Autoimmune pulmonary alveolar proteinosis mimicking *Mycoplasma* pneumonia in an adolescent

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A R T I C L E   I N F O

Keywords:
Autoimmune pulmonary alveolar proteinosis
Crazy paving pattern

A B S T R A C T

Pulmonary alveolar proteinosis (PAP) is a rare disease of abnormal surfactant production and accumulation. It is typically divided into three main categories: autoimmune, secondary and genetic. The genetic type is more common in children and adolescents, while the autoimmune type is most commonly seen in adults. Here we present an unusual case of autoimmune PAP presenting in an adolescent by mimicking findings of *Mycoplasma* pneumonia. Although both PAP and *Mycoplasma* pneumonia may reveal the same findings of the “crazy paving pattern” on computed tomography imaging, it is imperative to distinguish the two as treatment options are dissimilar.

1. Introduction

Pulmonary alveolar proteinosis (PAP) is a disease characterized by the increased accumulation of pulmonary surfactant proteins and lipids in the alveoli [1]. Granulocyte macrophage-colony stimulating factor (GM-CSF) is a cytokine at the center of this disease process and the pathophysiology of the disease is related to the aberrant signaling of this molecule [2].

The etiologies for PAP can be divided into autoimmune (previously known as idiopathic or primary), secondary or genetic, with the first two being more common in adults and the last being more common in children and adolescents [1]. Nevertheless, unique cases such as ours highlight the rare incidence of the autoimmune type as the cause in adolescents. In these autoimmune cases, there is a high concentration of anti-GM-CSF antibodies that bind to the GM-CSF molecules, hindering not only their activity but also their clearance by the alveolar macrophages [1,3].

2. Case presentation

A 17-year-old female with no significant past medical history presented to the emergency room with fever, nausea, headache and abdominal pain. Review of systems was negative for dyspnea and cough. Vital signs revealed mild tachycardia, but otherwise were within normal limits. On exam, she had diffuse abdominal tenderness without signs of an acute abdomen. The rest of the exam, including auscultation of chest was unremarkable. Laboratory testing demonstrated leukopenia, anemia and elevated inflammatory markers - C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Abdominal computed tomography (CT) scan illustrated an enlarged spleen along with bilateral groundglass opacities in the lower chest fields. A dedicated CT of the chest was obtained, which revealed the diffuse patchy opacities with superimposed intra-lobular septal thickening also known as the “crazy paving” pattern (Fig. 1). Infectious work-up was positive for *Mycoplasma pneumoniae* Immunoglobulin M (IgM); stool cultures were negative.

Treatment for *Mycoplasma* pneumonia was initiated with intravenous antibiotics. However, the medical team also recommended bronchoscopy for further investigation given the significant radiologic lung findings. The patient and family opted to hold off on the procedure at that time, given improvement in the symptoms. The patient was therefore discharged home with instructions to complete the antibiotic course and obtain another chest radiograph.

Unfortunately, chest radiography obtained at one- and three-months post hospitalization demonstrated bilateral patchy lung opacities unchanged from prior. The patient was also now developing new pulmonary symptoms of non-productive cough and exertional dyspnea. A...
Bronchoscopy was subsequently performed. Bronchial anatomy and mucosa were normal but milky fluid was noted on bronchoalveolar lavage (BAL; Fig. 2). Cultures were negative for infectious etiology. Histopathology of transbronchial biopsy samples showed alveolar spaces filled with granular proteinaceous material, which was positive for periodic acid Schiff (PAS) stain (Fig. 3). Serum GM-CSF autoantibody concentration was abnormally high at 584.4 mcg/ml (reference <5.0 mcg/ml). In addition, the STAT5 phosphorylation index test was also abnormal, indicating that GM-CSF signaling was not detected in leukocytes in whole blood. The patient was diagnosed with autoimmune PAP and is currently undergoing evaluation at a specialized center for GM-CSF supplemental therapy versus whole lung lavage.

3. Discussion

PAP is an uncommon but treatable disease. It should be part of a clinician’s differential diagnosis with chest CT findings of the “crazy paving” pattern. This case specifically illustrates the importance of pursuing an alternate diagnosis in the face of unresolving imaging abnormalities.

The “crazy paving” pattern is non-specific and can be seen in a myriad of other disease processes, such as acute respiratory distress syndrome (ARDS), acute interstitial pneumonia (AIP), drug-related hypersensitivity pneumonitis and even in Mycoplasma pneumonia [4]. Therefore, definitive diagnosis of PAP requires histopathologic analysis.

The GM-CSF autoantibody test is useful if an autoimmune etiology is suspected; it is measured using enzyme-linked immunosorbent assay (ELISA) and has a 100% specificity and sensitivity [5]. A value greater than 19 mcg/mL is considered specific [1]; our patient had a significantly higher level of 584 mcg/mL.
Recombinant supplemental GM-CSF therapy is a relatively novel treatment modality available for patients with autoimmune PAP and has been shown to be effective and lacking major adverse effects. The older whole lung lavage therapy still remains an alternative option; however, it carries a risk of complications such as pneumothorax, fever, hypoxic respiratory failure and pleural effusion [1].

In conclusion, autoimmune PAP can rarely occur in adolescents and timely diagnosis is key to appropriate management. This can be delayed due to radiologic mimickers such as *Mycoplasma* pneumonia, which is a much more common entity in this young age group.

Disclosures

This case report was presented as a poster at the Michigan Thoracic Society conference on 11th April 2019 in Novi, Michigan, USA.

Funding

None.

Declaration of competing interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgements

The authors thank Dr. Sayf Al-Katib for providing radiologic images for the case.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2020.101100.

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