July 2015 Pulmonary Case of the Month: A Crazy Case

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History of Present Illness

A 23-year-old woman presented in 2008 at outside institution with dyspnea and diffuse pulmonary infiltrates. She required intubation. After a surgical lung biopsy, she was transferred to the Mayo Clinic Hospital for further care.

Past Medical History

She has had a history of progressive dyspnea for several months, otherwise negative.

Physical Examination

Vital signs are stable. SpO₂ 94% on FiO₂ of 0.4. She is intubated and there is a chest tube in her right chest. Otherwise the physical examination is unremarkable.

Radiography

A thoracic CT scan was performed (Figure 1).

Figure 1. Representative images from the thoracic CT in lung windows.

Which of the following are **present on the thoracic CT scan?**

1. Diffuse ground-glass opacities
2. Interlobular septal thickening and intralobular reticular thickening
3. Right-sided pneumothorax
4. 1 and 3
5. All of the above

Correct!
5. All of the above

There is a residual pneumothorax from the open lung biopsy, a chest tube present, diffuse ground glass opacities and inter- and intralobular septal thickening (Figure 2).

Figure 2. Panels A-C: Thoracic CT scan showing pneumothorax (yellow arrows) and chest tube (green arrows). Panel D: enlargement of the right lung showing interlobular septal thickening (red arrow) and intralobular septal thickening (blue arrow).

The lung biopsy performed at the outside hospital was requested (Figure 3).

Figure 3. High power view of the open lung biopsy from the outside material showing positive periodic acid-Schiff (PAS) material in the alveoli.

What is the **diagnosis**?

1. Alveolar proteinosis
2. Idiopathic pulmonary fibrosis
3. Mycobacterial pneumonia
4. *Pneumocystis jiroveci* pneumonia
5. Sarcoidosis

Correct!

1. Alveolar proteinosis

The clinical course, the radiologic pattern and the open lung biopsy are all compatible with alveolar proteinosis. Both the "crazy paving" pattern seen on the thoracic CT scan and the positive PAS material are nonspecific but in this clinical context are diagnostic of alveolar proteinosis.

Which of the following would be **appropriate therapy** in this case?

1. Begin granulocyte macrophage-colony stimulating factor (GM-CSF)
2. Radiation to the whole lung
3. Whole lung lavage
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

There are 3 types of alveolar proteinosis (1):

1. Congenital
2. Secondary (allogeneic bone marrow transplant, hematologic malignancy, infections (Pneumocystis), acute toxic inhalations [silica, aluminum])
3. Acquired (autoimmune).

About 90% of the cases of alveolar proteinosis are acquired. This occurs when due anti-GM-CSF antibodies are formed which result in impairment of the alveolar macrophage clearance of surfactant. The surfactant accumulates clogging the alveoli resulting in the dyspnea and the positive PAS staining. Our patient's serum was positive for antibodies to GM-CSF.

The treatment of choice for severely ill patients is whole lung lavage (1). She was also begun on GM-CSF.

After whole lung lavage she was weaned off ventilator. After discharge pulmonary function tests (PFTs) showed a FVC of 80% of predicted, a TLC of 79% of predicted, and a DLco of 74% of predicted. A thoracic CT scan marked improvement in her "crazy paving" (Figure 4).

Figure 4. Representative images from the repeat thoracic CT scan showing improvement in the "crazy paving" compared to Figure 1.

By November, 2009 she had completed 4 months of GM-CSF and was feeling well, not requiring oxygen. She was subsequently lost to follow-up. In February, 2014 she was referred by her obstetrician because she was now pregnant with increasing dyspnea.

Repeat PFTs showed her FVC was 56% of predicted and her DLco was 42% of predicted. Chest x-ray showed diffuse consolidation.

Which of the **following are indicated** at this time?

1. Lung transplant
2. Rituximab
3. Therapeutic abortion
4. Whole lung lavage
5. None of the above

Correct!
5. None of the above

There are multiple treatment options available for alveolar proteinosis including (2):

1. Whole lung lavage
2. GM-CSF: systemic or inhaled
3. Rituximab (1 series of 10 patients)
4. Plasmapheresis (case reports)
5. Lung transplant (relapses reported)
6. Spontaneous remissions occur in up to 25% (no reported association with pregnancy)

None of these seemed appropriate in this situation and she was followed while on supplemental oxygen. She had a successful delivery in August, 2014 of a healthy child. She felt her breathing had improved after delivery and GM-CSF was restarted. Repeat PFTs in October, 2014 showed her FVC was 66% of predicted and her DLco 50% predicted although her chest x-ray continued to show diffuse consolidation (Figure 5).

Figure 5. Repeat chest x-ray showing diffuse consolidation.

She continued to improve and in April, 2015 her FVC was 80% of predicted and her DLco was 70% of predicted.

References

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2. Luisetti M, Kadija Z, Mariani F, Rodi G, Campo I, Trapnell BC. Therapy options in pulmonary alveolar proteinosis. Ther Adv Respir Dis. 2010;4(4):239-48. [\[CrossRef\]](#) [\[PubMed\]](#)