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Primary Ciliary Dyskinesia as a Cause of Repeating Atelectasis in the Neonatal Period

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, newborn
Final Diagnosis: Primary ciliary dyskinesia
Symptoms: Atelectasis • Respiratory distress
Medication: —
Clinical Procedure: Follow-up
Specialty: Pulmonology

Objective: Congenital defects/diseases

Background: Primary ciliary dyskinesia (PCD) is a disease characterized by motor ciliary dysfunction, which leads to the accumulation of secretions in the lower airways and, consequently, to atelectasis and repeated infections. During the neonatal period, diagnosis can be difficult because the symptoms are frequently associated with other respiratory diseases common in neonates. The laterality defects should warn the clinician of the need for further investigation using clinical criteria, but the confirmation depends on a genetic test.

Case Report: The objective of this report is to present a case of PCD manifesting in the neonatal period that was diagnosed due to respiratory failure associated with recurrent atelectasis and situs inversus totalis.

Conclusions: This disease is not well known by neonatologists, but early diagnosis decreases morbidity and improves patient quality of life.

MeSH Keywords: Ciliary Motility Disorders • Pulmonary Atelectasis • Situs Inversus

Abbreviations: **PCD** – primary ciliary dyskinesia; **NO** – inhaled nitric oxide; **HFNC** – high-flow nasal cannula; **CPAP** – continuous positive airway pressure; **PICADAR** – PrImary CiliARy DyskinesiA; **RSV** – respiratory syncytial virus

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Background

Primary ciliary dyskinesia (PCD) is an autosomal recessive disease characterized by motor ciliary dysfunction, resulting in atelectasis (with or without associated pneumonia) due to accumulation of secretions in the lower airways [1]. During the neonatal period, PCD is presumptively diagnosed based on persistent tachypnea, unexplained pneumonias, recurrent atelectasis, and associations with situs inversus totalis, dextrocardia, or other laterality defects [2,3]. The PrImary CiliARy DyskinesiA Rule (PICADAR) score was developed to help diagnose PCD in children beyond the neonatal period with persistent respiratory symptoms [4–6]. There is no defined treatment for PCD except for chest physiotherapy, vaccination against respiratory agents, and early antibiotic therapy for respiratory infections [7]. PCD manifests during the neonatal period and is not well known by neonatologists; however, early diagnosis improves patient prognosis and quality of life.

Case Report

Our patient was a term male newborn who was of normal size for gestational age and was prenatally diagnosed with situs inversus totalis. He was delivered in good condition and did not require resuscitation maneuvers. At 14 hours of life, he developed progressive respiratory discomfort and began receiving bubble continuous positive airway pressure (CPAP) therapy; an initial chest X-ray showed discrete infiltrate (Figure 1). He developed left pneumothorax requiring intubation for invasive ventilation and chest drainage (Figure 2). Due to worsening respiratory failure and echocardiographic evidence of pulmonary hypertension, inhaled nitric oxide (NO) was initiated, which led to clinical improvement. Antibiotics were started for suspect sepsis with ampicillin (100 mg·kg^{-1} dose every 12 hours) and amikacin (15 mg·kg^{-1} dose every 24 hours), as the institutional protocol for early onset sepsis. These were suspended after screening for infection provided negative results. Mechanical ventilation was withdrawn 24 hours after the administration of NO, and the patient was extubated after 48 hours; a significant discomfort due to upper airway obstruction was noticed, and managed by administration of nebulized epinephrine and intravenous dexamethasone. The chest drain was removed on the patient's 5th day of life. Subsequently, atelectasis developed in the right apex; the therapy with high-flow nasal cannula (HFNC) was stared at that time. On his 8th day of life, with an HFNC rate of 8 l/min, the patient continued exhibiting significant respiratory discomfort and persistent atelectasis in the right hemithorax and was returned to bubble CPAP therapy. He was then evaluated by a pulmonologist, who considered the hypothesis of PCD and recommended empirical use of hypertonic saline inhalation (3% sodium chloride) and N-acetylcysteine at 20 mg/kg/dose 3 times per

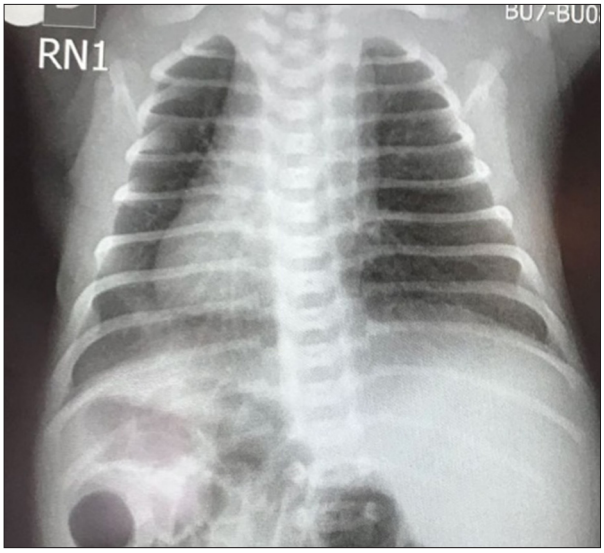

Figure 1. X-ray after respiratory distress and installation of bubble CPAP.

