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ODAD3-Related Primary Ciliary Dyskinesia in a Pediatric Patient with Recurrent Pneumonia: A Case Report

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ABSTRACT

Primary Ciliary Dyskinesia (PCD) is a rare, autosomal recessive condition impacting ciliary function, causing defective mucociliary clearance and chronic respiratory infection. Here we describe a 2-year-old female child born to consanguineous parents, with diagnosed situs inversus totalis and chronic pneumonia. She had a high-grade fever with productive cough and also a noteworthy history of neonatal respiratory distress and frequent lower respiratory tract infections. Her PICADAR score was 10, and further evaluation was warranted. Genetic testing established a homozygous nonsense mutation (p. Glu441Ter) in exon 10 of the ODAD3 gene, which is linked to PCD type 30 (CILD30). The patient was managed with intravenous Ceftazidime and daily therapy of hypernebulization. The case highlights the importance of bearing PCD in mind in children with situs anomalies and chronic respiratory illness. Early clinical scoring and genetic testing allow for early intervention, which is the key to preventing chronic pulmonary complications. The case also highlights the importance of genetic counselling in consanguineous marriages.

Keywords: Primary ciliary dyskinesia, situs inversus totalis, Dextrocardia, PICADAR score, ODAD3 gene, mutation, pneumonia.

INTRODUCTION

Primary ciliary dyskinesia (PCD) is a rare inherited disease that affects ciliary structure and function. PCD leads to severely impaired mucociliary clearance and a wide variety of symptoms primarily affecting the respiratory system. In addition, many males with PCD have immobile spermatozoa or dysfunction of cilia in the epididymal duct, leading to infertility. The prevalence of the disease is estimated to be between 1:2000 and 1:40000, but it is underdiagnosed [1]. Manifestations from other systems have also been reported. About half the patients have been described as presenting with situs inversus. Productive cough, rhinitis, and recurrent upper and lower respiratory tract infections have been described as leading symptoms. [2,3]. In this study, we aimed to report a case of a 2-year-old female child, the third child of a second-degree consanguineous marriage, who presented with high-grade fever for 10 days and productive cough for 2 days. She is a known case of situs inversus totalis and pneumonia.

CASE STUDY

A 2-year-old female child who was born to a second-degree consanguineous couple was born full term and had a known case of situs inversus totalis and pneumonia and was brought to the pediatric department complaining of a high-grade fever that had been present for 10 days, along with accompanying symptoms like vomiting and abdominal pain, as well as a wet productive cough that had been persistent for 2 days with yellow, non-blood-tinged, sticky sputum and no aggravating or relieving factors. The infant has a history of being admitted to the neonatal intensive care unit for 9 days after birth due to birth asphyxia caused by prolonged vaginal delivery. Dextrocardia was identified at 4.5 months of gestation, and the mother has had asthma for four years. At 3 months, she had a hospital admission with complaints of a cough for 15 days. Fever since the 8th day of examination, bilateral crepitations were heard. Relevant investigations were done, and she was started on inj. Cefotaxime for 7 days, intravenously. Amikacin for 5 days. On admission, she was conscious and oriented with a pulse rate of 122 bpm and a respiratory rate of 55 cycles per minute; her body temperature was found to be afebrile. On auscultation, the left axillary, left infra-axillary, and left infra-scapular regions showed reduced air entry, and fine crackles were heard over bilateral lung fields and were treated with Inj. Pantoprazole and Inj. Ceftriaxone for 5 days. Her laboratory investigation revealed that Hb was 8.3 gm/dL, the total count was 17570 cells/cm^3, neutrophils were 64%, packed cell volume (hematocrit) was 24.9%, MCV was 67.1 fl, MCH was 20.8 pg, MCHC was 31.1%, and C-reactive protein (CRP) was 433.75 mg/L.

