INTRODUCTION

Pulmonary alveolar proteinosis (PAP) is a rare diffuse lung disease caused by accumulation of surfactant in alveolar spaces.

- Primary PAP is associated with dysfunction or decreased levels of granulocyte-macrophage colony-stimulating factor (GM-CSF) causing dysregulation of surfactant clearance
- Secondary PAP accounts for less than 10% of all PAP cases
- The majority are associated with hematologic disorders, in particular myelodysplastic syndrome (MDS)

This case report focuses on a patient who developed PAP secondary to familial MDS.

CASE DESCRIPTION

30-year-old female with past medical history significant for familial MDS and nicotine dependence, who presented with fevers and chills with associated nausea and shortness of breath for six days.

- Found to have neutropenia (ANC 750) and diffuse interstitial infiltrates on chest X-ray. Admitted for sepsis, neutropenic fever and further work up of pulmonary infiltrates
- Diagnosed with familial MDS one-year ago. DNA sequencing was positive for germline GATA2 mutations
- Undergoing outpatient work up for bilateral upper lobe ground-glass opacities, interstitial thickening and bronchiectasis. Found on outpatient CT chest about two months before admission
- Repeat CT chest on admission significant for infiltrates in bilateral upper lobes and mediastinal lymphadenopathy (Figure 1 & 2)

CASE DESCRIPTION CONT.

Familial MDS accounts for a small percentage of patients with MDS. GATA2 germline mutations are among the more common mutations found in this patient population. GATA2 is a transcription factor involved in red blood cell and platelet production. It activates the expression of genes involved in stem cell maintenance and cell specification. GATA2 deficiency is associated with secondary PAP. It can lead to macrophage dysfunction and subsequent accumulation of surfactant into airway spaces. Overall this patient was at high risk for developing PAP due to history of familial MDS with GATA2 germline mutations.

IN THE FUTURE, PAP SHOULD BE CONSIDERED WHEN PATIENTS WITH HEMATOLOGIC DISORDERS PRESENT WITH UNEXPLAINED, DIFFUSE PULMONARY INFILTRATES ON IMAGING.

DIAGNOSIS:

- Flexible bronchoscopy with BAL and TBLB
- Test for serum antibodies to GM-CSF (depending on test availability)

Cytology and pathology findings of PAP:

- Positive PAS material
- Alveolar macrophages filled with PAS positive material
- Few inflammatory cells
- Stains and cultures for infectious causes are negative

TREATMENT:

Asymptomatic/Mild:
- Observation

Moderate to Severe:
- Whole lung lavage
- Recombinant GM-CSF
- Treatment of underlying cause

Refractory:
- Rituximab
- Therapeutic plasma exchange
- Lung transplantation

REFERENCES


DISCUSSION

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Figure 1: CT Thorax W/O Contrast Transverse view

Figure 2: CT Thorax W/O Contrast Coronal view

Pulmonology consulted. Status post bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB)

- Biopsy consistent with PAP: Pathology reported as intra alveolar filling with coarse granular eosinophilic material that is strongly positive with PAS and d-PAS. There is minimal interstitial inflammatory cell infiltrate, there are no granulomas and there is no fibrosis
- PAS – Periodic Acid Schiff
- D-PAS – Diastase resistant-Periodic Acid Schiff
- Biopsy stains and BAL negative for infectious processes

Due to severity of respiratory symptoms, the patient was discharged with plan for whole lung lavage at a specialized care facility

- Pulmonary symptoms improved with whole lung lavage
- Currently undergoing stem cell transplant for high risk MDS