A Term Newborn with Lung Collapse since Birth

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Abstract

Respiratory distress in a term newborn has a wide range of differential diagnoses. Lobar lung collapse as a cause of respiratory distress in a term newborn always raises the suspicion of congenital pneumonia but it is challenging to determine if (1) it presents since birth, (2) it has a migratory nature, and (3) infection was excluded as a cause. We report a case of lobar lung collapse in a full-term baby and present our management of the case until the underlying diagnosis was reached.

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Introduction

Respiratory distress is one of the most common causes of admission to neonatal intensive care units (NICU). Respiratory distress occurs in 5–7% of live births at term gestation [1]. Many risk factors can predispose to neonatal respiratory disease. These factors include prematurity,

cesarean section, meconium-stained amniotic fluid, maternal diabetes, chorioamnionitis, or some prenatal ultrasonographic findings, such as oligohydramnios or lung abnormalities [2]. We report a case of pulmonary lobar collapse in a nonmechanically ventilated full-term newborn since birth and our approach to reaching the diagnosis.

Case Report

A term baby boy weighing 2.6 kg was born at 37 weeks' gestation. He was a product of a first-degree consanguineous marriage. The mother was a primigravida, 22 years old, rubella immune with negative serology; she had gestational diabetes on metformin. Her antenatal scan was normal. A high vaginal swab was positive for *Candida* and a midstream urine sample showed mixed growth including Group B *Streptococci*.

The baby was delivered by normal vaginal delivery through clear liquor. He cried immediately after birth with an Apgar score of 9 and 10 at 1 and 5 min respectively. Initially, he was kept at the mother's side. However, after 10 h of age he was noticed to have color changes and respiratory distress, so he was transferred to the NICU for further management.

He was on noninvasive support and was started on intravenous antibiotics. Vital signs were stable. He was nondysmorphic with respiratory distress. There was prominent pectus excavatum clinically and in the chest X-ray (Fig. 1). Other systemic examination

was unremarkable including cardiac, neurological, and gastrointestinal examination.

His chest X-ray on different occasions showed recurrent lobar lung consolidation with migratory nature that resolved in an area and simultaneously appeared in another area (Fig. 2). Chest ultrasound showed upper and lower lobe consolidation. Septic screening and cultures were negative. Echocardiography and brain ultrasound were normal. Newborn screening including immune reactive trypsin was reported as normal. As the lung collapse was not improving, a chest CT was carried out which showed extensive bilateral patchy areas of pulmonary consolidation.

Our pulmonologist was involved in the case, and a diagnostic flexible bronchoscopy was performed which revealed vocal cord edema and adhesion of the apical part, tracheal obstruction caused by pectus excavatum with anterior wall extrinsic thoracic compression, excessive, thick, and sticky secretion predominantly in the right bronchial tree, inflammation, and edema of the bronchial mucosa.

A tracheostomy was performed and the infant could successfully be weaned to room air. The chest X-ray after tracheostomy showed right upper lobe collapse. Investigations did not show any situs abnormalities, but from the clinical course (unexplained multiple lobar atelectasis, unexplained prolonged respiratory distress, and pectus excavatum) and the investigation results (chest CT and bronchoscopy) primary ciliary dyskinesia (PCD) was suspected.

Unfortunately, electron microscopy to identify ciliary ultrastructural defects was not available, so genetic testing was requested. Molecular genetic testing by next generation sequencing identified homozygous duplication of 10 pairs in exon 1 of the *CCNO* gene (c.259_268dupGCCCAGCCCG) which leads to frameshift p.(Val90Glyfs*49), resulting in a premature stop codon. Pathogenic variants in the *CCNO* gene cause autosomal recessive PCD (OMIM: 615872). To the best of our knowledge, the variant has not been described in the literature to date (HGMD 2018.3). Other gene mutations associated with PCD listed in Table 1.

The infant was kept under cover of chest physiotherapy with nebulized saline 7%, budesonide, and salbutamol. He was off oxygen, and was on full oral feeding with tachypnea and recessions. Upon parental request, he was transferred abroad for further management.

Discussion

In our case, congenital pneumonia was ruled out by repeated negative septic screening and poor response to antibiotic therapy. We believe that severe pectus excavatum contributed to the clinical presentation but it did not fully explain the clinical course and the bronchoscopy findings, so our investigations were extended to rule out other etiologies.

Fig. 1. Chest X-ray lateral view shows pectus excavatum (marked by red arrow).

Fig. 2. Chest X-ray A/P view shows lobar lung collapse of the same patient on different occasions.

