

Wheezing in Childhood- not Always Asthma -Review

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Abstract

Wheezing in infancy and childhood is a common condition; however it is not a single disorder and can be due to causes other than asthma. Wheezing is a musical, expiratory sound due to narrowing and hyper responsiveness of the intra-thoracic and extra thoracic airways. Not all wheezing is asthma. Wheezing-associated respiratory illnesses in children are often described as asthma; however while most children with asthma show symptoms of wheezing. Wheezing, coughing and breathlessness are common in young children, and can all be symptoms of conditions other than asthma. Bronchiolitis refers to a first episode of wheezing, with respiratory distress triggered by a viral infection. Episodic wheezing refers to discrete episodes of wheezing without intermittent symptoms. Unremitting wheezing refers to distinct episodes of wheezing with intermittent symptoms, such as coughing or wheezing at night or in response to exercise, crying, laughter, mist, or cold air. Environmental conditions that increase the rate of bacterial and viral infections are risk factors for transient wheezing, but its relationship to asthma remains unclear. Children with frequent simple colds and other common childhood infections in infancy are less likely to develop persistent wheezing in later childhood. Many preschool children with viral induced wheezing will outgrow these symptoms, and do not have asthma. Generally, asthma is identified by the presence of cough, wheeze and breathing difficulty, together with features of atopy (or a family history of atopy or asthma) and impaired lung function evidenced by spirometry. It is important to explain to parents/carers that wheezing in an infant or preschooler does not mean the child will have asthma or allergies by primary school age. In preschool-aged children with recurrent wheeze (e.g. four or more episodes per year), consider using the Asthma Predictive Index, to estimate whether children are likely to have asthma during primary school years. Asthma Prediction Index has some major criteria and minor criteria. Major criteria are diagnosis of asthma in one or both parent, Diagnosis of atopic dermatitis during the first 3 yr. of life, Sensitization against >1 allergen, Minor criteria- Milk, egg, or peanut sensitization. Associated with respiratory infections, Eosinophilia >4%. In the first 3 years of life if anyone who have 1 major criteria or 2 minor criteria is present in one episode, the possibility of asthma in 6-13 years is 59% but 2 episodes possibility is 77%. Investigation -Chest X-Ray, spirometry, CT scan of Chest and Fiberoptic Bronchoscope. It is usually not necessary if history of "classic" asthma or patient response to salbutamol and or steroid; then only spirometry should be done. But need other investigation when Chronic cough (>1 month), recurrent pneumonia, persistent signs or symptoms are seen despite therapy. Bronchomalacia, esophageal dilatation, foreign body aspiration, vocal cord dysfunction, viral pneumonia allergic rhinitis, bronchiectasis, cystic fibrosis, heart failure, acute chest syndrome of sickle cell anemia, use of beta blockers, etc. All these conditions described can present with wheezing and certainly do not characterize asthma. Here we reported six case series having wheeze but ultimate diagnosis was not asthma.

Keywords: Wheezing; Asthma; Fiberoptic Bronchoscope; CT Chest

Introduction

Wheezing is a musical, expiratory sound due to narrowing and hyper responsiveness of the intra-thoracic also extra thoracic airways. Wheezing is a sign of asthma in children, but it does not always mean that a child has asthma. Children younger than 5 often develop wheezing during a respiratory infection. Children with a family history of allergies seem to be more likely asthma than other children to have one or more episodes of wheezing with colds. Children with certain viral infections, such as respiratory, rhinovirus (which causes the common cold), and influenza virus, also are likely to develop wheezing. Bronchiolitis refers to a first episode

of wheezing, with respiratory distress triggered by a viral infection. Episodic wheezing refers to discrete episodes of wheezing without intermittent symptoms. Unremitting wheezing or multiple-trigger wheezing refers to distinct episodes of wheezing with intermittent symptoms, such as coughing or wheezing at night or in response to exercise, crying, laughter, mist, or cold air. The distinction between Episodic viral wheeze (EVW) and multiple trigger wheeze (MTW) is not clear in all patients, some children retain a consistent pattern of EVW or MTW, but symptom patterns change over time in many patients and their airway pathology remains unclear [1].

Transient wheezers are commonest form of wheeze, decrease lung function at birth, no airway hyper responsiveness, non-atopic, no

immunoresponse to virus, resolves by 3 years. Persistent non-atopic wheezers are lung function abnormal at birth, reduced in later life. Non atopic, airway hyper-responsiveness, peak flow variability, RSV induced wheeze due to alteration in airway tone. Better outcome than persistent atopic wheezers. Persistent atopic wheezers are lung function normal at birth but deteriorate with recurrent symptom, increased symptoms with increasing age, airway liability, atopic, abnormal immune responses to viruses [1-3].

