A young child with persistent respiratory symptoms: Think beyond asthma

Respiratory diseases have a limited number of clinical manifestations with the most common being cough, cold, and breathlessness. Asthma is one of the leading causes of morbidity in children with varied prevalence in different parts of the world. Asthma commonly presents with recurrent cough, cold, and wheezing with seasonal variation and is commonly associated with other allergic diathesis in the form of rhinitis or eczema/dermatitis. The diagnosis of asthma is often clinical and is based on history and examination. Most children with asthma show a clinical response to treatment.

Children with atypical features may need pulmonary function testing (“spirometry”) to document reversible airflow obstruction. These atypical clinical features include neonatal onset, multi-site infections, failure to thrive, recurrent vomiting, clubbing, and persistent localized pulmonary signs. A careful review of history, physical examination, and course of illness in children diagnosed with asthma who have not shown an expected improvement to standard treatment should alert the treating physician about the possibility of an alternative diagnosis.

Chronic Respiratory Symptoms in Preschool Age Children: A Diagnostic Challenge

In the current issue of the journal a clinical grand round of an interesting case has been described. This 30-month-old boy had presented with worsening respiratory symptoms, failure to thrive, progressive hypoxemia, clubbing, hepatosplenomegaly, and progressively worsening abnormal chest radiographs was finally diagnosed as having Niemann–Pick disease Type C. This child had been treated for asthma with standard inhaled and oral medications without much relief in his symptoms. Detailed analysis of his clinical features and course of illness suggested that there was sufficient evidence to suspect an alternative diagnosis. Occasional wheezing is a very common problem in young children aged below 5 years of age and is estimated to occur in almost 50% of children by the age of 6 years. Its prevalence significantly decreases during the school-going age. While wheezing is considered to be synonymous with asthma in adults and older children, the same in preschool children may be due to multiple reasons. Early-onset wheezing in preschool children can be classified into two groups: (i) episodic wheezing due to a viral respiratory tract infection, and (ii) recurrent wheezing due to multiple reasons including asthma. Response to treatment with bronchodilators and inhaled steroids in preschool children with wheezing is variable. The course of illness is usually of a waxing and waning pattern rather than of progressive worsening. Therefore, persistent and progressive worsening of wheezing warrants consideration of an alternative diagnosis.

How to Distinguishing Asthma from Other Respiratory Disorders, Particularly Interstitial Lung Disease?

Reversible airway obstruction with underlying mucosal inflammation is inherent features of asthma. Diagnosis of asthma is considered when the symptoms are recurrent, seasonal, nocturnal, and aggravated by exercise or activity and when the symptoms are relieved by bronchodilators with/without anti-inflammatory medications. If a child diagnosed with asthma develops any of the following features during illness, the treating physician should review the diagnosis. These features include: (i) persistent symptoms which do not respond to bronchodilators, (ii) inspiratory or biphasic wheeze, (iii) hypoxia (as measured by pulse oximetry), (iv) clubbing and/or (v) failure to thrive.

In the index case, clinical features which gave clues for an alternative diagnosis included: (i) early age of onset of symptoms, (ii) lack of adequate response to standard asthma treatment, (iii) development of progressive respiratory difficulty, (iv) clubbing, (v) failure to thrive, (vi) presence of hepatosplenomegaly, and (vii) serial chest radiographs showing persistent lung field abnormalities.

What Should Be the Approach in Managing a Young Child with Recurrent or Persistent Respiratory Illness?

The common differential diagnoses in a young child having recurrent respiratory symptoms in spite of receiving standard treatment for asthma include: (i) conditions having problems of airway clearance like cystic fibrosis or primary ciliary dyskinesia, (ii) repeated aspirations or (iii) recurrent infections. A child having cystic fibrosis may present with a recurrent or a persistent cough and respiratory difficulty with...
The common differential diagnoses in a young child having persistent respiratory symptoms (with intermittent exacerbations) include: (i) congenital malformations (e.g., H-shaped trachea-esophageal fistula), (ii) dynamic airway obstructions like laryngotracheobronchomalacia or (iii) chronic infections including viral or tubercular. Children with dynamic airway obstruction are commonly confused as having asthma. However, in these instances, there is no response to bronchodilators. Young children with extrathoracic airway diseases resulting in an obstruction (e.g., postnasal drip, pharyngitis, sinusitis, and laryngitis) may have only inspiratory sounds and that can be easily identified by careful auscultation. However, young children with intrathoracic airway obstruction (e.g., chronic foreign body, mediastinal mass, vascular arch anomaly, and laryngotracheobronchomalacia) may present with wheezing. Wheezing may be biphasic if major airways (trachea and main bronchi) are involved or may be expiratory when peripheral airways are involved. Persistent symptoms with repeated exacerbations and no response to bronchodilators differentiate these conditions from asthma.