Table 1. Mutations in genes that cause PCD with ciliary ultrastructure and organ laterality defects

Genes	Ciliary EM	Laterality defect
DNAH5, DNAI1, DNAI2, DNAL1, NME8, CCDC114, CCDC151, ARMC4	ODA defect	Yes
DNAAF1, DNAAF2, DNAAF3, LRRC6, C21orf59, DNAAF5 (HEATR2), ZMYND10, DYX1C1 (DNAAF4), SPAG1, CCDC103	ODA+IDA defect	Yes
CCDC39, CCDC40	IDA defect + MTD	Yes
RSPH1, RSPH3, RSPH4A, RSPH9, HYDIN	RS/CP defect	No
CCDC164 (DRC1), CCDC65 (DRC2), GAS8 (DRC4)	Nexin link defect	No
DNAH11	Normal EM	Yes
DNAH1, DNAH8	EM not available	Yes
CCNO, MCIDAS	Oligo cilia	No
OFD1	PCD 1 XLMR	Yes
RPGR	PCD 1 XLRP	No

EM, electron microscopy; CP, central pair; RS, radial spoke.

Pectus excavatum is a dorsoventral narrowing and inward concave deformity of the caudal part of the sternum and associated costal cartilages. It extends caudally from around the 5th to 6th ribs and is most severe at the level of the 10th thoracic vertebra. It can lead to both displacement of the heart and lung compression. It is the most common anterior chest wall deformity. Incidence is 1 in 400–1,000 live births and it is three to five times more common in males. The clinical signs of pectus excavatum can be associated with tachypnea, cyanosis, and paradoxical movement of the deformity during inspiration, and chronic alveolar collapse that can contribute to hypoxemia by impairing gas exchange. Compression of the heart and kinking of great vessels can lead to heart murmurs or cardiac arrhythmias [3]. Pectus excavatum occurs in as many as 10% of patients with PCD versus 0.3% in the general population [4]. There is a high prevalence of scoliosis (5–10%) in PCD [5].

PCD has an estimated incidence of 1 per 10,000–20,000 births, based on population surveys of situs inversus and bronchiectasis [6]. The function of normal motile cilia is to clear mucus, bacteria, and toxic substances from the airways [7]. Pectus excavatum seen in the present patient could be secondary to severe respiratory distress.

Cilia have a complex (9 + 2) axonemal structure for their motility. They have microtubules of alpha and beta monomers of tubulin. Outer and inner dynein arms are present along the length of the peripheral microtubules. Nexin links (nexin-dynein regulatory complexes) connect the doublets, and radial spokes connect the doublets to the central pair for structural support during bending [8].

The earliest manifestations of PCD occur in the neonatal period, commonly in full-term neonates (80%). They are always misdiagnosed with transient tachypnea of the newborn and neonatal pneumonia [9]. Lobar collapse in term neonates is rare, yet it is seen in the majority of PCD cases. This suggests that PCD should be considered in the differential diagnosis if unexplained neonatal respiratory distress is associated with lobar collapse.

In our case, electron microscopy was not available so genetic testing was carried out based on the clinical suspicion, and the positive finding of pathogenic variants in the *CCNO* gene that cause autosomal recessive PCD may have caused ciliary dyskinesia, leading to presenting symptoms.

Situs abnormalities are present in more than 50% of pediatric patients, which may aid earlier recognition of PCD. This reflects abnormal function of motile cilia during embryogenesis [10]. There is a 200-fold increased probability of having structural congenital heart disease compared with the general population, with heterotaxy that includes polysplenia (left isomerism) and asplenia (right isomerism) [11].

As there is no “gold standard” diagnostic test for PCD, The European Respiratory Society (ERS) Task Force Guidelines for diagnosing PCD recommend that patients should be referred for diagnostic testing if they have several of the following features: persistent wet cough, situs anomalies, congenital cardiac defects, persistent rhinitis, chronic middle ear disease with or without hearing loss, or a history, in term infants, of neonatal upper and lower respiratory symptoms or NICU admission. Table 2 shows