Upon DNA testing, a homozygous nonsense variant in exon 10 of the ODAD3 gene (chr19:g.11422584C>A; Depth: 114x) was the pathogenic variant responsible for the reported phenotype. This variant results in a stop codon and premature truncation of the protein at codon 441 (p. Glu441Ter; ENST00000356392.9). This variation has a minor allele frequency of 0.0006% in the internal database and has not been observed in the 1000 Genomes, gnomAD, or topmed databases. Across species, the reference codon is conserved. Although the OMIM phenotype indicated primary ciliary dyskinesia, homozygous mutations in the ODAD3 gene (OMIM#615956) are the cause of 30 (OMIM#616037). Cough, situs inversus (in about 50% of patients), recurrent respiratory infections, newborn respiratory insufficiency, respiratory insufficiency caused by impaired ciliary clearance, recurrent dextrocardia, and electron microscopy of cilia are the hallmarks of CILD30.

To address the signs and symptoms, the treatment strategy involved daily hypernebulization and intravenous Ceftazidime 500 mg TID.

DISCUSSION

Primary ciliary dyskinesia (PCD) is a rare hereditary condition that affects ciliary structure and function. PCD leads to significantly decreased mucociliary clearance and a wide range of symptoms, mostly affecting the respiratory system. In addition, many males with PCD have immobile spermatozoa or failure of cilia in the epididymal duct, leading to infertility. The prevalence of the condition is believed to be between 1:2000 and 1:40000; however, it is underdiagnosed.[1] Common clinical features include chronic wet cough, recurrent sinusitis, otitis media with effusion, neonatal respiratory distress in full-term infants, and, in approximately half of the cases, situs inversus totalis-collectively known as Kartagener syndrome. In some cases, infertility may be observed due to defective ciliary action in the reproductive tract. [2,3]

Diagnosing PCD is difficult, as there is no 'gold standard'. Diagnostic methods include measuring nasal nitric oxide, assessing ciliary function with high-speed video microscopy, examining ciliary ultrastructure with TEM, and genetic testing. Performing and interpreting these tests requires

substantial knowledge of both normal and aberrant findings. [3,5] The PICADAR score is a simple diagnostic prediction tool that evaluates the likelihood of primary ciliary dyskinesia (PCD) using clinical data. Because PICADAR is specifically created for individuals with chronic respiratory symptoms that began in childhood, it initially inquires whether the patient has a daily wet cough. Patients are then asked seven easy questions in PICADAR, with each answer assigned a score ranging from one to four. Patients who were born full term and developed chest symptoms such as tachypnea, cough, and pneumonia during the newborn period, were hospitalized in the neonatal unit or had a congenital heart problem, received two points for each item. Patients with a situs anomaly (situs inversus) received 4 points, whereas those with perennial rhinitis or chronic ear or hearing complaints, such as glue ear, serous otitis media, hearing loss, and ear perforation, received 1 point for each. Patients with a score of more than 6 are advised to have a thorough assessment for PCD. Patients with a score of greater than 6 are recommended to undergo a detailed examination for a diagnosis of PCD. As our patient's PICADAR score was 10 points, we suspected PCD and performed genetic testing. [4,6] The genetic test reveals that the patient has a homozygous nonsense variant in the ODAD3 gene (c.1321G>T; p. Glu441Ter), located on exon 10, that results in a stop codon and premature truncation of the protein at codon 441 (p. Glu441Ter, ENST00000356392.9) was detected. This variant has not been reported in the 1000 Genomes, gnomAD (v3.1), gnomAD (v2.1), and topmed databases and has a minor allele frequency of 0.0006% in the internal database. In this patient, Primary ciliary dyskinesia, 30 (OMIM 616037) is caused by homozygous mutations in the DDAD3 gene (OMIM 615956). CILD30 is characterized by recurrent otitis media, nasal polyps and blockage, dextrocardia, neonatal respiratory insufficiency, respiratory insufficiency due to defective ciliary clearance, recurrent respiratory infections, cough, asthma, chronic bronchitis, bronchiectasis, and situs inversus (in about 50% of patients).

