

**CASE SERIES****PROTRACTED BACTERIAL BRONCHITIS IN CHILDREN:  
THE FIRST CASE SERIES FROM ETHIOPIA**Abate Yeshidinber Weldetsadik<sup>1</sup>, Wuhib Zenebe<sup>2</sup>**ABSTRACT**

*Though an old disease, Protracted Bacterial Bronchitis (PBB) is a new diagnostic entity in children described recently. Since then, many pediatric cough studies have confirmed the role of PBB as one of the commonest cause of chronic cough in children. We report here a series of 4 children diagnosed with protracted bacterial bronchitis in our clinics for the first time from Addis Ababa, Ethiopia, based on the European Respiratory Society protracted bacterial bronchitis clinical guideline criteria.*

**INTRODUCTION**

Cough is the most common reason for pediatric health care visits worldwide (1,2). Although a healthy child can have an average of 11 cough episodes in 24 hours (3), cough can also be a manifestation of serious and life-threatening medical conditions (4). It is thus important to approach pediatric coughs systematically so that the normal variants are not over diagnosed and the serious ones not overlooked.

Chronic cough is defined in children as a continuous uninterrupted cough for more than 4 weeks (5, 6). Amongst the commonest causes of chronic cough in children is protracted bacterial Bronchitis (PBB) accounting up to more than 50 % in some centers (6 - 8). PBB is the presence of persistent endobronchial bacterial infection typically manifested with wet cough lasting for more than 4 weeks in children in the absence of other systemic symptoms (6, 8). The diagnosis of PBB requires systematic ex-

clusion of other causes of chronic cough in children including asthma, tuberculosis and chronic suppurative lung disease (8-12). As a result, PBB diagnosis is difficult especially in resource limited settings and in younger children. While the burden of PBB is mainly unknown in low income settings, studies from high and middle income countries demonstrated the increasing role of PBB in children (6, 8,13-16).

A recent clinical diagnostic criteria recommended by the European Respiratory Society (ERS) can be applicable for the diagnosis and treatment of PBB across different settings (15). We here report the first series of cases from Ethiopia diagnosed with PBB based on ERS clinical criteria in our chest clinics over the last 3 years followed by short review of literature and practice recommendations. All the cases were followed for a minimum of 3 months post-treatment with no recurrence of cough with in the specified follow up period.

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**CASE 1**

A three and half year old female toddler was self-referred to pediatric chest clinic in Saint Paul's Hospital Millennium Medical College (SPHMMC) for cough of 4-5 months. Initially her symptoms started gradually with URTI but cough persisted despite resolution of the cold. Her cough was characterized as wet with no diurnal variation. No choking history, wheeze or allergy. No fever, weight loss or appetite problem. PE was unremarkable and investigation revealed negative allergy test, normal CBC, ESR and normal CXR. The child was then given Amoxicillin-Clavulanate for 2 weeks for PBB after which cough subsided completely with no recurrence on subsequent follow-up.

**CASE 2**

A six year old boy with cough of 6 months duration was referred from pediatric OPD to the chest clinic at SPHMMC. Had occasional intermittent worsening of cough and younger brother has allergic rhinitis with multiple positive skin prick test (SPT) for pollen, dust mite and milk.

No choking or URTI was recalled by the mother and symptoms progressed gradually. The cough was wet with night time worsening though he continuously coughs during the day as well but no wheeze or exercise limitation. No fever, weight loss or appetite problem. No contact with TB patient. PE was unremarkable and investigation revealed normal CBC and ESR. The CXR was also normal. Despite the atypical nature of his symptoms

for asthma, because of first degree relative allergy history and episodic symptoms with night time worsening, child received allergy and spirometry tests but both were normal. The child was thus considered as having possible PBB for which he was started on Amoxicillin-Clavulanate for 2 weeks after which cough improved significantly and continuation of antibiotics for a total of 4 weeks leads to complete resolution with no recurrence of cough on follow up.

**CASE 3**

An 11 year old female child with cough of 6 weeks duration presented to Girum General Hospital pediatric OPD. It started with cold and she was seen at the same hospital at two weeks of symptom, diagnosed with bronchitis and provided supportive therapy (home remedy) with no medications and advised to return if new symptoms appear or cough doesn't resolve in 2-4 weeks. The child was brought back after four weeks of persistent cough but worsening in the last two weeks with productive cough of yellowish sputum but no diurnal difference. No fever, night sweats or weight loss. No choking history. No wheeze, asthma or allergy history but complains mild exercise limitation.