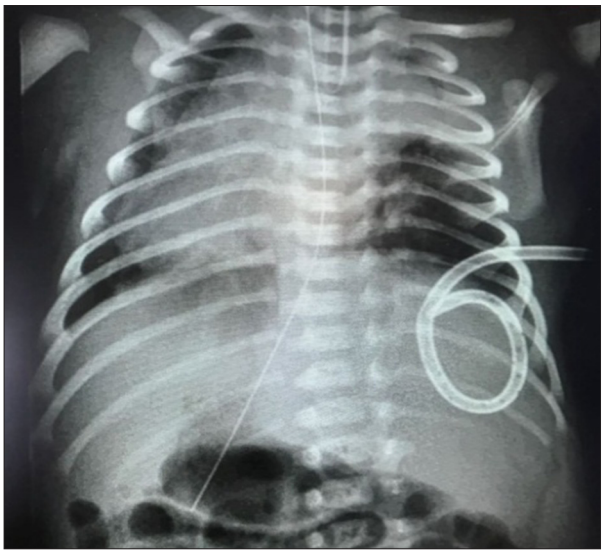

Figure 2. X-ray after left pneumothorax drainage.

day, as well as genetic panel testing for ciliopathy. The patient continued receiving CPAP therapy for 10 days, maintaining a respiratory pattern with tachypnea and retractions; an X-ray showed continued bilateral atelectasis. CPAP was slowly reduced, and on his 21st day of life, the treatment was transitioned to an HFNC, which was suspended for room air on the 27th day of life. The genetic panel identified 2 variants in the DNAH5 gene, one pathogenic variant, named c.10226>c(p.Trp3409Ser), and another intronic variant of unknown significance (c.9606-7A>G), which are findings consistent with PCD. The newborn was discharged at 33 days of life on room air; at this time, he was maintaining a baseline respiratory pattern of tachypnea and subdiaphragmatic retractions while receiving oral N-acetylcysteine and nebulization with saline solution.

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He was referred for follow up with a pediatric pulmonologist and was prescribed regular chest physiotherapy. During his hospital stay, he received a single dose of palivizumab to prevent respiratory syncytial virus (RSV) infection. During the time at the hospital, the newborn has received physical therapy 3 times a day as the institutional protocol for respiratory distress. After discharge, the interval of physical therapy will depend on the intensity of symptoms the patient manifests.

Discussion

PCD is a member of a varied group of genetic conditions characterized by changes in ciliary function. The estimated prevalence of PCD is 1: 10 000 to 1: 20 000 live-born children, but the true prevalence may be even higher [2,3,5,6,8]. The main finding of this case, the repeated atelectasis, is caused by the ciliary dysfunction that compromises the clearance of secretions from the respiratory tract, which leads also to recurrent respiratory infections, bronchiectasis, and loss of pulmonary function [5–9]. In the fetus, the motile cilia present in the embryonic node are responsible for the arrangement of organs on the left and right; as a result, ciliary dysfunction is associated with laterality defects [10]. Suspicion of PCD arises from a certain set of symptoms, and confirmatory tests include electron-microscopy of ciliated cells, videomicroscopy of ciliary beating, immunofluorescence studies of the cilia, nasal nitric oxide levels, and genetic studies [7]. While many diagnostic tests are applicable for PCD suspected cases, they are not straightforward to perform, and many patients remain with their PCD diagnosis incomplete [11]. In older children, the PICADAR score can be used successfully for screening PCD cases [4–6]. PICADAR scores accurately predict positive or negative test results in patients with daily lower respiratory tract symptoms throughout life. The PICADAR assessment should increase the awareness of symptoms associated with PCD, particularly in places with limited resources that lack diagnostic facilities, and this tool can be used to estimate the likelihood of a PCD diagnosis. The PICADAR score was not used for diagnosis for our patient because it is not for used during the neonatal period (it uses the patient's chronic symptoms) and we were led to suspect this diagnosis the persistent atelectasis and the defect in laterality. It is estimated that the vast majority of patients with PCD have not been diagnosed with this condition, which represents a major obstacle to providing adequate care [2–8]. Treatment also remains uncertain. There is no evidence of the effectiveness of airway humidifiers (for hypertonic inhalation or with saline solution) or mucolytic agents (such as N-acetylcysteine), although these treatments can minimize symptoms. Infections should be treated early to avoid loss of lung function [3–5]. The use of prophylactic antibiotics may be considered in patients with recurrent infections [3–7]. Chest physiotherapy and vaccines for respiratory agents are also lung-preservation measures; in particular, vaccination for pneumococcal disease and influenza and the use of palivizumab in children younger than 2 years of age are important in the prevention of early RSV infections [3].

Conclusions

PCD is a disease that is not well known to neonatologists but manifests during the neonatal period. This condition should be considered in the differential diagnosis of newborns with recurrent atelectasis, or unexplained respiratory distress, particularly when associated with laterality defects.

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