In this patient, the impaired ciliary function led to ineffective clearance of airway secretions, promoting mucus retention and creating an environment conducive to bacterial growth and ultimately resulting in pneumonia.

Treatment strategies for Primary Ciliary Dyskinesia (PCD) center on symptom management in addition to disease progression prevention, since disease-specific guidelines are nonexistent now. The main goals include airway clearance with improvement, respiratory infections that are prevented and then treated, and exposure to airway irritants such as passive smoke with minimization. [5] Daily chest physiotherapy is of great importance, as airway clearance techniques are as well. These techniques are postural drainage, autogenic drainage, active cycle breathing, positive expiratory pressure devices, as well as high-frequency chest wall oscillation vests. Regular workouts for improved mucociliary clearance are therefore recommended. Also, it does indeed improve respiratory muscle strength. These therapies, when inhaled, aid mucus thinning and removal, like nebulized hypertonic saline. With antibiotics, treat infections promptly, then monitor them routinely as key components of care.[7] In our patient, intravenous Ceftazidime(500mg) TID was administered, and hyper nebulization therapy OD was provided as a part of the treatment plan to treat pneumonia.

CONCLUSION

Primary Ciliary Dyskinesia (PCD) is an extremely rare genetic disorder that is often missed, often because of non-specific early symptoms and a complex diagnostic work-up. This case illustrates the need for clinical awareness especially in children with recurrent respiratory infections, situs inversus, and who experienced difficulties with breathing at birth. A high PICADAR score and genetic testing revealed a

homozygous harmful variant in the ODAD3 gene (c.1321G>T; p.Glu441Ter), confirming the diagnosis of PCD in this 2-year-old child. Early identification and diagnosis are key to starting the right treatment, preventing lung damage, and improving overall quality of life. Our case also highlights the need for genetic counseling, especially in consanguineous marriages, and the importance of working with a team that includes pediatricians, pulmonologists, and geneticists to manage this lifelong condition successfully.

Declaration by Authors

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REFERENCES

1. Goutaki M, Meier AB, Halbeisen FS, Lucas JS, Dell SD, Maurer E, Casaulta C, Jurca M, Spycher BD, Kuehni CE. Clinical manifestations in primary ciliary dyskinesia: systematic review and meta-analysis. European Respiratory Journal. 2016 Sep 30;48(4):1081-95.
2. Noone PG, Leigh MW, Sannuti A, Minnix SL, Carson JL, Hazucha M, Zariwala MA, Knowles MR. Primary ciliary dyskinesia: diagnostic and phenotypic features. American journal of respiratory and critical care medicine. 2004 Feb 15;169(4):459-67.
3. Lucas JS, Walker WT, Kuehni CE, Lazor R. Primary ciliary dyskinesia. Orphan Lung Diseases (ERS Monograph). Sheffield, European Respiratory Society. 2011 Dec 1:201-17.
4. Behan L, Dimitrov BD, Kuehni CE, Hogg C, Carroll M, Evans HJ, Goutaki M, Harris A, Packham S, Walker WT, Lucas JS. PICADAR: a diagnostic predictive tool for primary ciliary dyskinesia. European respiratory journal. 2016 Apr 1;47(4):1103-12.
5. Wee WB, Kinghorn B, Davis SD, Ferkol TW, Shapiro AJ. Primary ciliary dyskinesia. Pediatrics. 2024 Jun 1;153(6):e2023063064.
6. Hasegawa R, Suzuki S, Nishimata S, Kashiwagi Y, Inagaki N, Kawashima H. A case of primary ciliary dyskinesia caused by a mutation in OFD1, which was diagnosed owing to Clostridium difficile infection. Pediatric Reports. 2021 May 10;13(2):241-4.
7. Mirra V, Werner C, Santamaria F. Primary ciliary dyskinesia: an update on clinical aspects, genetics, diagnosis, and future treatment strategies. Front Pediatr. 2017; 5: 135 [Internet]. 2017

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