Pulmonary management of primary ciliary dyskinesia: a case report

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Introduction

Primary ciliary dyskinesia (PCD) is an autosomal recessive disorder with congenital reduction or absence of ciliary function. About 50% of the cases were associated with mirror image arrangement and constituted the classical Kartagener syndrome. The estimated prevalence for PCD is 1:15-30,000 live births. 1 PCD should be suspected in patients with chronic productive cough, rhinosinusitis and otitis media with effusion.

We presented a patient with primary ciliary dyskinesia with persistent Haemophilus influenzae infection and deteriorated progressively. We reviewed the current evidence on the pulmonary management of primary ciliary dyskinesia including the use of prolonged antibiotics, bronchodilator, mucolytics, chest physiotherapy and physical exercise.

Case report

An 11-year-old boy presented with chronic productive cough and nasal obstruction for 6 years. He was a new immigrant from mainland China. His parents were non-consanguineous. There was no family history of unexplained early death or recurrent infections.

Physical examination showed that his growth parameters were along the 25th percentile. His general condition was satisfactory. There was no clubbing of fingers. He was not in respiratory distress. His oxygen saturation in room air was normal. Chest examination showed increased antero-posterior diameter of chest and occasional crepitations over bilateral lung bases. His apex was located on the left side and was not displaced. There were thick purulent nasal discharge and a nasal polyp over the right side. Both of his tympanic membranes were congested.

The white cell counts were normal. Mantoux test was negative. Chest X-ray showed right middle and lower zone consolidation and bilateral lower zone haziness (Figure 1). CT thorax and nasal sinuses showed mild bronchiectasis over right middle lobe and pansinusitis. Sputum culture grew Haemophilus influenzae. Immunological workup showed no specific

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immunodeficiency. Sweat test was negative. Nasal brush biopsy for light microscopy showed that most cilia were immotile. Electron microscopy revealed absence of outer dynein arm, confirming the diagnosis of PCD.

He suffered from persistent *Haemophilus influenzae* infection in the subsequent years. There was moderate to heavy growth of *H. Influenzae* in his sputum, which was sensitive to amoxicillin with clavulanate, clarithromycin, chloramphenicol and cefaclor. White cell count in sputum varied from 2+ to 3+. Clinically, sputum volume remained similar at 30-40 ml per day, and remained yellowish. There was no fever or respiratory distress. Repeated courses of antibiotics including amoxicillin and clavulanate, clarithromycin, amoxicillin with courses varied from 4 weeks to 3 months were given. However, eradication of *H. Influenzae* was not achieved. After two years of almost continuous antibiotics, antibiotics was only prescribed when there were clinical signs of infection.

The patient had poor adherence to chest physiotherapy and physical exercise. Regular chest percussion and postural drainage was not possible as parents worked long hours. He defaulted physiotherapy sessions at the hospital because of busy schooling schedule neither did he exercise regularly.

His condition deteriorated gradually. About 3 years after the diagnosis of PCD, his sputum increased in volume and became greenish. His body weight dropped. His oxygen saturation dropped to low 90s in room air. His FVC decreased from 97% to 85% and FEV-1 dropped from 60% to 44% of predicted. He also suffered from a febrile pneumonic episode. Sputum culture grew *Haemophilus influenzae* sensitive to ampicillin and clarithromycin. Chest X-ray showed collapsed right middle and lower lobe. High resolution CT thorax showed completely collapsed right middle and lower lobe and bronchiectatic changes with basal predominance (Figure 2).

He was given intravenous amoxicillin and clavulanate 30 mg/kg three times per day for 2 weeks, followed by oral amoxicillin 500 mg and clavulanate 125 mg three times per day for 2 weeks. He had another episode of fever while on oral amoxicillin, hence antibiotics was changed to clarithromycin. High dose clarithromycin 500 mg twice daily was given for 4 weeks followed by 250 mg twice daily for 3 months. Bronchoalveolar lavage was performed to remove retained sputum. Supervised chest physiotherapy in ambulatory ward setting was performed twice weekly. The mother was taught successfully to perform chest percussion twice daily. Patient had good adherence to the use of positive expiratory pressure mucous clearance device, Flutter® every few hours and exercise at least daily.

