ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

https://patsjournal.org

Journal of the Pan African Thoracic Society

Case Report

Pulmonary alveolar proteinosis and whole lung lavage in Kenya: A case report

Evans Arnold Onyango[1], Jacqueline Wanjiku Kagima[2], George Mwamnemo Nyale[2], Edwin Oloo Walong[3], Jackson Omayio Atina[2]

[1]Department of Clinical Medicine and Therapeutics, University of Nairobi, [2]Department of Medicine, Kenyatta National Hospital, [3]Department of Human Pathology, University of Nairobi, Nairobi, Kenya.

***Corresponding author:**
Evans Arnold Onyango, Department of Clinical Medicine and Therapeutics, University of Nairobi, Nairobi, Kenya.

dreaonyango@gmail.com

Received: 16 May 2023
Accepted: 12 June 2023
EPub Ahead of Print: 10 July 2023
Published: 30 September 2023

DOI
10.25259/JPATS_13_2023

Quick Response Code:

ABSTRACT

Pulmonary alveolar proteinosis (PAP) is a rare interstitial lung disease. The ideal therapy to clear the accumulated lipoproteinaceous material is whole lung lavage (WLL). While there have been few cases of PAP in Sub-Saharan Africa, none have been reported in Kenya. We describe a case of a 36-year-old Kenyan lady with progressive dyspnea, cough, tachypneic, and respiratory crackles at presentation. A high-resolution computed tomography (HRCT) scan showed a "crazy-paving" pattern and a transbronchial lung biopsy revealed periodic acid-Schiff positive exudates. She was diagnosed with PAP and WLL was performed. She was discharged after 3 days with marked improvement. Unfortunately, she succumbed intraoperatively during the WLL of the contralateral lung 6 weeks later and a postmortem revealed widespread proteinosis. This case illustrates the diagnosis and treatment of a rare lung disease by WLL in a resource-limited setting with the assistance of a multidisciplinary team.

Keywords: Pulmonary alveolar proteinosis, Whole lung lavage, Case report

INTRODUCTION

Pulmonary alveolar proteinosis (PAP)/phospholipoproteinosis is a diffuse lung disease of alveolar accumulation of periodic acid-Schiff (PAS)-positive proteinaceous material. This rare disease first described by Rosen *et al.* in 1958[1] occurs due to disorders of surfactant production or clearance.[2] There are three main subtypes; Autoimmune, congenital, and secondary.[2-4]

Symptoms vary, with progressive exertional dyspnea being the most common. Cough, fatigue, and weight loss are also common. Physical examination yields limited findings but inspiratory crackles may be present.[5]

Chest radiography shows bilateral symmetric perihilar and basilar alveolar filling resembling pulmonary edema. Chest high-resolution computed tomography (HRCT) shows ground glass opacification (GGO) with intralobular and interlobular septal thickening adjacent to normal lung. This is classically referred to as "crazy-paving" but is neither sensitive nor specific.[5]

A restrictive pattern occurs on pulmonary function tests (PFT) in most patients.[6] Laboratory tests are rarely useful for diagnosis but high anti-granulocyte-macrophage colony-stimulating factor (GM-CSF) antibodies are important in diagnosing autoimmune PAP with almost 100% sensitivity and 98% specificity.[2,7]

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.
©2023 Published by Scientific Scholar on behalf of Journal of the Pan African Thoracic Society

Bronchoscopy can be used to evaluate the bronchoalveolar lavage fluid (BALF) which usually appears as a milky white fluid on gross examination. Additionally, transbronchial lung biopsy (TBLB), or open lung biopsy aid in diagnosis and excluding other conditions. Cytology of BALF and TBLB histopathology reveals PAS-positive, Grocott methenamine silver stain-negative, and eosinophilic material with enlarged foamy macrophages.[6,8]

Treatment varies from observation to supportive care, to whole lung lavage (WLL) depending on the symptoms. Recombinant inhalational and subcutaneous GM-CSF has not demonstrated a favorable response compared to WLL.[4,9]

CASE REPORT

A 36-year old female presented with a 5-month history of dyspnea, dry cough, and unintentional weight loss of 15 kg. She was a previously healthy high-school teacher with no history of exposure to organic or inorganic dust including insecticides, no cigarette smoking, and no family history of similar illness. She reported not to be on any medication including nitrofurantoin, amiodarone, methotrexate, corticosteroids, or any other chronic medication use.

