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Letter to the Editor

Secondary Pulmonary Alveolar Proteinosis Following Brief Toxic Gas Inhalation: A Case Report

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DEAR EDITOR,

Pulmonary alveolar proteinosis (PAP) is a syndrome characterized by impaired clearance of surfactant, leading to its accumulation within the alveoli and subsequent restrictive lung disease.[1-3] We present an instructive case of secondary PAP triggered by brief inhalation of a toxic gas to underscore the diagnostic importance of a detailed exposure history.

A 30-year-old Afghan male, an occasional smoker (2–3 pack-years) with no significant past medical history, presented with a one-year history of progressive dry cough and exertional dyspnoea (modified Medical Research Council grade 4). He reported a brief, 15-minute exposure to an unidentified irritant gas in a confined space at symptom onset. The exposure occurred in a domestic setting, while the patient was cleaning with a commercial cleaning agent in a poorly ventilated bathroom. The specific chemical composition of the agent was not identifiable; however, the acute onset of respiratory symptoms within minutes suggested a highly irritating gas, which could be chlorine- or ammonia-based. The patient had no prior history of respiratory or cardiac disease. He was not taking any regular medications and had no known allergies. An echocardiogram performed during the initial workup showed normal left ventricular systolic function and no evidence of pulmonary hypertension. Prior to the toxic gas exposure, he had no respiratory symptoms and had never undergone chest imaging. On admission, he was hypoxemic (SpO_2 86% on room air), requiring high-flow nasal oxygen (40 L/min, FiO_2 0.5). Auscultation revealed bilateral fine inspiratory crackles. The chest radiograph demonstrated diffuse bilateral alveolar opacities (Figure 1). A comprehensive etiological evaluation was performed to exclude other causes of secondary PAP. Complete blood count and peripheral smear showed no evidence of hematological malignancy. Serum human immunodeficiency virus serology and tuberculosis screening (sputum microscopy and GeneXpert) were negative. The patient had no history of occupational exposure to silica, metal dusts, or other inorganic particulates. Immunoglobulin levels and lymphocyte subset analysis were within normal limits, ruling out an underlying immunodeficiency. Serum anti-granulocyte-macrophage colony-stimulating factor antibodies were tested and found to be negative, ruling out autoimmune PAP. High-resolution computed tomography (HRCT) showed extensive bilateral ground-glass opacities with smooth interlobular septal thickening, the classic "crazy-paving" pattern of PAP (Figure 2). Bronchoscopy yielded an opaque, milky bronchoalveolar lavage (BAL) fluid (Figure 3). Cytology showed abundant acellular granular material that was strongly periodic acid-Schiff (PAS)-positive and diastase-resistant. Transbronchial biopsy confirmed alveolar filling with PAS-positive lipoproteinaceous material, establishing the diagnosis of PAP (Figure 4). He underwent sequential therapeutic

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whole lung lavage (WLL) under general anaesthesia. After approximately 25 litres of warmed saline were instilled into both lungs, oxygenation improved markedly, and he was weaned from high-flow oxygen within 48 hours. A follow-up chest radiograph at two weeks showed significant resolution (Figure 5). At three months, he was asymptomatic on room air.

This case exemplifies secondary PAP arising from an acute, non-occupational inhalational injury. Inhalational triggers of secondary PAP are diverse and include inorganic dusts such as silica, aluminum, titanium, and indium tin oxide, as well as acutely irritating gases like chlorine and nitrogen dioxide.[2,3]

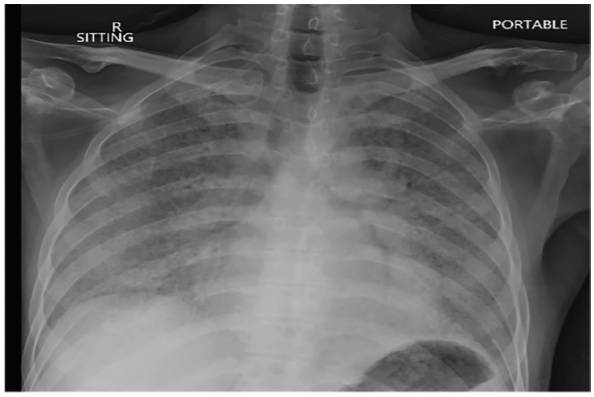

Figure 1. Initial anterior-posterior chest radiograph on presentation showing bilateral, diffuse, symmetrical alveolar opacities

