Case Series

Protracted Bacterial Bronchitis in children- shedding light on lingering cough

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ABSTRACT

Protracted Bacterial Bronchitis [PBB] in children, as the name suggests, is a prolonged wet cough of bronchial origin for more than four weeks. The affected children will be otherwise hale and healthy except for the disturbing diurnal cough. Unlike asthma, the cough is characteristically wet or productive, and there is no specific nocturnal variation of symptoms. It usually affects preschool children. The diagnosis is clinical in experienced hands without going in for an extensive workup. Responding to the treatment is one of the criteria to diagnose PBB as per consensus guidelines. Most patients respond to appropriate antibiotic therapy of 2-4 weeks duration, usually amoxicillin-clavulanate. Few children may go in for recurrence of symptoms; in such cases, bronchoscopic workup of the airway is warranted. Thus, clinicians should always have a high index of suspicion of this condition in otherwise healthy young children who have a chronic wet cough of more than four weeks duration. Timely management of such cases would prevent the development of chronic suppurative lung disease and long-term morbidity.

Key words: Child, Cough, Amoxicillin-Potassium Clavulanate Combination, Bronchoscopy, Clinical Trial

Cough is a protective airway reflex that prevents aspiration and enhances airway clearance. Excessive and protracted cough is a disabling complaint leading to a decreased quality of life. As per European Respiratory Society (ERS) and American College of Chest Physicians (ACCP) guidelines, chronic cough in children is defined as a daily cough lasting for more than four weeks [1, 2]. There are different consensus guidelines for the definition of chronic cough. CHEST guidelines define chronic cough as one that persists for more than 8 weeks [3, 4]. British Thoracic Society (BTS) guidelines also consider 8 weeks for a chronic cough [5]. Protracted Bacterial Bronchitis is a common cause of chronic wet cough in preschool children with the absence of symptoms and signs of other specific causes such as cystic fibrosis, primary ciliary dyskinesia, bronchiectasis, tuberculosis and upper airway cough syndrome. The exact prevalence of PBB in the community is not known since most of the cases go undiagnosed or misdiagnosed.

The diagnosis is made by clinical as well as microbiological methods, [6] with exclusion being the primary way of diagnosis. Investigations are done to rule out other causes of chronic wet cough in children. Resolution usually occurs with a two-to-four-week course of an appropriate antibiotic therapy. Amoxicillin-clavulanic acid is the preferred antibiotic for the management of PBB. It is given in conventional doses (30-50 mg per kg body weight per day in two or three divided doses).

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CASE DETAILS

Our first case was a 6-year-old male child who presented with complaints of a wet cough for two months. He was admitted with complaints of a recent onset of high-grade fever for four days. There were no recurrent ear or skin infections. On examination, his growth parameters were within the normal range. He was maintaining saturation in the room air. Examination of the respiratory system revealed normal upper airway findings; there were rattling sounds on auscultation of the chest. Bilateral air entry was equal. Chest X-ray was done, which showed increased broncho-vascular markings (Figure 1). His blood workup was normal, ruling out severe infections. Aquagenic wrinkling test, tuberculin sensitivity test and sputum for Acid Fast Bacilli (AFB) were all negative.

He was started on injection amoxicillin-clavulanate at 50mg/kg/day in two divided doses. His sputum culture showed *Streptococcus pneumoniae* with a significant colony count. The child was discharged with oral amoxicillin-clavulanate on day 3 of admission since he was afebrile for more than 24 hours. At one week follow-up, his cough subsided, and there was significant improvement after two weeks of the same treatment. The child fulfilled the clinical criteria for diagnosis of protracted bacterial bronchitis. He has been followed up for

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about a period of 8 months now, he is asymptomatic, and there is no recurrence of PBB reported in him.

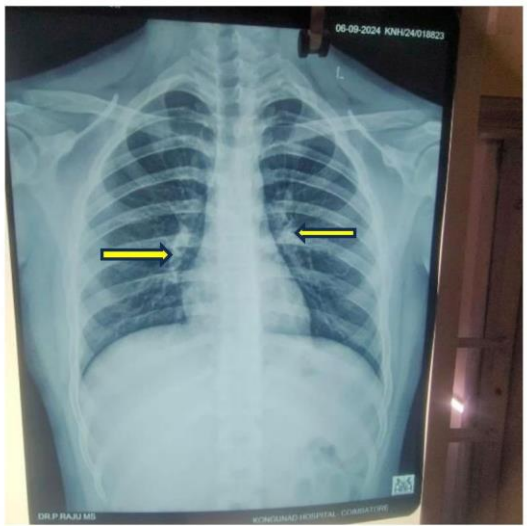

Figure 1: Chest X-ray of a 6-year-old male child showing bilateral increased broncho-vascular markings.

