An unPAPular etiology: Recognition of myelodysplastic syndrome as a rare cause of pulmonary alveolar proteinosis

Madiha Rasool, MD, Ravneet Randhawa, MD, Steve Butala, MD
University of Connecticut School of Medicine, Primary Care Internal Medicine

Introduction:
- Pulmonary alveolar proteinosis (PAP) is a rare syndrome characterized by accumulation of lipoproteinaceous surfactant in alveoli due to abnormal surfactant homeostasis.
- Primary PAP is autoimmune due to anti-GM CSF antibodies. Pulmonary macrophages depend on GM-CSF.
- Secondary causes include hematologic malignancies, of which myelodysplastic syndrome (MDS) is most common. Mechanism unclear but related to abnormal macrophage function
- Leads to impaired gas exchange and respiratory failure
- Treatment with whole-lung lavage can be life-saving

Case Description:
History of Presenting Illness
- A 30-year-old woman with a past medical history of myelodysplastic syndrome and psoriasis presented with 6-days of intermittent fevers, chills, and nausea.
- Earlier in the month, she experienced some nasal congestion, cough productive of green-yellow phlegm, diffuse headache, and increased bowel movements. These symptoms resolved; however, she remained weak and then went on to develop fevers for which she presented to the hospital.
- Social history: Polish immigrant, negative PPDs and QuantiFERON testing one year ago. No recent travel. Works in construction, including installation of insulation and piping. She was a five pack-year smoker. She denied other drug use.

Hospital Course:
- Admission vital signs included a temperature of 102.4 Fahrenheit and mild tachycardia.
- Laboratory workup revealed mild anemia and neutropenia with ANC of 1100.
- A chest x-ray revealed diffuse interstitial infiltrates. Chest CT demonstrated bilateral upper lobe predominant suprahilar ground-glass opacities, interstitial thickening, mediastinal lymphadenopathy, and bronchiectasis.
- Infectious workup was largely unrevealing, despite her continued daily fever spikes to 102 Fahrenheit.
- Bronchoscopy showed normal mucosa. BAL was negative for PJP, fungal culture and mycobacterial culture.
- She was found to be positive for GATA-2 mutation, and lung biopsy was diagnostic for pulmonary alveolar proteinosis. The patient was transferred to a higher level of care for whole lung lavage.

Discussion:
- Providers should maintain a high level of clinical suspicion for PAP in patients with MDS and evaluate for both whole lung lavage and stem cell transplant.
- Mechanism of secondary PAP poorly understood, some theories surrounding GATA-2 mutation.
- GATA-2 is a zinc finger transcription factor important for production and maintenance of hematopoietic stem cells and regulates phagocytosis of alveolar macrophages. GATA-2 mutation also associated with development of MDS, and possibly with PAP.
- Changes in cytokines in patients with hematologic malignancy can inhibit GM-CSF. Leads to abnormal quantity and function of macrophages.

References: