SVOA Paediatrics
ISSN: 2755-1660

ScienceVolks Open Access

Case Report

Autosomal Recessive Surfactant Metabolism Dysfunction Pulmonary III: A Clinical Case Report

Faizan Sadiq[1]*, Arooj Khan[1], Ali Nawaz[1], Syed Mohsin Ali Shah[1] and Shaista Azeem Khan[1]

[1] *Khyber Teaching Hospital, Pakistan.*

***Corresponding Author:** Faizan Sadiq, Khyber Teaching Hospital, Pakistan.*

DOI: https://doi.org/10.58624/SVOAPD.2024.03.085

***Received:** August 06, 2024* ***Published:** November 11, 2024*

Abstract

A female infant aging 4 months was presented with a history of respiratory distress and decreased oral intake since last 2 weeks with SpO2 of 84%. Intravenous antibiotic Ampicillin+ Cloxacillin & Cefotaxime was started, and supplemental oxygen was administered which improved SpO2 to 97%. The complete blood count demonstrated raised leukocyte count and chest radiography indicated lower RTI. Immunodeficiency workup was normal. Both MTB Gene Xpert as well as Fungal Hyphae were negative. HRCT chest revealed patchy subsegmental/subpleural atelectatic changes in the anterior and posterior segments of the right upper lobe, and the superior and basal segments of bilateral lower lobes. The patient's genetic study tests were sent to Germany. On Day 21, oxygen saturation began to drop. On Day 38, Genetic Study report mentioned a homozygous likely pathogenic variant in the ABCA3 gene leading to diagnosis of Autosomal Recessive SMDP3. The child died on day 45.

Keywords: *ABCA3 gene, Infants, Interstitial lung disease, Surfactant proteins, Respiratory disorders.*

Introduction

Interstitial lung diseases (ILDs) comprise a group of pediatric conditions characterized by remodeling of the lung interstitium and distal air spaces, leading to impaired gas exchange. There are varying degrees of inflammation, consequently, ILDs lead to progressive deterioration of lung function and exacerbation of respiratory symptoms. The pathological changes in the interstitium disrupt the normal alveolar-capillary interface.[1]

Autosomal Recessive Surfactant Metabolism Dysfunction Pulmonary III (SMDP3) is a rare and severe genetic disorder affecting the respiratory system, particularly in newborns and infants. This condition belongs to a group of ILD, characterized by disruptions in pulmonary surfactant metabolism, leading to acute respiratory distress (ARD) and potentially life-threatening complications.[2]

Surfactants (surface-active-agent) is a compound of phospholipids and proteins that is synthesized and secreted by type II epithelial cells in the alveoli, where it reduces surface tension, maintains alveolar expansion, and facilitates lung compliance. Surfactant proteins (SP) A, B, C, D make up approximately 8% of all components, but they play an important role in optimizing the rapid adsorption and distribution of phospholipids. Surfactant expression increases with gestational age and is critical for proper lung function at birth. The complex interplay between surfactant components allows near-zero surface tension at the end of exhalation, preventing alveolar collapse and forming a protective barrier against inhaled pathogens.[3] The ABCA3 gene are located on chromosome 16p13.3 and encodes an ATP-binding cassette protein which is essential for surfactant metabolism. Mutations in genes encoding SP-B, SP-C, and ABCA3 are associated with respiratory disorders and ILDs in children.[4]

Case Presentation

A 4 month old female infant was presented to the outpatient department of Khyber Teaching Hospital Peshawar with history of respiratory distress and decreased oral intake since last 2 weeks. The patient's oxygen saturation (SpO2) at the time of presentation was 84% in room air. The patient was shifted to High Dependency Unit (HDU) after initial stabilization.

The patient was admitted there and put on IV antibiotic Ampicillin+ Cloxacillin & Cefotaxime at optimum doses as per weight. She was Nil per Mouth and maintenance fluids were started. Supplemental oxygen was administered via nasal cannula at a flow rate of 5 L/min, resulting in an improvement of the patient's SpO2 to approximately 97%. The complete blood count (CBC) demonstrated raised leukocyte count and lower respiratory tract infection (LRTI) was indicted at chest radiography. Liver function tests, renal function tests and serum electrolytes were in normal ranges. Over the subsequent 48 hours, the patient demonstrated significant clinical improvement. Oral intake was resumed, and oxygen requirements were reduced. The patient maintained adequate SpO2 on low-flow oxygen therapy at 1 L/min, approaching levels sustainable on room air and shifted to our pediatric ward.

Upon reviewing the patient's medical history, we noted multiple previous hospitalizations for recurrent respiratory infections at various facilities. Prior immunodeficiency workup had been conducted, with all results within normal limits, ruling out immune disorders as a contributing factor to the patient's recurrent infections. The patient's genetic study tests (Centoxome) were sent to Germany.

On day 7, the patient starts deteriorating on the low flow oxygen. The patient was again shifted to HDU and started on 7L/min oxygen with O2 mask which showed slight improvement. Over the next 4 days the patient did not show any significant improvement. The antibiotics were change to Ceftazidime and Linezolid and regulars' nebulization were continued. Over the next week the patient remains in static condition. The patient was started on IV Antifungal prophylactically & Gastric Aspirate sample for MTB Gene Xpert as well as Fungal Hyphae were sent which both came negative.

On Day 21, the patient's saturation started dropping and was decided to put on manual Continuous Positive Airway Pressure (CPAP) which improved the saturation. Considering low response to the previous antibiotic, it was decided to shift the patient to Clarithromycin and Meropenum along with continuing the antifungal. From Day 21 to 38 patients remained in static condition without significant clinical response & improvement. The patient's respiratory rate remained above normal for age with subcostal recessions and bilateral crepts and wheezes on auscultation. One of the two siblings of the child had Severe Combined Immunodeficiency (SCID) Syndrome who died at age of 9 months with recurrent chest infections, we repeated the immunodeficiency work up which came normal in all aspects.

On Day 38 of admission, the genetic study report came. A homozygous pathogenic variant (HPA) was reported in the ABCA3 gene. It was consistent with genetic diagnosis of Autosomal Recessive SMDP3. The patient started on 3% saline nebulization with a mild improvement.

The patient's parents were counselled regarding the genetic result and prognosis of the disease. Unfortunately, the child died on 45 days of admission in our unit at the age of 5 months and 15 days.

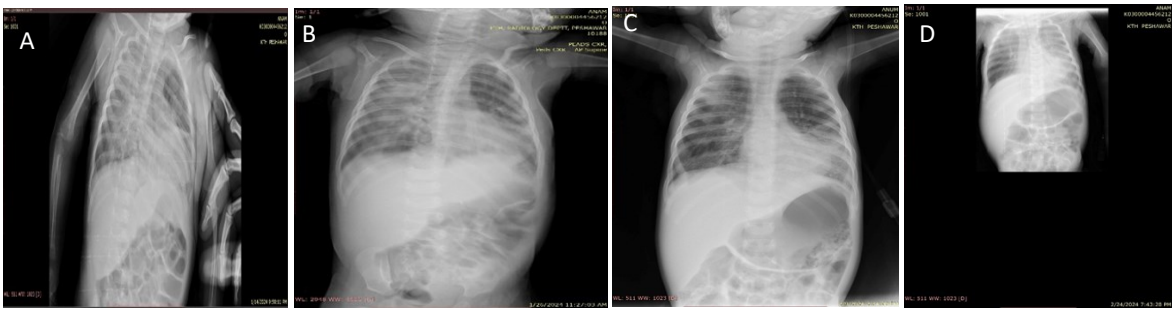

***Fig: A-D**: Showing Patchy subsegmental/subpleural atelectatic changes along anterior & posterior segment of right upper lobe, Superior and basal segment of bilateral lower lobe.*

Table 1. Investigations.

Blood Culture	No growth of microorganisms obtained after 5 days of aerobic incubation at 37°
Urine Culture	No growth of microorganism obtained after 48 hours of aerobic incubation at 37°
PCR for Covid-9	Not detected
Primary Immunodeficiency workup	Normal
Gastric Aspirate for Gene Expert	MTB Not detected
Fungal Hyphae	No fungal hyphae seen in KOH preparation
Stool for reducing substances	Positive
Serum Anti HIV 1 & 2	Non-Reactive
CT Chest	Patchy subsegmental/subpleural atelectasis in • Right upper lobe: anterior and posterior segments • Bilateral lower lobes: superior and basal segments
Gene Study	HPA in ABCA3 gene

Discussion and Conclusion

The cases of Autosomal Recessive SMDP3 although rare but important to diagnose at earlier days especially in our health care set ups where health facilities and budgets are limited.

Rogulska reported a case of a 36-week preterm male neonate who developed severe ARD shortly after birth. Despite antibiotic treatment, the patient's condition deteriorated, requiring escalating respiratory support from nCPAP to mechanical ventilation and eventually high-frequency oscillation. Two doses of exogenous surfactant were administered without significant improvement. Genetic analysis revealed two heterozygous ABCA3 gene variants, consistent with surfactant metabolism dysfunction. The infant died at 99 days. Genetic counseling was recommended for the family due to recurrence risk.[6]