Physical exam was completely normal and CBC with 5 differential and acute phase reactants were all normal. The CXR was unremarkable except for mild hyperinflation (Image 1). PBB was considered as a provisional diagnosis for which she was started on Amoxicillin-Clavulanate and after a total of

four weeks cough resolves completely with no recurrence. This child was diagnosed earlier compared to the other three with only six weeks of cough (the other three coughed  $\geq 4$  months) likely because of consistent follow

and appropriate steps of management while the other 3 had visits to multiple providers with no regular follow up, multiple OTC drugs and antibiotics without proper diagnostic and therapeutic goal.



Figure 1. CXR of an 11 year old child with PBB showing mild hyperinflation (straight and deep coastophrenic angles with more than 9 posterior ribs and small, CTR)

#### CASE 4

A 12 year old adolescent girl presented with cough of four months. She had history of upper respiratory Infection (URTI) symptoms initially which subsided later with the cough persisting. Cough was reported as productive, paroxysmal with post-tusive vomiting, whooping sound but no fever. No similar illness at school or home and child is vaccinated according to the expanded program of immunization (EPI). Given different drugs in-

cluding Azithromycin for pertussis, different OTC cough syrups, antihistamines and augmentin for one week. No weight loss, no self or family history of allergy. No wheeze or episodic symptoms and no night worsening but mild exercise limitation.

Examination was normal and laboratory tests with complete blood count (CBC) and acute phase reactants are normal. CXR is remarkable only for peri-bronchial thickening (Image 2).



Figure 2. CXR of a 12 year old girl with PBB with peri-bronchovascular thickening

Child was then started on Amoxicillin-Clavulanate for two weeks after which cough improved significantly and continuation of antibiotics for a total of four weeks leads to complete resolution with no recurrence.

### Discussion

#### Epidemiology

PBB is an old disease though not recognized as a diagnostic entity (7,9). Some astute clinicians had recognized this entity many years back, though they were not able to bring it in wide attention of clinicians and researchers (9,10). It was first described in 2006 by the Australian group for the first time as a diagnostic entity (11,12). PBB is now recognized as a separate entity and accounted for a significant (up to 40%) of pediatric chronic coughs in specialized centers. It is commonly seen in under-five children though it can occur as late as more than 12

years children (11,16, 18-20). Males are documented to be more affected than females in some studies (8,20). However, the burden and etiologies of PBB are not well documented in low resource settings (20).

#### Definition and diagnosis

PBB is a bacterial endobronchial infectious process associated with neutrophilic inflammation and risk of chronic suppurative lung disease (CSLD) and bronchiectasis (BE) at least in some group of children if not detected and treated (13-16). The commonest bacteria responsible for PBB are *Hemophilus influenzae* (47–81 %%), *Streptococcus pneumoniae* (24–39 %%), *Moraxella catarrhalis* (19–43%), and sometimes mixed with aerobic and anaerobic bacterial isolates (11,16).

The diagnosis of PBB can be made based on clinical or microbiologic criteria (Table1) (15,16). The microbiologic diagnosis require bronchoscopic collection of lower airway

samples and is invasive that it is done only in atypical cases or repeated cases of PBB. The ERS guideline criteria for PBB diagnosis (Table 2) is a simplified clinical criteria

based on 3 validated components and is easily applicable in low resource settings like ours (15,16).

Table 1. Diagnostic Criteria for Protracted Bacterial Bronchitis (16)

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1. Original microbiologic-based case definition (also termed PBB-micro)
    - i. Presence of chronic wet cough (>4 weeks)
    - ii. Lower airway infection (recognized respiratory bacterial pathogens growing in sputum or at BAL at density of a single bacterial species  $10^4$  colony-forming units/ml)
    - iii. Cough resolved following a 2-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate)
  2. Modified clinical-based case definition (also termed PBB-clinical)
    - i. Presence of chronic wet cough (>4 weeks)
    - ii. Absence of symptoms or signs of other causes of wet or productive cough
    - iii. Cough resolved following a 2-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate)
  3. PBB-extended : PBB-clinical or PBB-micro, but cough resolves only after 4 weeks of antibiotics
- Recurrent PBB: recurrent episodes (>3 per year) of PBB
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The diagnosis of PBB is thus provisional at least initially when the first 2 criteria are (Table 2) met and to be confirmed after treatment trial succeed in cough resolution. This approach is reasonable in those children as other serious causes of chronic cough are

relatively rare in these groups of children and avoids performance of expensive, invasive investigations or unnecessary treatment including prolonged steroids for presumed asthma only to understand finally that it was not asthma!(12,15,17).

