

## CASE REPORT

# Management of a child with primary ciliary dyskinesia

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## Abstract

Primary ciliary dyskinesia (PCD) is an autosomal recessive condition characterized by dysmotile cilia. Typically associated with defects in the cilia structure, it results in impaired mucociliary clearance of pathogens from the lungs and sinuses. Consequently, patients suffer from recurrent sinopulmonary and middle ear infections. We report on the management of a 5-year-old boy who presented with increased work of breathing, fever and crepitations, with an existing diagnosis of PCD with situs inversus totalis. Chest X-ray imaging revealed right lower lobe collapse. He was managed with intensive physiotherapy, nebulized mucolytic agents and antibiotics. However, due to a poor response, he underwent flexible bronchoscopy, which allowed removal of a mucus plug and subsequent re-expansion of his collapsed lobe. Although there is limited evidence for the management of PCD, here we discuss the accepted strategies for its management, based on expert opinion and guidelines for other suppurative lung diseases.

## INTRODUCTION

Primary ciliary dyskinesia (PCD) consists of a rare heterogeneous group of conditions that can affect ~1 in 10 000 live births and causes impaired mucociliary clearance [1]. Motile cilia are situated at numerous sites in the body including the respiratory tract and middle ear. Hence, PCD is characterized by recurrent sinopulmonary infections and otitis media with effusion (OME), which develop into bronchiectasis and conductive hearing loss respectively [2]. Additionally, cilia play a crucial role in determining left–right orientation in embryonic development with almost half of PCD patients having organ laterality defects [3]. A further complication of PCD is reduced fertility in females as well as a high rate of infertility in males as a result of immotile sperm [3].

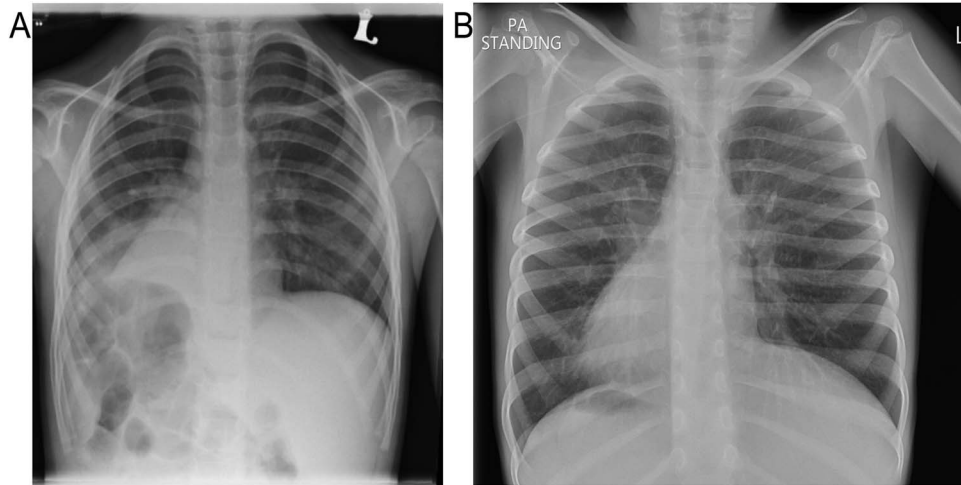
## CASE REPORT

A 5-year-old boy presented to a tertiary hospital with 1-week history of pyrexia and cough. He was diagnosed with PCD at 1 month of age, having been noted to have both dextrocardia and persistent neonatal respiratory distress. Diagnostic investigations demonstrated static cilia throughout the sample on high-speed video microscopy analysis and an outer dynein arm defect on ciliary ultrastructure analysis by transmission electron microscopy. Subsequent testing showed he had extremely low levels of nasal nitric oxide (nNO) at 25 parts per billion (8.33 nl/min) and genetic tests demonstrated that he is heterozygous for two known disease-causing mutations in the dynein axonemal intermediate chain 1 (DNAI1) gene.

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**Figure 1:** Chest X-ray imaging of patient at admission (A) and 10 days after treatment (B). (A) Antero-posterior view of chest showing extensive consolidation/collapse of right lower zone with volume loss. (B) Postero-anterior view of chest showing marked improvement of the previous right-sided X-ray changes with re-expansion of the right lower lobe and clearer lung fields.

It is often challenging in children with PCD to identify respiratory exacerbations as, even when well, they have a persistent wet cough [4]. However, in the three months prior to presentation, he had received 2 courses of oral antibiotics for respiratory exacerbations. These had presented with increased productive cough, wheeze and fever. Both courses of antibiotics led to his symptoms temporarily improving to his baseline daily cough but deteriorating soon after the course was complete.