Sputum amount decreased significantly, white cell count in sputum also decreased. Temporary clearance of *H. Influenzae* was achieved intermittently. He regained his body weight to his original centile. Oxygen saturation normalised. Pulmonary function showed no further deterioration, FEV1 increased from 44% to 56% of predicted.

**Discussion**

In the current case of PCD, aggressive management of infection and intensive chest physiotherapy halted...
the deterioration of lung function. Early diagnosis of PCD is important first step in the management. PCD should be suspected in patients with chronic productive cough, rhinosinusitis and otitis media with effusion. Screening for PCD with saccharin test is unreliable, particularly in children. Nasal nitric oxide is low in PCD and has been used as a screening with reasonable sensitivity. However, overlap with other respiratory conditions is common and further diagnostic testing is required. The gold standard for diagnosis is the examination of ciliary ultrastructure by electron microscope. Nasal brush is used for collection of nasal epithelium. Other diagnostic tests include assessment of ciliary beat frequency, beat pattern analysis and ciliary disorientation. Majority of PCD are due to lack of outer dynein arm. The initial test may be equivocal in about 10%, repeated brushing should be performed.

Once diagnosed, patient should be monitored regularly with pulse oximetry, lung function test and sputum cultures. Appropriate medical treatment has been shown to prevent deterioration in lung function.

Bacterial colonisation was thought to perpetuate inflammatory change in PCD. As a result of cilia dysfunction, mucous accumulates and became liable to infections causing inflammation, releasing pro-inflammatory mediators which further damage the respiratory tract, causing scarring and airway dilatation. Common infective organisms include Haemophilus influenzae, Staphylococcus aureus, Streptococcus pneumoniae and Pseudomonas aeruginosa. Prolonged antibiotics treatment was proposed as one of the strategy to interrupt the infection-inflammation vicious cycle. One study on non-cystic fibrosis (CF) bronchiectasis children showed that clarithromycin for 12 weeks in adjunct to supportive therapy significantly decreased 24 hours sputum volume, IL-8, total cell count and neutrophils ratio in bronchoalveolar lavage but had no impact on pulmonary function. Another study showed that roxithromycin for 12 weeks significantly lowered sputum leukocyte and purulence scores. A meta-analysis on 9 trials on prolonged antibiotics for purulent non-CF bronchiectasis in children and adults, showed that antibiotics given for 4 weeks to one year, had significant favourable effect on clinical response in terms of patients diary card and physician assessment, but conferred no benefit in reducing exacerbation or lung function. The American College of Chest Physician guideline concluded that prolonged systemic administration of antibiotics may produce small benefits in reducing sputum volume and purulence, but may also be associated with intolerable side effects. The risk of facilitating the emergence of resistant organisms should not be disregarded. Expert opinion was that prophylaxis antibiotics should only be considered if repeated courses of antibiotics were required. Should there be any sign of deterioration in symptoms or lung function, high-dose oral antibiotics should be given.

There is no evidence to recommend routine use of mucolytics. Bromhexine was shown to ease sputum expectoration and reduce sputum production, but a higher than recommended dose was used in the reported study and it was uncertain whether the improvement was due to concomitant use of antibiotics. Recombinant human DNase showed no benefit in lung function and was associated with influenza-like side effects. Regular bronchodilators are not useful.

Chest physiotherapy is considered mainstay in treatment of PCD. Hospital-supervised chest physiotherapy for one month has been shown to improve lung function at 12 months. However, there is no evidence to confirm the effectiveness of non-supervised chest physiotherapy. Adherence is of paramount importance, the options of various modes of physiotherapy should be tailored to the individual. Physical exercise was shown to achieve greater degree of bronchodilation than inhaled beta-2 agonists, and the effect persisted for 30 minutes post-exercise. Physical exercise should therefore be encouraged.

From our experience, aggressive management of infection and a tailored made physiotherapy and physical exercise program had been successful in preventing the deterioration of lung function.
References