2nd case was a 4-year-old female child who presented as an outpatient with a wet cough for the past 6 weeks. Her growth parameters were within normal limits. There was no digital clubbing. Screening for tuberculosis was negative. Blood counts showed neutrophilic leukocytosis, and the chest X-ray was normal (Figure 2). The child was given oral amoxicillin-clavulanate of 30-50 mg/kg/day in divided doses for 2 weeks. Cough has significantly subsided, and blood counts have returned to normal upon follow-up. This child fulfilled the clinical criteria for PBB. Four months down the line, the child is completely asymptomatic.

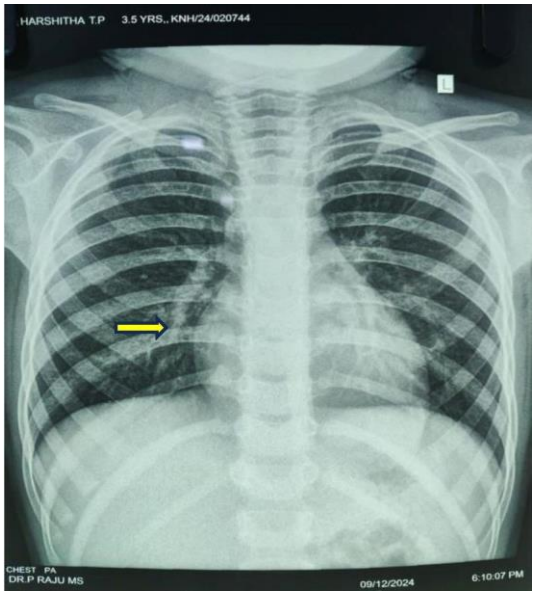

Figure 2: Chest X-ray of a 4-year-old female child with increased broncho-vascular markings on the right.

3rd case (Figure 3) was a 5-year-old female child with a similar presentation, chronic wet cough of one month duration, she was healthy with normal growth parameters and no other comorbidities. She also responded well to oral amoxicillin-clavulanate of 30-50 mg/kg/day in two divided doses for two weeks, which was started after ruling out other causes. On the first monthly follow-up after completion of the treatment, the child has a complete resolution of cough.

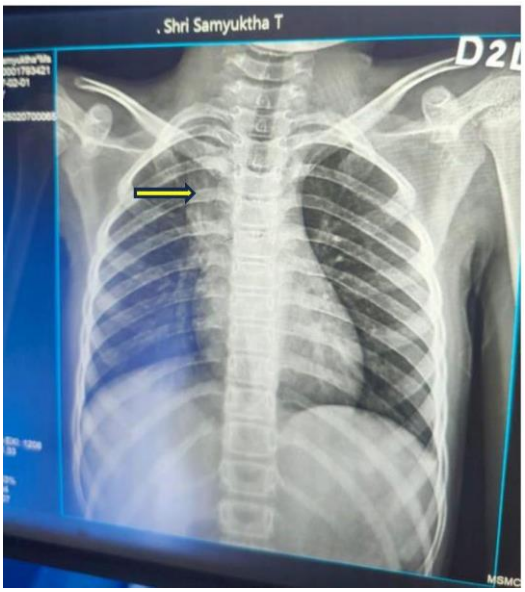

Figure 3: Chest X-ray of a 5-year-old child with normal lung fields and prominent thymic shadow.

In all three cases, the diagnosis of PBB was arrived at by exclusion of other causes. Forced Oscillation Technique (FOT) was also done in them to assess the pulmonary function, which had reactance and resistance in normal ranges with no significant bronchodilator reversibility, thus ruling out bronchial asthma and Interstitial Lung Disease (ILD).

DISCUSSION

PBB was first proposed as a new disease entity in the year 2006 [7, 8]. This term was first described by the Brisbane group and was recognized then in guidelines as a cause of chronic wet cough in children. Pediatric chronic cough (in children aged < 15 years) is defined as a daily cough lasting for > 4 weeks. This time frame was chosen based on the natural history of upper respiratory tract infections in children and differs from the definition in adults [1].

Any child with a wet cough of early onset, usually within 6 months of life and failure to thrive should have a suspicion of other causes like primary ciliary dyskinesia, cystic fibrosis and structural anomalies of the lung or heart. Children with PBB differ from these by cough usually of late onset, though cases of infantile PBB have been reported; it is less frequent in those under 6 months of age [8]. Children with PBB appear well; their growth and development are normal, and they lack signs of chronic suppurative lung disease such as digital clubbing, chest wall deformity, lung signs or radiological changes. Lung function tests- spirometry, FOT values are usually normal unless in those with concurrent asthma [7].

