Case Report

Primary ciliary dyskinesia in an infant with post-infectious bronchiolitis obliterans and failure to thrive: A case report

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ABSTRACT

We report the case of a 9-month-old male infant with recurrent severe viral pneumonia, culminating in bronchiolitis obliterans and chronic respiratory morbidity. The clinical course was marked by multiple pediatric intensive care unit admissions, prolonged oxygen dependency, and recurrent bacterial superinfections. High-resolution computed tomography revealed bronchiectasis and fibrotic changes. Given the chronicity of symptoms, a clinical suspicion of Primary Ciliary Dyskinesia (PCD) was raised. Genetic analysis detected heterozygous variants of uncertain significance in the *DNAH1* and *LRRC6* genes. This case highlights the diagnostic and management complexities in infants with post-viral chronic lung disease and the importance of early consideration and evaluation for underlying genetic etiology, such as PCD.

Key words: Bronchiectasis, Bronchiolitis obliterans, Chronic lung disease, Primary ciliary dyskinesia

Primary ciliary dyskinesia (PCD) is a genetically heterogeneous, autosomal recessive disorder of motile cilia that leads to impaired mucociliary clearance, recurrent sinopulmonary infections, situs abnormalities in approximately 50% of cases, and progressive bronchiectasis [1,2]. The estimated prevalence of PCD is 1 in 10,000–20,000 live births worldwide, though underdiagnosis likely results in a higher true prevalence [3,4].

Bronchiolitis obliterans (BO) is a chronic obstructive lung disease that can occur following severe viral lower respiratory tract infections (LRTI), most commonly adenovirus infection in infants and young children [5]. Although BO is a recognized post-adenoviral complication, unusually severe, recurrent, or prolonged respiratory illness should prompt evaluation for underlying conditions such as primary immunodeficiency, cystic fibrosis (CF), or ciliary motility disorders [6].

We report this case of an infant with severe recurrent respiratory illness, post-adenoviral BO, and heterozygous variants of uncertain significance (VUS) in *DNAH1* and *LRRC6* genes. This report highlights the diagnostic challenges of differentiating post-infectious BO from genetic disorders causing chronic lung disease and underscores the importance of early suspicion and workup for PCD to enable multidisciplinary management and genetic counseling.

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CASE REPORT

A 9-month-old boy was brought in March 2023 with complaints of fever, cough for 5 days, and respiratory distress for 2 days. He had increased breathing with SpO_2 in the 80 s in room air. He appeared sick, pale, and had bilateral wheeze in the chest. He was started with nebulization and shifted to the pediatric intensive care unit (PICU) for further monitoring and care. His initial workup revealed anemia, neutrophilic leukocytosis (17000/cu mm), and C-reactive protein (134 mg/L). Chest X-ray (CXR) showed features of hyperinflation. Upper respiratory viral panels were positive for adenovirus, influenza (H3N2), and parainfluenza. Oseltamivir (3 mg/kg/dose twice a day) and other antibiotics were also started. He needed a high-frequency nasal cannula (HFNC) for 72 h, which was later weaned to oxygen by nasal cannula. Work-up for anemia was attributed to a nutritional cause; there was no hemoglobinopathy. Anemia was managed with a packed red blood cell transfusion. He recovered over the next few days and hence could be discharged after 12 days of stay in the hospital. However, he continued to need nebulization at home, and parents were instructed to be in close follow-up.

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Twenty days later, he was brought to the emergency room with respiratory distress for 1 day. He had tachypnea with increased work of breathing and a reduced level of consciousness. His SpO_2 in room air was in the 80 s. He was again shifted to PICU, started on oxygen support, nebulization, and later put on HFNC support. He was started on fluids, IV antibiotics, and other supportive care. His upper respiratory panel revealed adenovirus and parainfluenza type 3. CXR showed bilateral patchy opacities. Once stabilized, high-resolution computed tomography (HRCT) chest was done, which revealed multifocal patchy areas of subacute infiltrates in bilateral lungs with residual sub-segmental consolidation and fibro-bronchiectasis changes (Fig. 1). Bronchoalveolar lavage identified *Pseudomonas aeruginosa*. Antibiotics were modified accordingly. An opinion from a pulmonologist was taken, who suggested managing conservatively. With a background of bronchiolitis, beta D-glucan level was sent, which was negative. An Echo was performed, which ruled out any structural cardiac lesion. After a week's stay in the hospital, he started having a high-grade fever. Blood reports showed neutrophilic leukocytosis, whereas blood culture revealed growth of methicillin-resistant *Staphylococcus aureus*, which was managed with IV antibiotics. He was also noticed to have an undescended testis for which a surgical opinion was taken; however, interventions were postponed till stabilization. He became oxygen dependent and had difficulty weaning off oxygen. He needed oral steroids (prednisolone at 2 mg/kg/day), azithromycin (10 mg/kg/day), nebulization with salbutamol, budesonide, and tobramycin, and other supportive care. He was started on regular physiotherapy. He could be discharged home after 50 days of stay in hospital with supplemental oxygen, nebulization, macrolides in anti-inflammatory doses, and other supportive care under close supervision. He was started on hydroxychloroquine as an anti-viral/immunomodulator.