Generally, asthma is identified by the presence of cough, wheeze and breathing difficulty, together with features of atopy (or a family history of atopy or asthma) and impaired lung function evidenced by spirometer. It is important to explain to parents/carers that wheezing in an infant or preschooler does not mean the child will have asthma or allergies by primary school age. In preschool-aged children with recurrent wheeze (e.g. four or more episodes per year), consider using the Asthma Predictive Index, to estimate whether children are likely to have asthma during primary school years [4, 5].

Asthma Prediction Index has some major criteria and minor criteria. Major criteria are Diagnosis of asthma in one or both parent, Diagnosis of atopic dermatitis during the first 3 yr of life, Sensitization against >1 allergen, Minor criteria- Milk, egg, or peanut sensitization. Wheezing not associated with respiratory infections. Eosinophilia (> 4%. In the first 3 years of life if anyone who have 1 major criteria or 2 minor criteria is present in one episode, the possibility of asthma in 6-13 years is 59% but 2 episodes possibility is 77% [4, 5].

API is a validated clinical model for childhood asthma defined on a cohort of children who wheeze at least one time during the first 3 years of life. The primary criteria to identify the score are ≥ 4 episodes of wheezing in 1 year and the secondary are clinician diagnose of parental eczema or asthma, allergic sensitization to aeroallergen, wheezing unrelated to cold, eosinophilia ≥ 4 percent. A positive index was defined as at least major criterion plus at least one major or two minor criteria.

API sensitivity is low, suggesting that the test is poor for predicting later asthma development. Nevertheless API has a high negative predictive value, meaning that it can identify children who have a low probability to develop asthma with a negative test [5].

A modified version (mAPI) was tested in a cohort of high risk children with a family history of allergy and/or asthma. A positive mAPI increased the probability to identify patient at risk to develop future asthma. In past 12 months, 4 wheezing episodes (>24h), with at least 1 physician-confirmed, plus major criteria are

1. Parental history of asthma
2. Atopic dermatitis.
3. Sensitization to > 1 aeroallergen.

Plus minor criteria are

1. Allergic sensitization to milk, egg or peanut.
2. Wheezing apart from colds.
3. Eosinophilia.>5% [4-6].

Differential diagnosis of Wheezing in Infants and Young Children

1. Viral wheezing
2. Asthma
3. Chronic aspiration (Gastro esophageal reflux diseases, GERD or vocal cord or swallowing dysfunction, silent aspiration may

also be the cause of persistent wheezing in many infants and young children who do not respond to bronchodilator and steroid treatments. Infections pertuses, mycoplasma, Chlamydia, TB)

4. Infection (pertuses, mycoplasma, Chlamydia, TB) .
5. Broncho pulmonary dysplasia, BPD
6. Foreign body
7. Anaphylaxis
8. Cystic fibrosis (CF)
9. Vascular tracheal compression
10. Tracheobronchial malformations
11. Mediastinal masses
12. Bronchiolitis obliterans
13. Immune deficiency
14. Primary ciliary dyskinesia
15. Heart failure [1, 6-8].

Viral Respiratory Infections

The two most common respiratory viruses that affect the pediatric population are rhinovirus and respiratory syncytial virus (RSV) [9]. Patients with rhinovirus present with nasal congestion, sneezing, nose and eye pruritus (itching), cough, dyspnea, wheezing and tightening or pain in the chest.

Patients with RSV present with a cough, nasal congestion, sore throat, fever, listlessness, poor sleeping, poor feeding and possibly brief periods of apnea. It has been recognized through clinical observation that children who suffer from RSV and acquire bronchiolitis early in life are at increased risk for the development of childhood asthma [10].

Infants who suffer from viral respiratory infections and atopic sensitization (a predisposition toward developing an IgE- mediated reaction or hypersensitivity) are at increased risk for the development of childhood asthma and to suffer from asthma into adulthood [7].

Bronchiolitis

Bronchiolitis is a common lung infection in young children and infants. Bronchiolitis, with an underlying diagnosis of RSV, was the number one cause of infant hospitalization in the United States from 1997-2000 [11]. An estimated 96,000 infants were hospitalized nationwide during that three year period. Patients with bronchiolitis may present with fever, difficulty feeding, wheezing, tachycardia, tachypnea, accessory muscle use, nasal flaring, intercostal retractions, peripheral cyanosis and developing hypoxia.

