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CASE REPORT

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Pulmonary alveolar proteinosis with an unusual bronchoscopic complication

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Abstract

Pulmonary alveolar proteinosis (PAP) is a rare respiratory syndrome, which can be challenging to diagnose given its non-specific presentation and imaging findings. While most primary cases of PAP have an autoimmune basis, the triggers for the disease are uncertain with occupational factors increasingly thought to be important. We report the unusual complication of pneumomediastinum and bilateral pneumothoraces following endobronchial ultrasound-guided transbronchial needle aspirate in the setting of PAP. We discuss the possible physiological mechanisms of this complication, which appears to be more common in conditions with reduced lung compliance.

KEYWORDS

autoimmune disease, interstitial lung disease, pneumothorax, radiology and other imaging, rare lung diseases

INTRODUCTION

Pulmonary alveolar proteinosis (PAP) is a rare syndrome characterized by accumulation of surfactant proteins and lipids within the alveoli, leading to impaired gas exchange and ventilatory mechanics.[1] Due to rarity and its non-specific presentation, the diagnosis can be challenging. However, a combination of imaging, bronchoscopic, cytological and serological findings can support the diagnosis. We report an unexpected complication of bronchoscopy superimposed on this infrequent condition.

CASE REPORT

A 30-year-old Caucasian male with no prior medical history presented to the emergency department with subacute-on-chronic dyspnoea and cough productive of brown sputum. The patient reported 12 months of progressive dyspnoea, fatigue and 10 kg of unintentional weight loss. In the month preceding presentation, his breathlessness progressed to the extent that he was unable to climb stairs, accompanied by the development of night sweats and fevers.

The patient had previously smoked tobacco until 2 years prior to presentation (10 pack-year history) and inhaled tetrahydrocannabinol via a water pipe multiple times per week. He had worked as a concreter and landscaper, which included exposure to soil and stone cutting without respiratory mask precautions. His home contained caged parrots in the living area. Family history revealed an unclassifiable interstitial lung disease in his mother. Clinical examination at admission demonstrated resting hypoxaemia (peripheral capillary oxygen saturation [SpO_2] 87%) and inspiratory crackles; systemic examination was otherwise unremarkable.

Initial laboratory investigations revealed mild neutrophilia (8.4×10^9/L) and marked hypoxaemia (partial pressure of oxygen [PaO_2] 52 mmHg) with a widened

