure 2. Portable AP of chest (Panel A) and representative lung window from thoracic CT scan (Panel B) performed after intubation.

What is the **most common** cause of respiratory decompensation in interstitial lung disease (ILD) patients? (click on correct answer to move to next panel)

1. Complication of immune suppressing treatment
2. Congestive heart failure
3. Idiopathic
4. Infection
5. Pulmonary hypertension
6. Venous thromboembolism

Correct!
3. Idiopathic

Acute exacerbation is one of the main prognostic factors predicting increased mortality of ILD patients. For instance, the mortality rate of acute exacerbation in IPF patients is 60~100%, and it is the main cause of death. The definition of an acute exacerbation in ILD patients includes the following criteria (2).

- Concurrent diagnosis of interstitial lung disease;
- Aggravating symptoms;
- Hypoxemia worse than pre-exacerbation (decreased PaO₂/FiO₂);
- New ground glass opacities or consolidations on images;
- Exclusion of other causes that can cause aggravation of symptoms such as infection, pulmonary hypertension, congestive heart failure and pulmonary embolism.

Multiple factors including infection, pulmonary embolism, heart failure, chemo- or radio-therapy for lung cancer, BAL, and complication of immune suppressing agents, can exacerbate underlying ILD, however a clear etiology cannot be found in the majority of ILD patients with acute exacerbation. Several hypothesis such as genetic factors, occult aspiration and viral infection have been suggested although no clear evidence to support any of these (2).

The patient is now on mechanical ventilator in the volume control mode with a positive end expiratory pressure (PEEP) of 14 cm H₂O, respiratory rate 14 breaths/min, tidal volume (TV) 380 ml, and the fraction of inspired oxygen (FiO₂) of 60%. ABGs were as follows:

ABG: pH 7.34, pCO₂ 45.4 mmHg, pO₂ 168.3 mmHg HCO₃⁻ 24.8 meq/L, SaO₂ 96.3 %

What is the **most appropriate ventilator mode** in diffuse interstitial lung disease? (click on correct answer to move to next panel)

1. High PEEP, high tidal volume
2. High PEEP, low tidal volume
3. Low PEEP, high tidal volume
4. Low PEEP, low tidal volume
5. None of the above

Correct!

2. High PEEP, low tidal volume

Repetitive opening and closing of alveoli upon mechanical ventilation can cause injury in lung parenchyma, which is called ventilator induced lung injury (VILI). It can lead to multi-organ failure through dissemination of proinflammatory cytokines and enzymes, therefore, a protective ventilation strategy is pivotal in patients with ARDS or ALI. The ARDS Clinical Network recommends a low tidal volume (≤ 8 ml/kg PBW) with a goal plateau pressure ≤ 30 cm H₂O (3). A recent meta-analysis showed high PEEP might increase survival in ARDS patient, but may be harmful in ALI patients without ARDS (4). However, most of these studies excluded patients with known interstitial lung disease such as idiopathic pulmonary fibrosis and cryptogenic organizing pneumonia, and it is unclear whether these mechanical ventilator strategies for ARDS or ALI work the same way in ILD patients. One recent retrospective study with ILD patients showed a high PEEP > 10 cm H₂O was associated with a significant survival benefit (5). Although there is no definitive evidence, a low tidal volume with high PEEP is the current recommendation for ILD patients who need mechanical ventilation to minimize volutrauma, atelectotrauma and maximized oxygenation.

There was little improvement in our patient with antibiotic treatment, and ventilator weaning was difficult. The diffuse chest x-ray and CT findings along with the nonspecific BAL cytology suggested the diagnosis of cryptogenic organizing pneumonia.

What is the **best initial treatment** for an acute exacerbation of cryptogenic organizing pneumonia? (click on correct answer to move to next panel)

1. Antibiotics
2. Anticoagulation
3. Cyclophosphamide
4. Glucocorticoids
5. Pirfenidone

Correct!
4. Glucocorticoids

Cryptogenic organizing pneumonia (COP) is one of the many causes of diffuse interstitial lung disease. Histologic findings of COP include extensive proliferation of granulation tissues affecting distal bronchioles and alveolar walls with patchy and peribronchiolar distribution (5). Patients with COP most commonly present with flu-like symptoms including cough, dyspnea, fever and general weakness, which are resistant to antibiotic treatment. There is no specific laboratory test for COP, and only 50 % of patients have leukocytosis. Glucocorticoids with careful attention to their adverse effect are recommended as an initial treatment for COP patients with persistent or worsening symptoms (6,7). Cytotoxic agents such as cyclophosphamide can be an alternative option for the patients who are refractory to steroid treatment.

High dose glucocorticoids were started. The patient's respiratory status improved rapidly, and he was extubated successfully.

Which of the following disease is **not** included in steroid responsive interstitial lung disease? (click on correct answer to move to next panel)

1. Acute interstitial pneumonia (AIP)
2. Desquamative interstitial pneumonia (DIP)
3. Idiopathic pulmonary fibrosis (IPF)
4. Nonspecific interstitial pneumonia (NSIP)
5. Respiratory bronchiolitis interstitial lung disease (RBILD)

Correct!

3. Idiopathic pulmonary fibrosis (IPF)

Most of the interstitial lung diseases respond well to steroid treatment except IPF. No treatment has been shown to be effective in IPF. Azathioprine, N-acetylcysteine and a steroid combination is often used, however, combination therapy cannot change the course of IPF. Additionally, a recent clinical trial showed combination therapy is associated with a higher mortality and more adverse effects than placebo (8).

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