Bronchiolitis exacerbation is more common in the winter months and commonly affects children with exposure to people with symptomatic respiratory infections. Pertinent medical history findings such as premature birth, congenital heart disease, immune deficiency, hypoxia and chronic lung disease are conditions that can complicate the course of bronchiolitis [12].

Shortness of Breath Acronyms: NEHI and ChILD

Neuroendocrine cell hyperplasia of infancy (NEHI) is a form of childhood interstitial lung disease. Patients with NEHI present with rapid and labored breathing, hypoxia, crackles, and wheezing. NEHI may initially be mistakenly diagnosed as asthma or prolonged respiratory infections.

Children's interstitial and diffuse lung diseases (chILD) are a category of rare pediatric lung diseases characterized by tachypnea,

hypoxia, and crackles that present without a diagnosed underlying disease process [13, 14].

Pneumonia (Viral and Mycoplasma)

Pneumonia is lung inflammation caused by a bacterial or viral infection. Viral and mycoplasma pneumonia in children present with a high fever, intractable cough, sweating, chills, flushed skin, peripheral cyanosis, wheezing or grunting, dyspnea, tachypnea, intercostal retractions and nasal flaring.

It is important to note physical assessment findings in the pediatric patient who may be dehydrated, including dry mucous membranes, sunken fontanels and decreased urine output.

Cystic Fibrosis

Cystic fibrosis is a genetic disorder that produces excess, thick mucus that affects the lungs presenting with wheezing, pancreas and digestive system. Infants are screened for cystic fibrosis with genetic testing and blood tests that determine whether the infant’s pancreas is working. If cystic fibrosis is not diagnosed with testing in infancy, it is recognized and tested for if a child has had repeated lung infections or severe growth problems [15]. Patients with cystic fibrosis present with persistent cough, wheezing, dyspnea, and inflamed nasal passages.

Vocal Cord Dysfunction

Vocal cord dysfunction refers to the abnormal motion of the vocal cords during inspiration. Normally, the vocal cords open widely during inspiration; however, in vocal cord dysfunction, they narrow. The result is an obstruction at the level of the vocal cords. Athletes describe wheezing that occurs very early in exercise, wheezing during high anxiety situations, a sense of smothering, rapid resolution of the wheeze after exercise, and a lack of symptoms when calm.

Few findings are evident during a physical exam; however, if the wheeze is present, it should be heard best over the throat. If this diagnosis is suspected, direct visualization of the vocal cords may be necessary. This is done during forceful breathing with a flexible scope inserted through the nose. A diagnosis is made when the vocal cords close during inspiration. Specialized therapists can teach the athlete to breathe correctly. This diagnosis can be confused with exercise-induced bronchospasm (asthma), because athletes sometimes respond to the inhaled medications used for asthma.

Bronchoscopy with airway survey that identifies an anatomical cause of Wheezing confers several potential benefits. Finding tracheomalacia, bronchomalacia, or tracheobronchomalacia usually leads to conservative management, which has a high success rate and other benefits including relief from the burden, cost, and potential harms of further diagnostic testing for infants with persistent wheezing despite treatment with bronchodilators, inhaled corticosteroids, or systemic corticosteroids, we suggest airway survey via flexible fiber optic bronchoscopy. Finding vascular rings, vascular slings, and airway compression by a vascular structure leads to surgical therapy with an 88-100% success rate. Now let us discuss some case reports with wheezing problems but ultimately diagnosis was not asthma.

Case No 1: A 4 years old girl presented with cough and recurrent wheezing. Her Chest CT scan showed

Increase in transparency of the medial and lateral (Right middle

Lobe) RML segments. The RML bronchus seems to be reduced in caliber due to right principal bronchomalacia, shown in Figure 1 and air trapping occur in the distal segment [1].