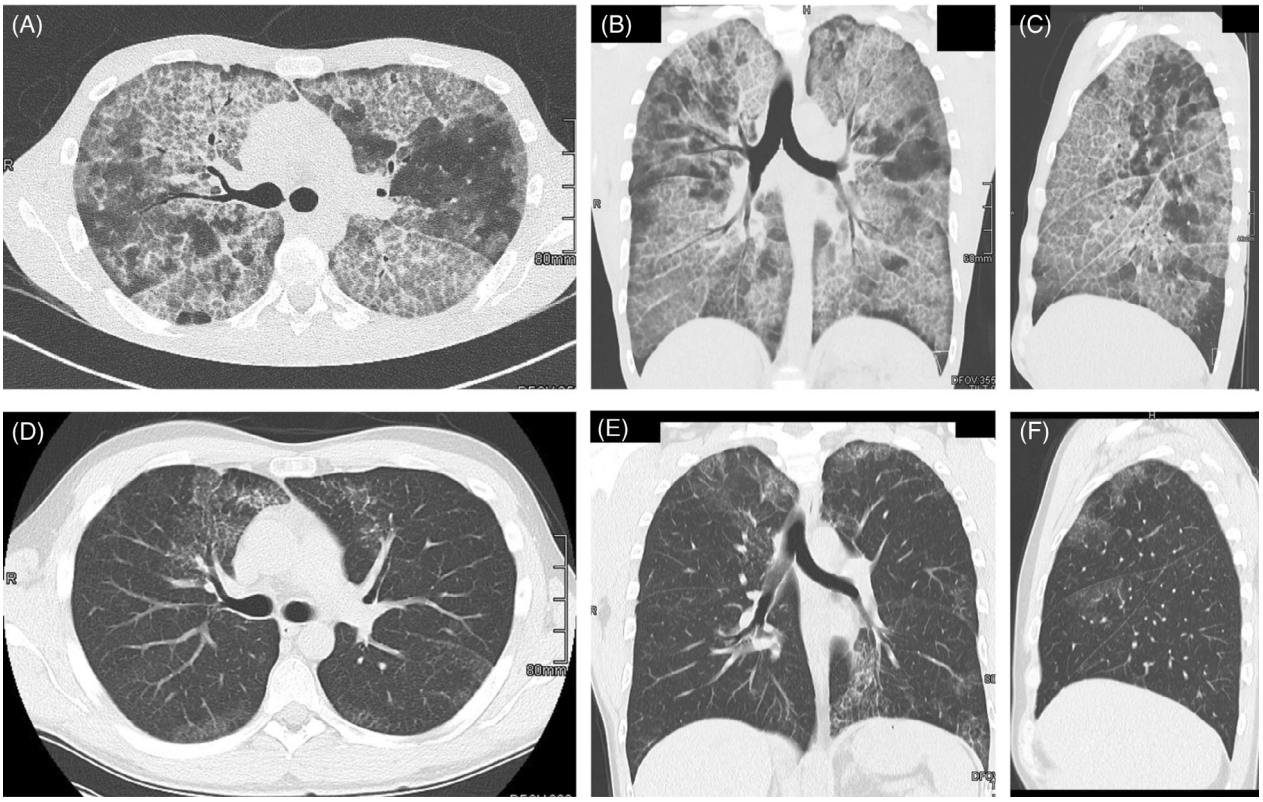

FIGURE 1 Chest computed tomography images demonstrating a 'crazy-paving' appearance of interlobular septal thickening and associated ground-glass interstitial opacities without zonal predominance at presentation (A–C) with marked improvement in magnitude and extent of abnormalities following sequential whole-lung lavage (D–F)

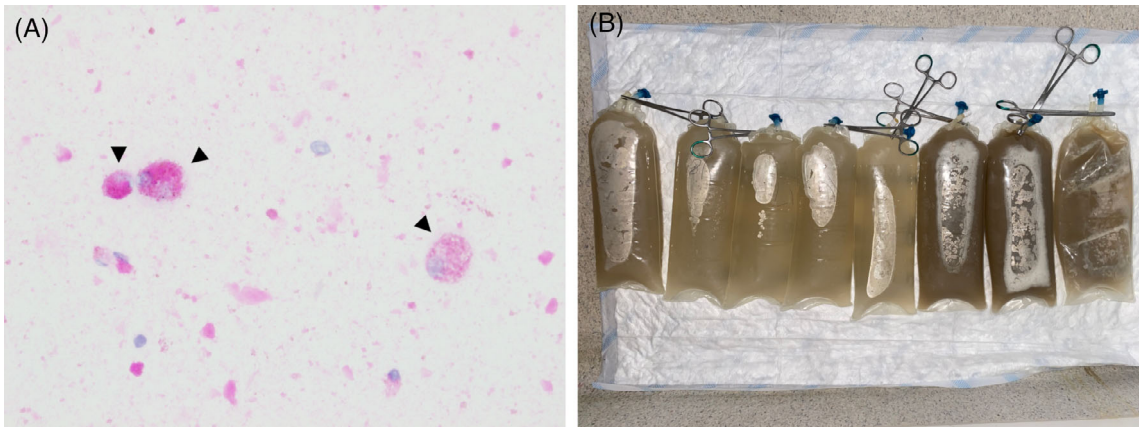

FIGURE 2 Chest x-ray (A) and computed tomography (B, C) images demonstrating pneumomediastinum, bilateral pneumothoraces and subcutaneous emphysema

alveolar-arterial (A-a) gradient (49 mmHg). Microbiological investigations were negative for respiratory viruses and sputum cultured *Aspergillus fumigatus* complex. Computed tomography (CT) of the chest demonstrated a 'crazy-paving' appearance of bilateral diffuse interstitial ground-glass opacities with interlobular septal, a small left upper lobe cavitating nodule and mediastinal lymphadenopathy (Figure 1A–C).

The clinical impression was that of non-infectious interstitial pneumonitis with a possible superimposed infectious process. Broad-spectrum antibiotics were initiated in combination with voriconazole for possible invasive aspergillosis. Flexible bronchoscopy and endobronchial ultrasound-guided transbronchial needle aspirate (TBNA) of an enlarged subcarinal lymph node were undertaken via an endotracheal tube, with a milky-turbid bronchoalveolar