At the emergency department, her vitals were normal. She had no pallor, finger clubbing, cyanosis, ankle edema, or lymphadenopathy. Her oxygen saturation (SpO_2) was 63% on room air and her respiratory rate was 28. Chest auscultation revealed bilateral crackles. Other systems were unremarkable. She was initiated on oxygen therapy through a non-rebreather mask at 15 L/min.

Laboratory investigations on admission revealed polycythemia and elevated lactate dehydrogenase (LDH). In subsequent days, tests to rule out secondary causes were done; the hemogram and blood smear did not reveal any hematological malignancy. Her arterial blood gas revealed hypoxemia on room air: partial pressure of oxygen (6.2 kPa). She was human immunodeficiency virus (HIV)-negative. A COVID-19 antigen test was negative and so was the Gene-Xpert for *Mycobacterium tuberculosis*. Antinuclear antibodies, antineutrophil cytoplasmic autoantibodies, and extractable nuclear antigens were negative. Anti-GM-CSF antibodies were not tested due to unavailability locally and prohibitive costs abroad.

The admission chest radiograph revealed a reticular nodular pattern [Figure 1] and a HRCT revealed a "crazy-paving" appearance bilaterally with GGO and interlobular septal thickening suggestive of PAP [Figure 2]. Her PFT revealed a restrictive pattern. Incentive spirometry was also initiated.

After 1 week, her oxygen requirements decreased, transitioned to a face mask but continued to experience exertional dyspnea and low SpO_2 levels. At this point, the working diagnosis was an interstitial lung disease likely PAP with differentials of pulmonary alveolar hemorrhage and interstitial pneumonitis.

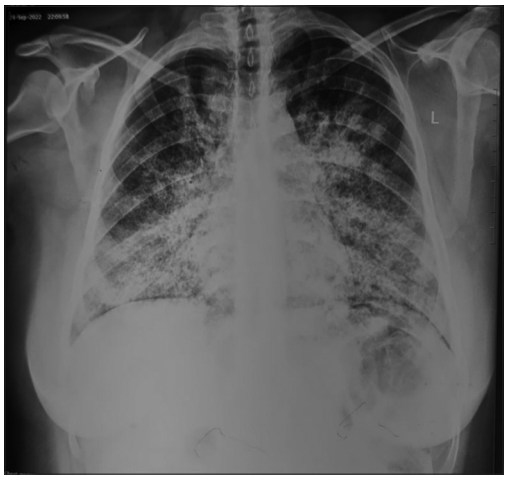

Figure 1: A 36-year-old lady with pulmonary alveolar proteinosis who presented with progressive dyspnea and cough. A posterior-anterior chest radiograph showing a reticular nodular pattern of bilateral perihilar and basilar infiltrates.

The cytological examination of the BALF showed large, foamy alveolar macrophages. Microbiological tests were negative, ruling out infection, and no malignant cells were found. The absence of hemosiderin in the BALF on Pearl's Prussian blue stain ruled out pulmonary hemorrhage. The cytology showed PAS-positive eosinophilic material [Figure 3] and TBLB revealed intra-alveolar granular material which was also strongly PAS-positive [Figure 4].

Despite successful tapering of oxygen therapy, her oxygen requirements remained at 3–5 L/min on nasal prongs due to desaturation and dyspnea. She underwent WLL approximately 5 weeks after admission and there was a significant improvement in her symptoms and exercise-related desaturation. Our patient was also on prophylactic dose of enoxaparin and omeprazole.

WLL treatment

The left lung underwent WLL first in the operation theater. A double-lumen endotracheal tube (ETT) was used for intubation. The left lung was degassed and warm saline was instilled through the ETT. Fourteen liters (7 lavages) were utilized, making the "milky" fluid with high sedimentation less opaque [Figure 5]. This lasted approximately 4 h with no complications during or after WLL. A physiotherapist performed chest percussion.