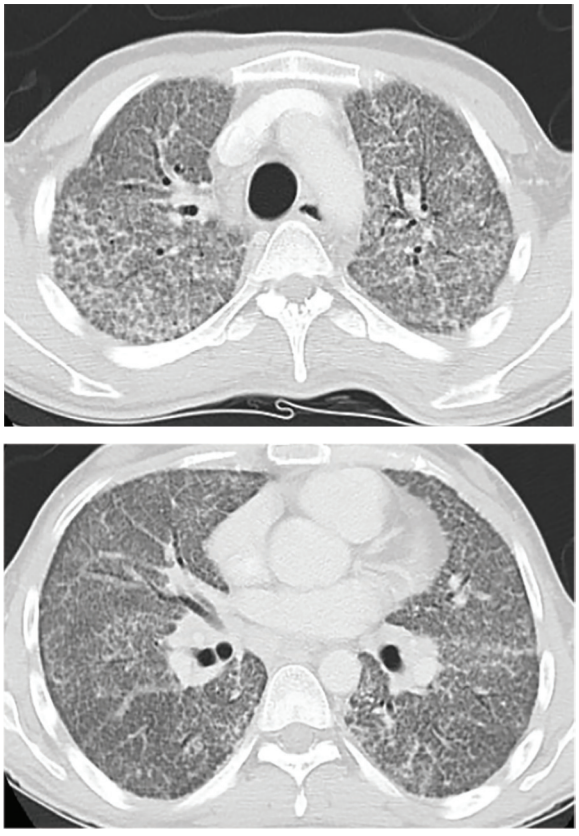

Figure 2. Axial high-resolution computed tomography scan of the thorax demonstrating the classic "crazy paving" pattern, characterized by extensive ground glass opacification with superimposed smooth interlobular septal thickening pattern indicative of PAP

PAP: Pulmonary alveolar proteinosis

The underlying mechanisms vary by agent, but commonly involve direct alveolar epithelial injury, impaired clearance, or a combination of these mechanisms. Our patient's clear temporal link with exposure to a toxic gas strongly supports this mechanism. HRCT is pivotal; the "crazy-paving" pattern, while not pathognomonic, is a highly characteristic sign that should prompt immediate suspicion of PAP.[4] In such a context, BAL cytology demonstrating PAS-positive, lipid-laden acellular debris is often sufficient for diagnosis, as in our patient.[3] Histopathological confirmation remains the diagnostic gold standard. For symptomatic, hypoxemic patients, WLL is the established first-line therapy. It is a highly effective mechanical method of removing the accumulated alveolar material, leading to sustained physiological and clinical improvements in the majority of patients, as we observed.[5] The prognosis of secondary PAP is intrinsically linked to the underlying cause, and secondary cases can follow a more variable course than autoimmune PAP.[1] A limitation of this report is the absence of post-treatment HRCT imaging; however, the marked clinical improvement and chest radiograph resolution support the efficacy of WLL.

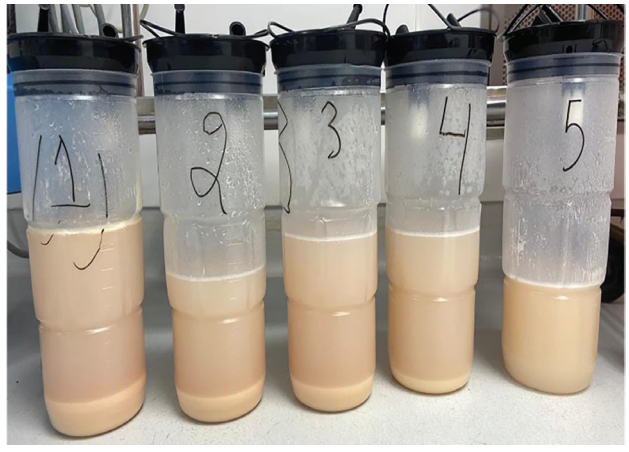

Figure 3. Fiberoptic bronchoscopy showing opaque and milky bronchoalveolar lavage fluid characteristic of PAP