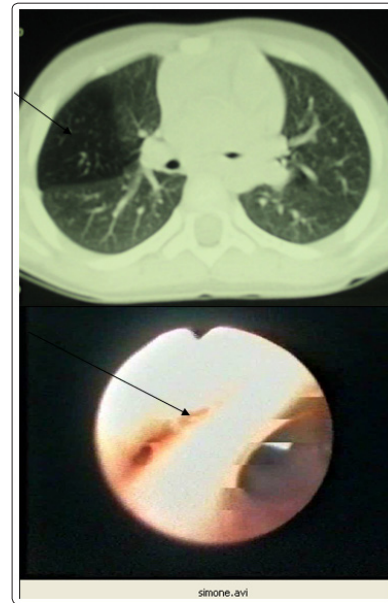


Figure 1: Fiber-optic Bronchoscope showed RML bronchomalacia

Case No 2: A 12 year old boy presented with recurrent episodic of “inspiratory wheezing”. Methacholine test was negative but His fiberoptic bronchoscope showed VOCAL CORD DYSFUNCTION, shown in Figure 2 is an abnormal adduction of the vocal cords during inspiration (less commonly during expiration) that produces airflow obstruction at the level of the larynx Wheezing in Vocal cord dysfunction, the exact cause of this condition is not clearly defined and may be multi-factorial but the underlying pathophysiology involves a hyper functional and inappropriate laryngeal closure reflex triggered by exertions, psychological factors and irritants , laryngopharyngeal reflux, rhinitis, sinusitis, recurrent upper airway viral infections, environmental allergens and/or pollutants and occupational irritant fumes [1, 16].

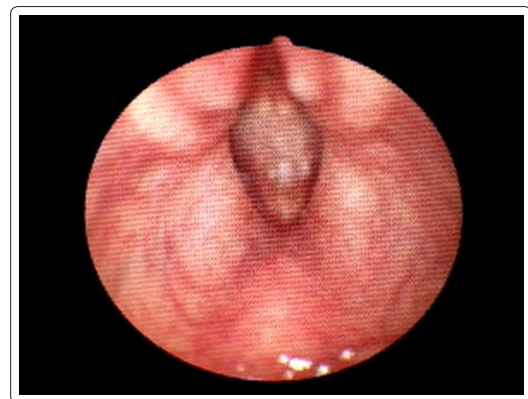


Figure 2: Showing adduction of vocal cord during expiration

Case No 3: A 13 year old girl presented with Nocturnal cough and wheezing , Her Fiberoptic bronchoscope showed Flattening of posterior wall ultimately lead to narrowing of the airpassages and esophageal endoscope showed dilation, shown in Figure 3. Spirometry was normal.

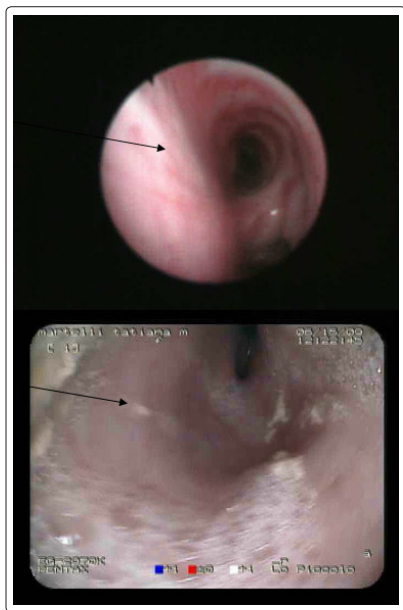


Figure 3: Esophageal dilatation

Case No 4: An 11 year 10 months old girl had a history of recurrent wheezing and respiratory infections. Spirometry was normal but Fiber-optic bronchoscope showed Bronchmalacia, and wheezing due to narrowing of airway [1, 17].

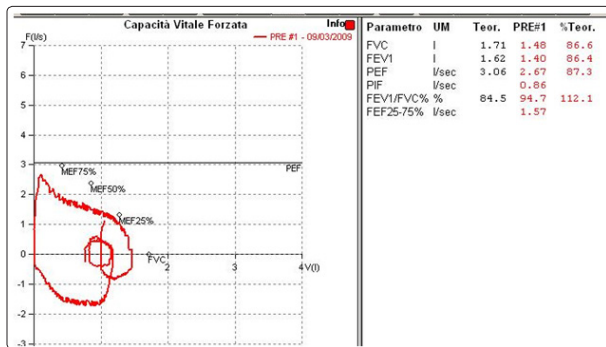


Figure 4A: Showed normal spirometry



Figure 4B: showed narrowed Bronchus in Fiberoptic Bronchoscope

Case No 5: A 13 year old girl presented with recurrent Wheezing and shortness of breath during exercise. Her CT Angiogram showed Right aortic arch + aberrant left subclavia artery with Kommerel diverticulum. But Fiber-optic Bronchoscope showed normal finding

and Spirometry was also normal.