She was observed in the critical care unit, transferred to the ward, and discharged after 3 days with no dyspnea, no oxygen requirement, and a SpO_2 of 95%. She was initiated on

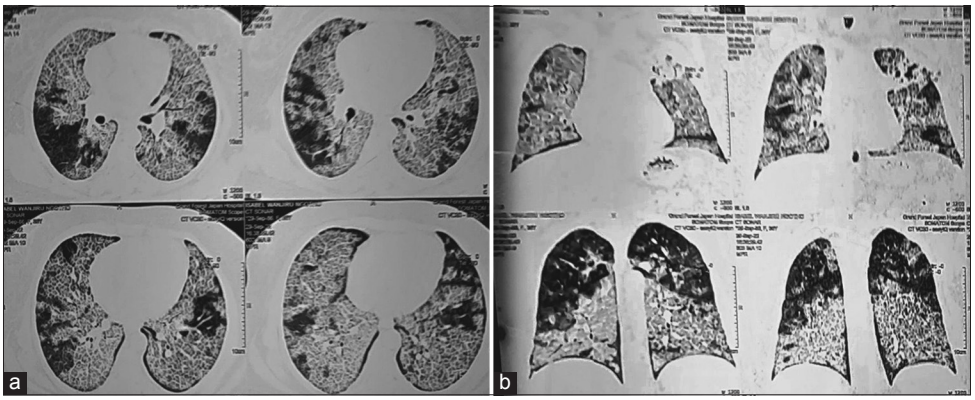

Figure 2: A 36-year-old lady with pulmonary alveolar proteinosis who presented with progressive dyspnea and cough. A cropped grayscale lung window high-resolution computed tomography of the chest demonstrates a "crazy paving" pattern as; (a) Extensive diffuse bilateral thickening of the lung interstitium with superimposed interlobular septal thickening in the axial view. (b) Bilateral diffuse, symmetrical ground-glass attenuation in the coronal view.

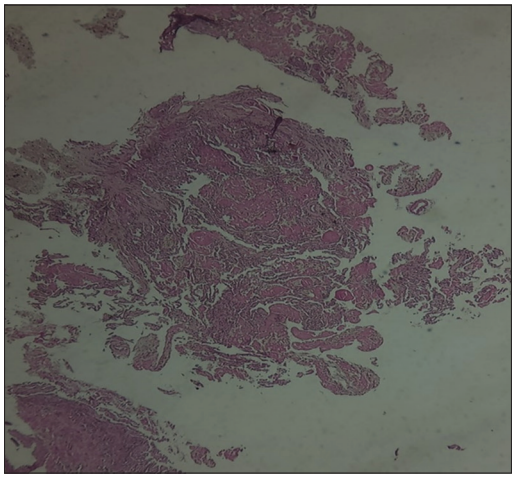

Figure 3: A 36-year-old lady with pulmonary alveolar proteinosis who presented with progressive dyspnea and cough. Cell block of bronchoalveolar lavage showing granular and globular eosinophilic material that is Periodic acid-Schiff positive.

Figure 5: A 36-year-old lady with pulmonary alveolar proteinosis who presented with progressive dyspnea and cough. Collection jars with effluent from whole lung lavage show an initially "milky" appearing effluent with a high sediment level (Jar 1) that gradually turns less opaque with a lower sediment level (Jar 3).

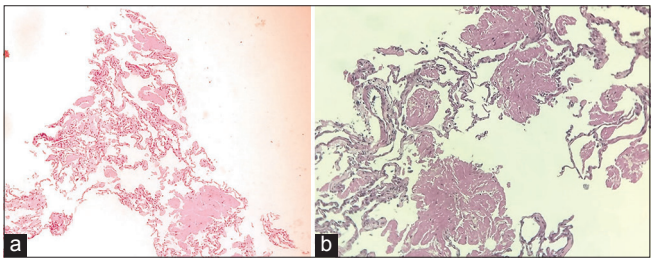

Figure 4: (a and b) A 36-year-old lady with pulmonary alveolar proteinosis who presented with progressive dyspnea and cough. Transbronchial lung biopsy showing intra-alveolar exudates that are periodic acid-Schiff positive.

glycopyrrolate and atropine for bronchial secretions after the WLL.

Six weeks later, a WLL was performed on the contralateral lung due to hypoxia but the patient unfortunately succumbed during the procedure. A postmortem revealed asphyxia due to widespread alveolar proteinosis as the cause of death.

DISCUSSION

A definite diagnosis of PAP requires a lung biopsy but the presence of progressive dyspnea, worsening hypoxemia, high serum LDH, "crazy-paving" pattern on radiology, and BALF characteristics may aid in diagnosis.[2,10]

Bronchoalveolar lavage alone can be diagnostic with a transbronchial biopsy increasing the diagnostic yield of PAP.[4] The BALF revealed PAS-positive proteinaceous exudates and our patient had an elevated serum LDH although it is non-specific.[2]

Although we did not perform genetic testing to identify mutations associated with congenital PAP, congenital PAP was excluded due to the age at which the symptoms appeared and the absence of any previous respiratory symptoms during childhood or adolescence. The history, physical examination, and investigations did not identify any secondary cause. Secondary PAP is due to reduced alveolar macrophages caused by chronic infections or inflammatory conditions, hematological dyscrasias, and exposure to various substances.[2] We eliminated the possibility of secondary causes of PAP including hematological disorders, and infections including HIV based on the medical history, clinical examination, laboratory tests, and BALF. In addition, there was no history of exposure to organic or inorganic dust or fumes. Once congenital and secondary PAP were ruled out, autoimmune PAP emerged as the most probable cause of PAP despite not being able to perform GM-CSF tests on serum or BALF for confirmation.