PAP: Pulmonary alveolar proteinosis

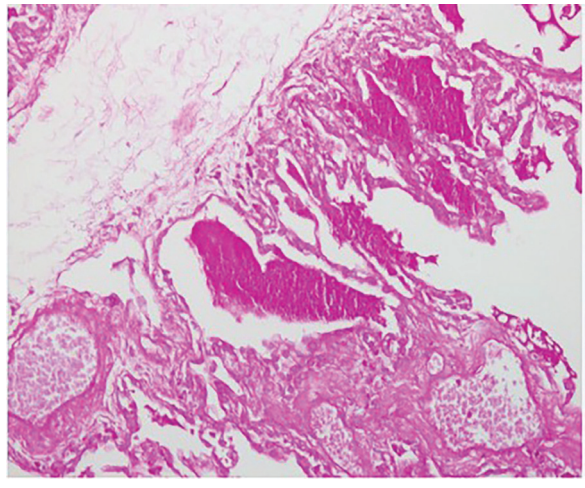

Figure 4. Histopathology of transbronchial lung biopsy [periodic acid-Schiff (PAS) stain, original magnification ×40]. Alveolar spaces are filled with granular, PAS-positive lipoproteinaceous material, confirming the diagnosis of pulmonary alveolar proteinosis. Alveolar architecture is preserved

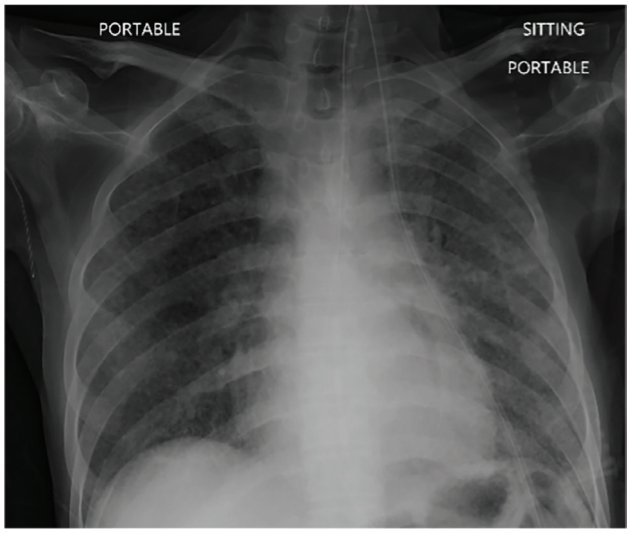

Figure 5. Follow-up chest radiograph obtained two weeks after sequential whole lung lavage, demonstrating marked resolution of the previously noted bilateral alveolar opacities

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We thank the patient for consenting to share their medical case and for contributing to the advancement of medical knowledge through this publication.

Footnotes

Informed Consent: Informed consent was obtained from the patient for anonymized information to be published in this article.

Declaration on the use of Artificial Intelligence (AI):

The authors declared that OpenAI's ChatGPT was used only for language editing, grammatical correction, and sentence refinement. The content, data analysis, interpretation, and conclusions remain the sole responsibility of the authors.

Authorship Contributions

Concept: A.U.A., M.A., M.S., M.I., M.U.G., H.N., T.K., Design: A.U.A., M.A., M.S., M.I., M.U.G., H.N., T.K., Data Collection or Processing: A.U.A., M.A., M.S., M.I., A.S.A., H.N., T.K., Analysis or Interpretation: A.U.A., M.A., M.S., M.I., M.U.G., H.N., T.K., Literature Search: A.U.A., M.A., M.S., M.I., M.U.G., A.S.A., H.N., T.K., Writing: A.U.A., M.A., M.S., M.I., A.S.A., H.N., T.K.

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