On admission, he had bilateral wheeze and crepitations at lung bases, which were more evident on the right side. His chest X-ray showed extensive collapse of his right side lower lobe with volume loss (Fig. 1A). He was initially treated with aggressive airway clearance physiotherapy before administration of hypertonic 7% saline nebulisers and intravenous (IV) antibiotics (Cefuroxime 50 mg/kg, four times daily). However, his clinical signs did not improve and hence he went on to have a flexible bronchoscopy under general anaesthetic. This demonstrated mucus plugging of the right-sided lower bronchial division, which was suctioned out. At the time of his bronchoscopy, a peripherally inserted central catheter (PICC) line was placed to facilitate a prolonged course of IV antibiotics.

A week after bronchoscopy, with ongoing use of airway clearance physiotherapy, mucolytic agents (hypertonic saline and Dornase alfa (recombinant human deoxyribonuclease (DNase) nebulisers) and IV antibiotics, a further chest X-ray demonstrated re-expansion of the right lower lobe (Fig. 1B), accompanied by an alleviation of his respiratory symptoms. He was discharged two weeks after admission with ongoing hypertonic 7% saline nebulisers, to be given twice daily prior to physiotherapy, and 2.5 mg DNase nebulizer, to be given once daily after physiotherapy.

## DISCUSSION

The principal goal of care for children with PCD is to reduce the frequency of recurrent infections and slow the decline in respiratory function. There is currently limited evidence surrounding its management and thus guidelines are derived from other chronic suppurative lung diseases, such as cystic fibrosis (CF), and clinical experience [5, 6]. Children and their families are trained in conducting airway clearance physiotherapy twice

daily, increasing at times of respiratory exacerbations. In addition, some children may be prescribed mucolytic agents, such as hypertonic saline (starting on 3% and possibly trialling 7% sodium chloride depending on age and tolerance) to aid airway clearances. For any respiratory exacerbations, a microbiology sample should be obtained, preferably a sputum sample if not a cough swab/laryngeal aspirate, and a 2-week course of oral antibiotics should be commenced if the exacerbation lasts more than 3–4 days. Pending the results of the microbiology testing, antibiotic choice should be based on previous cultures from that child and cover typical respiratory pathogens, including *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Staphylococcus aureus* [5]. Depending on age, a number of nasal treatments are also considered including nasal drops, Sterimar nasal spray and, when old enough, nasal douching which, if tolerated, in our centre's experience is the most effective.

In this case, in addition to hypertonic saline nebulizers, we also used nebulized DNase. There is limited evidence for its use in patients with PCD, with no randomized control trials and only three case reports to date [7–9]. Although these found that commencing DNase therapy improved respiratory symptoms and function in children, a large study in adults with non-CF bronchiectasis found that it led to increased hospitalization rate and poorer lung function [10]. Given this, in our centre and the other three UK PCD centres, DNase is used as a second line mucolytic agent where hypertonic saline is not tolerated or not found to be effective. Its use is carefully trialled and discontinued where no benefit is observed. If physiotherapy and mucolytic treatments are not effective in re-expanding areas of collapse/consolidation, as in this case, bronchoscopy should be considered.

In PCD, it is important to consider the possible non-respiratory complications that may arise. For instance, children with PCD often suffer with chronic OME. Historically, to treat this, children with PCD would have undergone surgical insertion of myringotomy tubes (grommets). This had limited benefit and can lead to multiple further insertions, which increased the risk of tympanic membrane perforation [11]. Although grommet insertion is occasionally undertaken in children with PCD, it should be carried out following advice from an ear, nose and throat (ENT) surgeon with expertise in this patient group. A known complication of OME is conductive

hearing loss; therefore, hearing should be routinely tested. Depending on the severity, the child might require hearing aids or extra educational support [1]. An additional serious complication of PCD is infertility. Hence counselling should be provided to patients as they approach adulthood. For those interested in raising a family, *in vitro* fertilization could be considered [12].

It is recommended that paediatric patients have regular follow up appointments every 3 months. Annually, the child should have a review with the specialist PCD multidisciplinary team (MDT) [1]. These comprise of, but are not limited to, a respiratory consultant, ENT surgeon, specialist PCD nurses, physiotherapists and audiologists [13]. During each review, patients undergo lung function tests to monitor disease progression. Carriage of pathogens are also detected through sputum cultures or cough swabs, although the latter has lower sensitivity [14]. Patients with PCD are also a high priority group to receive seasonal vaccinations.

PCD is a relatively rare condition with multisystem involvement. Currently, the evidence-base for the management of children with PCD is limited. However, ensuring early diagnosis by education of the presenting features of the condition and the MDT approach to its management will help ensure optimal outcomes for patients.

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## CONFLICT OF INTEREST STATEMENT

None declared.

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## ETHICAL APPROVAL

No ethical approval was required for this report.

## CONSENT

As the patient was an underage child, his parent has provided written consent for the publication of his information.

## GUARANTOR

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