Autoimmune PAP, the most common subtype accounts for 90% of cases and is due to neutralizing anti-GM-CSF antibodies.[8] This test is not widely available and the expensive in specialized centers abroad.

The case emphasizes the importance of a multidisciplinary team in diagnosing and managing PAP when clinical suspicion, HRCT findings, histopathology, and the surgical team work in concert. This collaborative approach enabled the performance of WLL, the cornerstone of therapy. This procedure is safe and provides symptomatic, physiological, and radiological improvement by physically removing the proteinaceous material.[2] The initial WLL appeared to be effective based on symptom resolution. Hypoxia necessitated the contralateral lung lavage and during the procedure, the patient suffered a cardiac arrest. Resuscitation was performed but was unsuccessful. We suspect that the cardiac arrest may have been caused by hypoxia resulting from severe alveolar proteinosis, which could have been aggravated by potential pulmonary edema during the procedure. While poor response to treatment is considered a poor prognostic factor, we are still faced with the question of whether performing the second WLL earlier would have altered the outcome.

CONCLUSION

Even in settings with limited resources, a diagnosis of PAP can be confirmed by utilizing a combination of HRCT patterns, BALF evaluation, and lung biopsy characteristics in a multidisciplinary approach. This concerted effort enabled the first-ever performance of WLL at the tertiary referral hospital in Kenya.

Acknowledgment

We express gratitude to the cardiothoracic, theater teams, and nursing staff for their dedicated care. Special thanks to respiratory nurse Joan Kagema and Dr. Grace Kang'ethe for excellent care.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Rosen SH, Castleman B, Liebow AA. Pulmonary alveolar proteinosis. N Engl J Med 1958;258:1123-42.
2. Marwah V, Katoch CD, Singh S, Handa A, Vardhan V, Rajput AK, *et al*. Management of primary pulmonary alveolar proteinosis: A multicentric experience. Lung India 2020;37:304-9.
3. Suzuki T, Trapnell BC. Pulmonary alveolar proteinosis syndrome. Clin Chest Med 2016;37:431-40.
4. Kumar A, Abdelmalak B, Inoue Y, Culver DA. Pulmonary alveolar proteinosis in adults: Pathophysiology and clinical approach. Lancet Respir Med 2018;6:554-65.
5. Patel SM, Sekiguchi H, Reynolds JP, Krowka MJ. Pulmonary alveolar proteinosis. Can Respir J 2012;19:243-5.
6. Salvaterra E, Campo I. Pulmonary alveolar proteinosis: From classification to therapy. Breathe (Sheff) 2020;16:200018.
7. Hawkins P, Chawke L, Cormican L, Wikenheiser-Brokamp KA, Fabre A, Keane MP, *et al*. Autoimmune pulmonary alveolar proteinosis: A discrepancy between symptoms and CT findings. Lancet 2021;398:e7.
8. Sweeney DJ, Munsif M, Pilcher D, Stirling RG, Leong TL. Pulmonary alveolar proteinosis with an unusual bronchoscopic complication. Respirol Case Rep 2021;9:e0856.
9. Venkateshiah SB, Yan TD, Bonfield TL, Thomassen MJ, Meziane M, Czich C, *et al*. An open-label trial of granulocyte macrophage colony stimulating factor therapy for moderate symptomatic pulmonary alveolar proteinosis. Chest 2006;130:227-37.
10. White DA, Klugman SR, Weil R, Zigiriadis E, Green RJ. Pulmonary alveolar proteinosis in a child from an informal settlement: 12 litres of fluid drained from the lungs and successful use of ECMO. S Afr J Child Health 2013;7:155-7.

How to cite this article: Onyango EA, Kagima JW, Nyale GM, Walong EO, Atina JO. Pulmonary alveolar proteinosis and whole lung lavage in Kenya: A case report. J Pan Afr Thorac Soc 2023;4:152-5.