Although interstitial lung diseases (ILD) include about 300 illnesses with diverse etiologies, data from India are limited. A recent case series of ninety children diagnosed as having ILD over a 12-year period in our pediatric chest services unit has highlighted the rarity of this condition.

Common underlying diagnoses in these ninety patients were langerhans cell histiocytosis, pulmonary hemosiderosis, and hypersensitivity pneumonitis. None of the ninety patients with ILD had a diagnosis of a storage disease (as in the index case). However, we do come across children having ILD (albeit rarely) with an underlying storage disease such as Gaucher’s disease, Niemann-Pick disease, or GM1 gangliosidosis. Since these patients have significant extrapulmonary manifestations, they are not enrolled in our pediatric chest services.

Persistent or recurrent respiratory symptoms for long periods with extrapulmonary manifestations like hepatosplenomegaly may be the result of rare diseases such as storage disease or immune deficiency disease (due to abscesses as in chronic granulomatous disease).

**Conclusion**

We reiterate that because of a very high burden of wheezing disorders in young children, a diagnosis of asthma is commonly done and its treatment started empirically. In most of these further specialized investigations are not warranted. However, a physician should be ready to review the diagnosis of asthma if the symptoms persist and do not show a response to bronchodilators. It is important to remember that, although rare, the proportion of children with an alternative diagnosis is relatively more common in this young preschool age group of patients. Both over- and under-diagnosis of wheezing disorders and depriving afflicted children of appropriate treatment is unfortunately not uncommon.

With clues from history, examination, and course of illness, appropriate investigations should be planned to make a correct diagnosis. A chest radiograph is the first diagnostic test. In asthma, it may be normal or show some hyperinflation. Further characterization of abnormalities on chest radiograph (infiltrates, soft tissue shadow) should be achieved by performing a computerized tomography scan of the chest. Other diagnostic workup including bronchoscopy for airway abnormalities and obtaining bronchoalveolar lavage, specialized investigations for immune deficiencies and primary ciliary dyskinesia, and sweat chloride testing for cystic fibrosis can be planned according to the clues obtained from history and examination.

Since the availability of specialized diagnostic tests and specialists is limited in India, it is advisable to seek the help of pulmonologists if a child with chronic respiratory illnesses is not responding to treatment on expected lines.

**References**

1. Pearce N, Alt-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, et al. Worldwide trends in the prevalence of asthma symptoms: Phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax 2007;62:758-66.
2. Baij S, Muranjan M, Karande S, Prabhat D. Rare disease heralded by pulmonary manifestations: Avoiding pitfalls of an “asthma” label. J Postgrad Med 2017;63:122-7.
3. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. N Engl J Med 1995;332:133-8.
4. Brand PL, Baraldi E, Bisgaard H, Boner AL, Castro-Rodriguez JA, Custovic A, et al. Definition, assessment and treatment of wheezing disorders in preschool children: An evidence-based approach. Eur Respir J 2008;32:1096-110.
5. Lodha R, Puranik M, Natchu UC, Kabra SK. Recurrent pneumonia in children: Clinical profile and underlying causes. Acta Paediatr 2002;91:1170-3.
6. Sankar J, Pillai MS, Sankar MJ, Lodha R, Kabra SK. Clinical profile of interstitial lung disease in Indian children. Indian Pediatr 2013;50:127-33.
7. Chen Q, Chu H, Tao Y, Huang H, Peng L. Lessons learned from 35 cases of laryngeal foreign bodies undergoing misdiagnosis in pediatric population. Ann Otol Rhinol Laryngol 2017;126:146-151.
8. Levitas A, Krymko H, Ioffe V, Zalzstein E, Broides A. Anomalous left coronary artery from the pulmonary artery in infants and toddlers misdiagnosed as myocarditis. Pediatr Emerg Care 2016;32:232-4.
9. Park DB, Dobson JV, Losek JD. All that wheezes is not asthma: Cognitive bias in pediatric emergency medical decision making.
10. Østergaard MS, Nantanda R, Tumwine JK, Aabenhus R. Childhood asthma in low income countries: An invisible killer? Prim Care Respir J 2012;21:214-9.
11. Kurokawa La Scala CS, La Scala CR, Wandalsen GF, Malozzi MC, Naspitz CK, Solé D. Childhood tuberculosis diagnosed and managed as asthma: Case report. Allergol Immunopathol (Madr) 2006;34:276-9.
12. Lodha R, Kabra SK. Recurrent/persistent pneumonia. Indian Pediatr 2000;37:1085-92.