Table 2. Characteristic symptoms in patients with PCD, stratified by age

Neonates	Situs abnormalities Normal situs (~47%) Situs inversus totalis (~47%) Situs ambiguus with or without cardiac defects (~6–12%) Neonatal respiratory distress At term with no risk factors Prolonged oxygen requirement Atelectasis on radiography Persistent rhinorrhea Family history of PCD
Children	Wet cough Typically starts in infancy Persistent, year-round, does not completely resolve with antibiotics Bronchiectasis Sometimes present in pre-school year Chronic rhinitis Typically starts in infancy; persistent, year-round even when “well” Otitis media with effusion (“glue ear”) Conductive hearing loss Variability within and between patients, normal to requiring hearing aids Mucopurulent discharge complicates ventilation tube insertion (evidence poor)
Adolescents and adults	As for children, plus: Bronchiectasis, almost universal by adulthood Rhinosinusitis, variability within and between patients; symptoms might include persistent nasal blockage and discharge Conductive hearing loss Sinusitis Anosmia Nasal polyposis Male infertility (not 100% and incidence unclear) Female fertility issues (incidence unclear)

characteristic symptoms in patients with PCD, stratified by age [12].

No validated PCD-specific therapies are available. Therefore, therapies for PCD extrapolated from other diseases, such as cystic fibrosis and non-cystic fibrosis bronchiectasis, like antibiotic therapy (commonly macrolides) and anti-inflammatory agents [13].

We recommend considering the diagnosis of PCD in neonatal respiratory distress especially in the following cases: term baby, late onset of respiratory distress (12 h of age), longer duration of required oxygen therapy, and higher frequency of atelectasis and/or lobar collapse. Other features that increase the suspicion are association with pectus excavatum, situs abnormalities, and structural congenital heart defects. Other causes of neonatal respiratory distress should always be excluded first, especially congenital pneumonia and transient tachypnea of the newborn.

Statement of Ethics

Written consent was obtained from the parents of the infant.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

F.A.: analysis, review, design, critical analysis, and final approval. A.M.E.: conception, data acquisition, manuscript drafting, critical analysis, and final approval.

References

- 1 Chowdhury N, Giles BL, Dell SD. Full-term neonatal respiratory distress and chronic lung disease. *Pediatr Ann*. 2019 Apr;48(4):e175–81.
- 2 Hibbard JU, Wilkins I, Sun L, Gregory K, Haberman S, Hoffman M, et al.; Consortium on Safe Labor. Respiratory morbidity in late preterm births. *JAMA*. 2010 Jul;304(4):419–25.
- 3 Fokin AA, Steuerwald NM, Ahrens WA, Allen KE. Anatomical, histologic, and genetic characteristics of congenital chest wall deformities. *Semin Thorac Cardiovasc Surg*. 2009; 21(1):44–57.
- 4 Kennedy MP, Noone PG, Leigh MW, Zariwala MA, Minnix SL, Knowles MR, et al. High-resolution CT of patients with primary ciliary dyskinesia. *AJR Am J Roentgenol*. 2007 May;188(5):1232–8.
- 5 Knowles MR, Daniels LA, Davis SD, Zariwala MA, Leigh MW. Primary ciliary dyskinesia. Recent advances in diagnostics, genetics, and characterization of clinical disease. *Am J Respir Crit Care Med*. 2013 Oct;188(8):913–22.
- 6 Torgersen J. Transposition of viscera, bronchiectasis and nasal polyps; a genetical analysis and a contribution to the problem of constitution. *Acta Radiol*. 1947 Feb;28(1):17–24.
- 7 Tilley AE, Walters MS, Shaykhiev R, Crystal RG. Cilia dysfunction in lung disease. *Annu Rev Physiol*. 2015;77(1):379–406.
- 8 Satir P, Christensen ST. Overview of structure and function of mammalian cilia. *Annu Rev Physiol*. 2007;69(1):377–400.
- 9 Mullowney T, Manson D, Kim R, et al. Primary ciliary dyskinesia and neonatal respiratory distress. *Pediatrics*. 2014 Dec;134(6):1160–6.
- 10 Basu B, Brueckner M. Cilia multifunctional organelles at the center of vertebrate left-right asymmetry. *Curr Top Dev Biol*. 2008;85:151–74.
- 11 Brueckner M. Impact of genetic diagnosis on clinical management of patients with congenital heart disease: cilia point the way. *Circulation*. 2012 May;125(18):2178–80.
- 12 Kuehni CE, Lucas JS. Diagnosis of primary ciliary dyskinesia: summary of the ERS Task Force report. *Breathe (Sheff)*. 2017 Sep;13(3):166–78.
- 13 Shapiro AJ, Zariwala MA, Ferkol T, Davis SD, Sagel SD, Dell SD, et al.; Genetic Disorders of Mucociliary Clearance Consortium. Diagnosis, monitoring, and treatment of primary ciliary dyskinesia: PCD foundation consensus recommendations based on state of the art review. *Pediatr Pulmonol*. 2016 Feb;51(2):115–32.