The common organisms causing PBB are *Hemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Staphylococcus aureus.* According to European Respiratory Society data, *Hemophilus influenzae* is the most common organism, found in 28 to 58% of children. *Streptococcus pneumoniae* (13 to 58%) and *Moraxella catarrhalis* (17 to 59%) are the two other most frequently detected organisms. Most *Hemophilus influenzae* are likely to be non-typeable strains [9]. Few studies have shown other organisms, like *Klebsiella pneumoniae* [10] and *Staphylococcus aureus*, too. The most common virus detected in children with PBB in a few studies was human adenovirus, with a few cases reporting the presence of rhinovirus, human bocavirus and human coronavirus.

The true prevalence of PBB cases presenting to a physician is unknown. Most of the cases go undiagnosed because of a lack of knowledge about this condition. Reports of chronic cough in populations vary between 1% in India, 9% in Eastern Europe and 5-12% in China, with a higher rate in areas with higher air pollution [2]. Various studies from Australia and Turkey have primarily shown an incidence of PBB between 11% and 41%. The median age of occurrence from these studies is 1.8 to 4.8 years [7]. The risk factors for developing PBB include structural airway lesions and host airway inflammatory and immune responses. There is a slight male predominance, and this occurs more commonly in the pre-school children with a median age range of 10 months to 4.8 years [2, 9].

According to European Respiratory Society guidelines, the modified clinical criteria for diagnosing PBB are as follows [9]:

1) Presence of chronic wet cough (>4 weeks)
2) Absence of symptoms or signs of other causes of wet or productive cough, and
3) Cough resolved following a 2-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate).

The original microbiological criteria for PBB (PBB-micro) are

(i) Presence of chronic wet cough (>4 weeks)

(ii) Lower airway infection (recognized respiratory bacterial pathogens growing in sputum or bronchoalveolar lavage at density of a single bacterial species >10000 CFU/mL) and

(iii) cough resolved following a 2-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate)

PBB extended – PBB resolving only after 4 weeks of an appropriate oral antibiotic.

Recurrent PBB - more than 3 episodes of PBB in a year.

Studies have shown that there will be intense airway neutrophilia along with raised total cell count. Airway eosinophilia is not a feature in these cases, unlike asthma [9]. A marked inflammatory response was also found in the Bronchoalveolar lavage (BAL) fluid of children with PBB.

Regarding the management of PBB, the choice of antibiotic is mostly empirical since sputum culture is not possible in most children as they are too young to expectorate. The antibiotic of choice would be based on targeting the common microorganisms involved in PBB and based on the local antibiotic sensitivity pattern. The appropriate antibiotic in the treatment of PBB is amoxicillin-clavulanate, which is active against beta-lactamase-producing strains of Hemophilus *influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus* and *Streptococcus pneumoniae*. The alternatives can be oral second or third generation cephalosporins, trimethoprim/sulfamethoxazole or macrolides, though the efficacy is still not proven [11].

Since PBB is just one among the various causes of chronic wet cough in children, any child who is not responding to 2-4 weeks of oral amoxicillin therapy should be further investigated. A Lancet study has provided a conclusion that a 4-week course of amoxicillin-clavulanate for children with suspected PBB has offered little advantage compared to the 2-week course in achieving clinical cure by 28 days [11].

A 5-year prospective cohort study conducted in Australia for the outcome of PBB showed that a significant portion of children had ongoing symptoms on 5-year follow-up. The risk factors for developing bronchiectasis were identified to be recurrent PBB within one year of follow-up and the presence of *Hemophilus influenzae* in BAL [12].

CONCLUSION

Protracted Bacterial Bronchitis, a common cause of chronic wet cough in young children, often responds to a course of appropriate antibiotic, amoxicillin-clavulanate. Early recognition and initiation of treatment promptly relieve the cough and school absenteeism in the affected children. Few children may go in for recurrent PBB; improperly treated cases may develop chronic suppurative lung disease. Recurrence or persistence of symptoms even after treatment needs bronchoscopic evaluation of the airway and culture of the bronchoalveolar fluid for microbiological diagnosis of PBB. Henceforth, any child diagnosed with protracted bacterial bronchitis should be closely followed up by either telephonic enquiry about ongoing symptoms or by direct visits until complete resolution of symptoms. PBB typically responds to a 2-4-week course of oral antibiotic therapy. Knowing this condition is crucial in day-to-day practice to avoid unnecessary extensive workup and also to prevent progression of the disease.

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