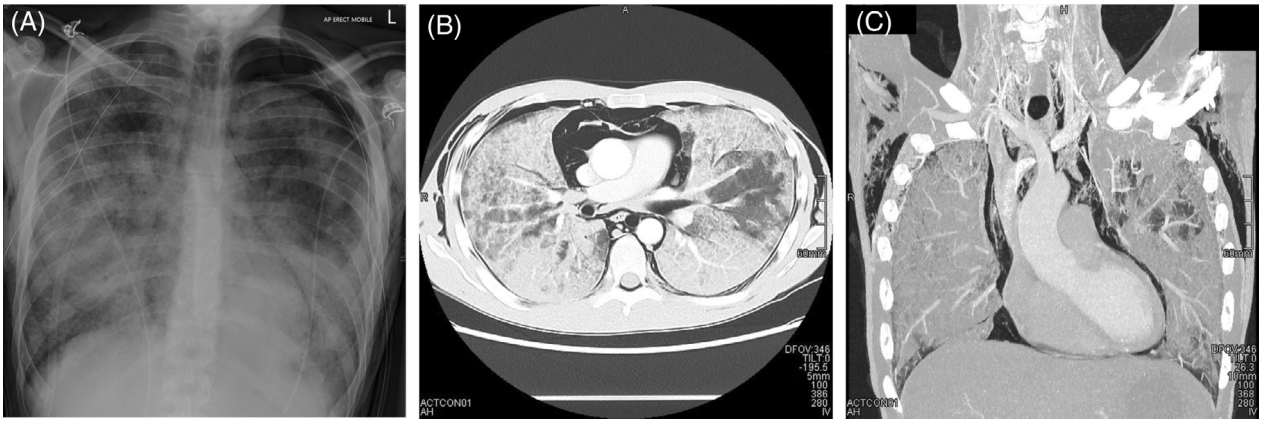

FIGURE 3 (A) Cytology smears showed a dispersed population of macrophages containing cytoplasmic periodic acid-Schiff (PAS)-positive material (arrows) with background proteinaceous fluid (PAS stain ×400); (B) whole-lung lavage return with a milky-turbid appearance

lavage fluid return. There were no immediate procedural complications. After 8 h, however, the patient reported severe pleuritic chest pain, and chest x-ray demonstrated pneumomediastinum, further characterized on CT chest (Figure 2). Insertion of bilateral intercostal catheters was required due to progressive subcutaneous emphysema and dysphonia, following initial conservative observation.

Subsequent analysis of the bronchoalveolar washings demonstrated proteinaceous globules which were periodic acid-Schiff (PAS) positive (Figure 3A), diagnostic of PAP, with benign lymph node cytology. Anti-granulocyte-macrophage colony-stimulating factor (GM-CSF) antibody later resulted positive on the bronchoalveolar lavage fluid. Serum anti-GM-CSF antibody was elevated at an optical density index of 0.81 (normal range < 0.23).

Due to progressive respiratory failure, the patient was transferred to intensive care. Following clinical stabilization and resolution of pneumomediastinum, he proceeded to sequential-day, bilateral single lung lavage via a dual-lumen endotracheal tube using 25 L of warmed saline and chest percussion (Figure 3B). Pre-procedural A-a gradient was 225 mmHg on 50% fraction of inspired oxygen (FiO_2) and 24 h post-procedural A-a gradient was 32 mmHg on FiO_2 21%. This resulted in significant clinical and radiographic improvement (Figure 1D,E).

DISCUSSION

PAP is a rare syndrome with a reported prevalence of 6–7 cases per million.[2] Autoimmune PAP accounts for 90% of cases and is associated with high levels of GM-CSF autoantibodies leading to functional impairment of surfactant clearance by alveolar macrophages. While causative mechanisms are uncertain, tobacco smoke and environmental exposures (including occupational dusts) are common and postulated as triggers.[1]

Given non-specific presenting symptoms, diagnosis of PAP can be challenging, and bronchoscopy is generally required for diagnosis and to exclude other pathologies. Bronchoalveolar lavage fluid is characteristically milky, with microscopy demonstrating proteinaceous globules. PAS staining confirms the presence of polysaccharides, glycolipids, proteins and mucins, and is strongly positive in PAP. These changes have been shown to correlate with the presence of multi-lamellated structures originally described on electron microscopy and aid in differentiation from other causes of interstitial fluid accumulation.[1] The crazy-paving appearance, while initially described in PAP, can be seen in a number of other conditions including interstitial pneumonias and mucinous bronchoalveolar carcinoma. Given hilar and mediastinal lymphadenopathy is only infrequently reported in PAP, nodal sampling was felt necessary due to the consideration of infective, infiltrative and malignant pathologies.[3]

During the procedure, the patient was invasively ventilated with a volume control strategy. While the mechanism of injury cannot be determined with certainty, we hypothesize that pneumomediastinum was related to barotrauma in the context of pleural disruption caused by TBNA. Due to the high resistance caused by poorly compliant lungs, high inspiratory driving pressures are required to achieve targeted ventilatory volume. While barotrauma is a well-recognized cause of pneumomediastinum and pneumothorax,[4] especially in mechanically ventilated patients with underlying parenchymal abnormalities,[5] it has not previously been suggested as a potential contributor to pneumomediastinum post TBNA. Amongst the eight cases we identified in the literature, seven had significant parenchymal abnormalities.

While various management strategies for PAP are described, our practice is to perform sequential whole-lung lavage with subsequent GM-CSF therapy once the accumulated alveolar fluid is removed. The presence of a persistent air leak, implying communication between the airways and the pleural space, initially delayed proceeding to whole-lung lavage due to concern of introducing instilled fluid into the mediastinum. This was subsequently performed once the air leak had subsided.

This case highlights the diagnostic challenges of diffuse parenchymal abnormalities, and the importance of exercising caution with ventilation strategies during bronchoscopy in patients with poorly compliant lungs, especially when interventions that disrupt the pleura are performed.

ACKNOWLEDGMENT

Allan Pham provided the description and images of the cytology smear.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

All authors contributed to the patient's treatment. Duncan J. Sweeney, Maitri Munsif, Rob G. Stirling and Tracy L. Leong all contributed to the writing and editing of the manuscript, with the final version approved by all authors.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for publication of this case report and accompanying images.

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