Table 2 . European Respiratory Society modified clinical diagnostic Criteria for Protracted Bacterial Bronchitis (15)

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- 1) Presence of continuous chronic (>4 weeks' duration) wet or productive cough
  - 2) Absence of symptoms or signs (i.e. Specific cough pointers\*) suggestive of other causes of wet or productive cough
  - 3) cough resolved following a 2–4-week course of an appropriate oral antibiotic
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\* **Specific cough pointers** Symptoms: chest pain, history suggestive of inhaled foreign body, dyspnea, exertional dyspnea, hemoptysis, failure to thrive, feeding difficulties (including choking/vomiting), cardiac or neurodevelopmental abnormalities, recurrent Sino pulmonary infections, immunodeficiency or epidemiological risk factors for exposure to tuberculosis Signs: respiratory distress, digital clubbing, chest wall deformity or auscultatory crackles; Tests: chest radiographic changes (other than perihilar changes) or lung function abnormalities.

**Pathophysiology**

Although upper respiratory infections may precede onset of chronic cough and some studies identify viruses from PBB patients, current evidences don't suggest significant role of Viruses in PBB pathobiology (6, 8,15,16,20). PBB is characterized by neutrophilic endobronchial persistent inflammation caused by bacterial infections and defective mucociliary clearance (6,8,16,21). No systemic or local immune deficiencies are documented except for a reduced alveolar phagocytosis (6,16). Flexible bronchoscopy reveals presence of airway malacia in most patients although the causative relationship is not yet clearly outlined (8,11,16,21).

**Treatment**

The treatment of choice for PBB is amoxicillin-clavulanate as it covers all the commonly responsible organisms. The 1st and 2nd generation cephalosporins are the other options of PBB treatment. Macrolides are the alternatives for penicillin and cephalosporin allergy patients but with limited evidence on the effectiveness of these drugs (12, 15, 17,19). The duration of management should base on the response of the child but generally ranges from a minimum of 2 weeks to up to 6 weeks of continuous treatment (15-17, 19-22). A child with no improvement by a 4 weeks course of antibiotics should be considered for further workup while a 6 weeks course could be considered if significant improvement is documented (6,15,16).

It is important to strictly adhere to the initial two ERS criteria not to delay an early diagnosis of other serious conditions including foreign body aspiration and tuberculosis before a therapeutic decision is made in these children especially in our setting. It is also important to remember that many conditions can have bacterial super infection and some improvement may be seen but only complete resolution should make the criteria met for PBB before ruling for PBB as a final diagnosis and closing the case. Children with Suspected PBB but no response to treatment or showed inadequate response despite adequate dose and duration of antibiotics should be referred to appropriate centers for further work up including lung function, allergy, high-resolution computed tomography (HRCT) and bronchoscopy. Parents should also be counseled about the development of chronic cough in their children following a visit to acute respiratory infection, as an underlying respiratory condition is not uncommon (23).

Our case series has limitations that all cases were diagnosed and treated empirically short of microbiologic studies and we didn't perform spirometry although it is not mandatory in all patients with PBB. The diagnosis of these few cases in our centers may also reflect that we may be missing children with this problem in the primary settings. However, we like to note that regular follow up with a systematic diagnostic and

therapeutic approach will allow the diagnosis and treatment of those children with chronic cough early in the course of their disease with a reasonable cost on the child and families.

### Prognosis

PBB is associated with good prognosis with proper diagnosis and optimal treatment. (15,16). PBB can recur after treatment and may require repeated doses of antibiotics. Frequency of recurrence and H. influenzae isolation has been associated with increased risk of progression to chronic suppurative lung disease (CSLD), and bronchiectasi (BE) (15-17,19). Treatment for at least 4 weeks may decrease the risk of recurrence as shown from a recent clinical trial(22).

### Conclusion

Protracted Bacterial Bronchitis should be considered in all children with chronic wet cough in the absence of cough pointers but only to be confirmed after a therapeutic trial lead to complete resolution of the cough. However, children with chronic cough and cough pointers or abnormal physical exam, Lab or Imaging should be approached differently and are not candidates for therapeutic trial with antibiotics, unless superinfection is present, and should get a diagnosis as early as possible without waiting for a response for prolonged antibiotic.

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