Mohamed YA reported a case of a 2-hour-old neonate with ARD and respiratory failure. The infant required non-invasive ventilation for 58 hours before intubation due to desaturation and increased oxygen needs. Hemoptysis occurred during intubation, and chest radiography showed diffuse ground-glass opacities. Multiple doses of exogenous surfactant temporarily improved the condition, allowing extubation for 5 days. Genetic analysis in Germany confirmed a homozygous pathogenic variant in the ABCA3 gene, diagnosing autosomal recessive SMDP3. The patient died at 43 days of birth.[7]

Cambaceres C reported a 6-month-old boy presenting with cyanosis and ARD. Chest X-ray showed interstitial infiltrate, pneumomediastinum, and bilateral pneumothorax. Maternal history revealed prolonged oxygen therapy in infancy and current chronic hypoxia. Chest CT demonstrated ground-glass opacities, septal interstitial thickening, and air trapping. Lung biopsy and genetic study confirmed SMDP. The patient was transferred back to the referring hospital for ongoing oxygen therapy and management.[8]

A Tunisian case reported a full-term female infant with ARD and inherited SP-B deficiency. Chest CT at 29 days showed ground-glass opacities and interlobular septal abnormalities. Genetic analysis confirmed homozygosity for a rare SFTPB variant, with both parents being heterozygous carriers of the mutation. Monthly high-dose pulse methylprednisolone began at two months. By 12 months, the patient showed weight gain and was weaning off oxygen. The researchers emphasized considering congenital SP-B deficiency in term or near-term infants with persistent acute respiratory failure beyond five days of age.[9]

Our case report is similar to the cases discussed above and focuses on diagnosis of genetic surfactant disorders which is a rare respiratory diseases yet associated with high mortality and morbidity. It should be considered in infants with persistent severe ARD. While imaging and bronchoalveolar lavage fluid analysis guide initial assessment, definitive diagnosis requires genetic testing. Despite limited therapeutic options, early intervention is crucial for delaying the onset of pulmonary fibrosis.

Conflict of Interest

The authors declare that they have no competing interests.

Acknowledgement

None.

References

1. Althobiani MA, Russell AM, Jacob J, Ranjan Y, Folarin AA, Hurst JR, et al. Interstitial lung disease: a review of classification, etiology, epidemiology, clinical diagnosis, pharmacological and non-pharmacological treatment. Front Med (Lausanne). 2024;11:1296890. doi: 10.3389/fmed.2024.1296890.
2. Gjeta I, Sala D, Bakalli I, Celaj E, Kola E. Surfactant Deficiency Causing Severe Pneumonia in a Child. Curr Health Sci J. 2023;49(1):134-138. doi: 10.12865/CHSJ.49.01.134
3. Cambaceres C, Viggiano V, Parellada C, Esteguy F, García S, Castaños C. Pulmonary surfactant metabolism dysfunction: A pediatric clinical case report. Arch Argent Pediatr. 2024;122(3):e202310084. doi: 10.5546/aap.2023-10084.eng.
4. Beers MF, Mulugeta S. The biology of the ABCA3 lipid transporter in lung health and disease. Cell Tissue Res. 2017;367(3):481-493. doi: 10.1007/s00441-016-2554-z.
5. Chua WC, Chen IC, Liu YC, Wu YH, Lo SH, Hsu JH, Liang PI, Chen HL, Dai ZK. Congenital Surfactant C Deficiency with Pulmonary Hypertension-A Case Report. Children (Basel). 2022;9(10):1435. doi: 10.3390/children9101435.
6. Rogulska J, Wróblewska-Seniuk K, Śmigiel R, Szydłowski J, Szczapa T. Diagnostic Challenges in Neonatal Respiratory Distress—Congenital Surfactant Metabolism Dysfunction Caused by *ABCA3* Mutation. *Diagnostics*. 2022; 12(5):1084. https://doi.org/10.3390/diagnostics12051084.
7. Mohamed YA, Sherif AH, Saadi MMA, Aldamanawi MM, Fouad H. Surfactant Metabolism Dysfunction Type 3 (SMDP3). Sch J Med Case Rep. 2023;11(07):1368-72.
8. Khalsi F, Chaabene M, Romdhane MB, Trabelsi I, Hamouda S, de Becdelièvre A, Boussetta K. Congenital surfactant protein B (SP-B) deficiency: a case report. Pan Afr Med J. 2023;44:158. doi: 10.11604/pamj.2023.44.158.35316.
9. Cambaceres C, Viggiano V, Parellada C, Esteguy F, et al. Pulmonary surfactant metabolism dysfunction: A pediatric clinical case report. Arch Argent Pediatr. 2024;122(3):e202310084.

Citation: Sadiq F, Khan A, Nawaz A, Shah SMA, Khan SA. Autosomal Recessive Surfactant Metabolism Dysfunction Pulmonary III: A Clinical Case Report. *SVOA Paediatrics* 2024, 3:6, 176-179. doi:10.58624/SVOAPD.2024.03.085