At 14 months of age (September 2023), he was brought again with another such exacerbation. He was again admitted to PICU, started on frequent nebulization, respiratory support by HFNC, and steroids (prednisolone), magnesium sulfate (50 mg/kg every 4–6 h), and antiviral prophylaxis. He could successfully be weaned off oxygen and sent home after 8 days of stay.

The child received multiple courses of antibiotics, systemic steroids, inhaled bronchodilators, aminoglycosides, and antiviral agents. Following the third hospitalization, he was stable off oxygen, although for some time during the day. He was continued on supplemental oxygen through oxygen concentrator for several months after discharge. He still needs oxygen support during respiratory tract infections. The child continues to follow up in outpatient department, occasionally needing oxygen support. He seems developmentally age appropriate, but has severe failure to thrive. His current anthropometric measurements at 3 years were: Weight was 9 kg (<1st centile), height was 84 cm (<1st centile), and head circumference was 42 cm (<3rd centile).

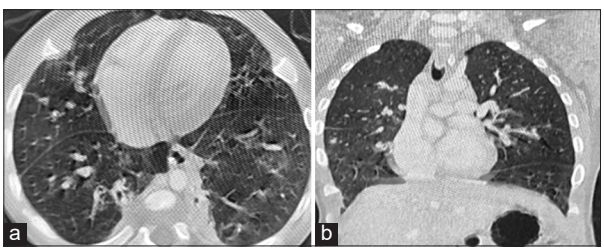

Figure 1: (a and b) High-resolution computed tomography chest showed multifocal patchy areas of subacute infiltrates in bilateral lungs with residual sub-segmental consolidation and fibro-bronchiectasis changes.

Given his prolonged course and recurrent hospital admissions with LRTI and bronchiectatic changes on HRCT chest, workup for CF was initiated. A sweat chloride test was done, which was negative. He was then subjected to genetic testing for PCD, which revealed abnormalities in the *DNAH1* and *LRRC6* genes, consistent with the diagnosis of PCD. Both genes were associated with autosomal recessive forms of PCD. No second pathogenic variant was identified, and both variants were classified as VUS.

DISCUSSION

This case illustrates a severe post-viral BO phenotype following multiple respiratory viral infections in infancy, most notably adenovirus. While post-infectious BO is a recognized entity, the persistence and severity of symptoms, along with multiple hospital admissions due to LRTIs, raised the suspicion of underlying genetic disorders such as CF or PCD. Given the negative sweat chloride test and recurrent LRTIs with bronchiectasis, a genetic workup for PCD was pursued.

PCD is a rare, genetically heterogeneous disorder affecting motile cilia function, typically inherited in an autosomal recessive pattern. Mutations in more than 50 genes have been associated with PCD, including DNAH1 and LRRC6, both of which are implicated in axonemal assembly and function [1-3]. Although only heterozygous VUS were detected in our patient, both variants have been previously reported in association with PCD phenotypes, supporting a likely role in disease pathogenesis [2,4].

Emerging literature emphasizes that PCD may present as a spectrum, and children with heterozygous VUS, especially in the context of classic symptoms, should not be dismissed without further clinical correlation [1,5]. In such cases, ancillary testing, including nasal nitric oxide measurement and electron microscopy of ciliary ultrastructure, can aid in confirming the diagnosis [1,6,7].

The presence of undescended testes in our patient may reflect a broader ciliopathy-related phenotype, although this association is not consistently reported. Multidisciplinary involvement – including pulmonologists, geneticists, and physiotherapists – was

essential for this patient's stabilization and long-term care plan [3,4,6,7].

This case underlines the importance of suspecting PCD in infants with severe or recurrent viral pneumonias and bronchiectasis, especially following adenoviral infections. Early genetic testing, even if yielding inconclusive or VUS results, provides a framework for further workup and family counselling.

The differential diagnosis for recurrent severe LRTIs and bronchiectasis in infancy includes CF, primary immunodeficiency syndromes, post-infectious BO without underlying genetic etiology, congenital airway malformations, and aspiration syndromes [8-10]. In our patient, sweat chloride testing excluded CF, and there was no clinical evidence suggestive of immunodeficiency or aspiration. The persistent severity of illness and presence of bronchiectasis prompted evaluation for a mucociliary clearance disorder such as PCD, which was supported by genetic findings.

CONCLUSION

Bronchiolitis is a common respiratory infection in the pediatric population. Adenoviral pneumonia can lead to chronic progressive disease of the developing lungs, characterized by inflammation and scarring, leading to BO. Persistent or recurrent respiratory symptoms with bronchiectasis should prompt evaluation for underlying disorders such as CF, anatomical defects, and PCD. Genetic findings of VUS require careful clinical correlation and family testing. A multidisciplinary approach is essential for the long-term care of children with post-viral chronic lung disease.

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