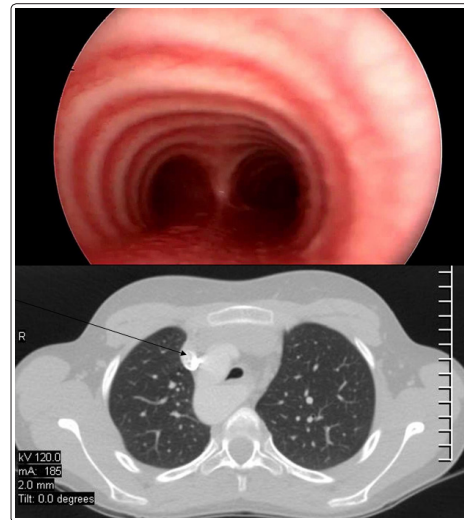


Figure 5: Showed CT and Bronchoscopic finding of Right Aortic Arch+aberrant left subclavian artery with Kommerel

Case No - 6. A 2 year old boy having history of recurrent wheezing and persistent pneumonia. His

- Chest X Ray showed
(Right lower Lobe) RLL opacity, partially due to sub-atelectasis. Patency of the correspondent segmental bronchi.
- Chest XRay
RLL opacity, partially due to sub-atelectasis. Patency of the correspondent segmental bronchi.

And Chest CTscan showed
RLL area of segmental atelectasis with granular para-atelectasis density and was diagnosed Foreignbody Inhalation.

Figure 6 & 7: Showing increased attenuated area due to foreign body infection

Discussion

Wheezing is a common finding in patients with bronchospasm and airway obstruction. There is no doubt that one of the most common causes of wheezing complaints, or of auscultation of wheezing on physical examination, is due to bronchial asthma. Nevertheless, numerous other diseases can present with this sign. Examples of these conditions include tracheal stenosis, bronchomalacia, esophageal dilation, vocal cord dysfunction, vascular anomalies, central airway tumors, pulmonary edema, and pulmonary aspiration may lead to narrowing as well as hyper responsive airways [17-20]. In our case series review the same finding leading to wheeze.

This is certainly the type of knowledge that is expected to be a required component of the basic education of all physicians, even of no specialists in respiratory medicine. However, to surprise, in recent years, it has been found that many clinical cases referred to our facility or private health care clinic for evaluation with a diagnosis of “severe asthma” or “difficult-to-control asthma” that are in fact cases involving completely different diseases, as I have

been seen in this case series. Many of these patients report for the appointment after long periods of investigation and unsuccessful treatments. Atopy testing and allergy desensitization therapy are common. Long-term use of high doses of systemic corticosteroids is the rule. The presence of severe side effects related to the last treatment is a constant, and these side effects contribute substantially to the deterioration of the patient's overall clinical status.

Asthma is a highly prevalent disease, and chronic recurrent episodes of dry cough, dyspnea, chest tightness, and wheezing are important for characterizing the disease [19]. It should be borne in mind that not always all of these findings are present, which can make it difficult to diagnose asthma. On physical examination, wheezing is in fact the most common finding. Bronchial hyper responsiveness is a characteristic of individuals with asthma, although it is not always present, depending on the treatment given or the type of definition employed [19]. However, bronchial hyper responsiveness can also be found in many other conditions, such as allergic rhinitis, COPD, right after respiratory infections, bronchiectasis, cystic fibrosis, heart failure, acute chest syndrome of sickle cell anemia, use of beta blockers, etc [20-22]. All these conditions described can present with wheezing and certainly do not characterize asthma.

The approach to patients complaining of wheezing, presenting with physical examination findings of wheezing, or both, requires careful clinical history taking, with an emphasis on triggers, improvement factors, duration of wheezing, and course of wheezing over time. It is essential that, in addition to upper airway symptoms and digestive and cardiac symptoms, all types of respiratory symptoms present be properly assessed. The personal histories should be carefully investigated, especially regarding history of diseases, smoking, and occurrence of environmental exposure. Physical examination must be complete and cannot be limited only to pulmonary auscultation. Routine chest X-rays and spirometry, Fiber optic Bronchoscope and CT Chest or angiogram should be done when non-response to salbutamol or steroid. Ideally with printing of the flow-volume curve and evaluation of bronchodilator response, are usually the most useful ancillary tests in this assessment.

Conclusion

Children with wheezing, not a single disorder like asthma and need extensive evaluation to reach a proper diagnosis.

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