Coughing and Kids: When It’s Not Just Asthma

Satellite Conference and Live Webcast
Thursday, May 16, 2013
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Video Communications and Distance Learning Division

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Presentation Overview
• Case Presentation and Parent Interview
  – 20 minutes
• Functional and Pathophysiologic Cough
• Airway Clearance – Innate Defense

Presentation Overview
• Diagnostic Evaluation of Cough
  – 40 minutes
  – Break (15 minutes)
• Case Reviews
  – 25 minutes
• Questions
  – 5 minutes

Disclosures
• Dr. Hoover
  – No personal disclosures
  – Cystic Fibrosis Research Funding
    • Cystic Fibrosis Foundation
    • Gilead Pharmaceuticals
  – Will indicate non-FDA approved treatment strategies (**)

5/13/2013
Disclosures
• Ms. Bradford has no disclosures

Objectives
• Explore the parental experience of dealing with chronic cough and undiagnosed illness
• Identify the functional nature of coughing
• Associate the relationship of coughing to pathologic states in the respiratory tract

Objectives
• Identify differential diagnoses associated with chronic coughing that may indicate diagnoses other than asthma

Chronic Cough: A Parent’s Perspective

Jacob’s Medical Journey
• Concern
• Frustration
• Disappointment
• Hope
• Resolution
• Maintenance

Jacob’s Cough
• Began at age two
• Rarely productive but occasionally produces green sputum
Jacob’s Cough

- Multiple visits with few answers and little improvement
  - Recurrent use of antibiotics, cough and cold medicines, allergy medicines, inhalers
  - Nothing seemed to work

Frustration

“I knew something was wrong with him but did not know where to turn.”

Disappointment

“I figured that a doctor, if there was something really wrong, would find it and fix it.”

Chronic Fever and Cough

- Jacob, age 12, experienced fevers over 9 months up to 103°F associated with cough
- Ultimately he was evaluated by a new physician and referred to infectious disease specialist following a CT scan demonstrating bronchectasis

Hope

“This was the first time I thought that a doctor actually cared about my child.”

Chronic Fever and Cough

- Subsequent referral to pulmonary for evaluation of chronic cough
  March 2012
Jacob’s Cough and Bronchiectasis

- Jacob’s differential diagnosis
  - Asthma
  - Cystic Fibrosis
  - Immune Deficiency
  - Primary Ciliary Dyskinesia
  - Hypersensitivity Pneumonitis
  - Aspiration of foreign body

Evaluation

- History and PE
  - Chronic wet productive cough
- PFTs confirm asthma
- CT sinuses: Pan Sinusitis
- Immune w/u negative
- Sweat CL: negative

Evaluation

- IgE elevated 531 and Rast c/w Environmental Allergies (ABPA neg)
- Admitted with pneumonia May 2012
  - Bronchoscopy: Purulent Bronchitis

Bronchoscopy

- Alveolar Lavage
  - G+ Cocci
  - 12,815 WBC/uL
  - 440 RBC/uL
  - 93% PMNs
  - 500,000 CFU
  - Strep Pneumonia

Ciliary Dyskinesia

- Electron Microscopy Revealed Normal Ultrastructure
- PCD Gene Sequence Identified Heterozygous Mutation in DNAH11

Ciliary Dyskinesia

Diagnosis of PCD

- Difficult diagnosis with emerging tools
  - Gold standard: nasal brushing and EM
  - Demonstrating ultrastructural abnormality has a high specificity for disease
  - Normal structure does NOT rule out our PCD

- Genetics
  - Ready for prime time?
  - Much debate
- Nasal NO
  - Good NPV / limited availability

Diagnosis of PCD

- Ciliary motility study
  - Difficult / affected by virus
- See references for further reading

Treatment for PCD and Asthma

- Daily chest physiotherapy
- Mometosone / Fomoterol 100/5mcg 2 puffs BID with spacer
- Montelukast 5mg QHS
- Albuterol HFA 2-4 puffs prn with spacer

Treatment for PCD and Asthma

- Azithromycin 250mg Mon., Wed., and Fri.**
- Gentamicin 80mg nebulized BID QOM**

“Relieved”

“Now I finally know what is wrong with Jacob.”
Staying Healthy is Hard Work!

"I don't feel Jacob's care is a burden. He is able to actively play sports and lead an almost normal life."

Mechanical Defenses of the Lung
• Nasal and upper airway filtration of larger particles (>10um)
• Muscosal surface and mucous secretion
• Mucociliary clearance

Mechanical Defenses of the Lung
• Neurally mediated responses
  – Cough
  – Sneezing
  – Bronchoconstriction

Mucociliary Clearance
• Ciliated cells present at 13 WGA
• Present on mucosal surfaces with up to 200 cilia present per cell
• Beat in frequency at 12-22 hz to sweep mucous along mucosal surfaces
• Ciliary function can be disrupted due to structural or dyskinetic beat

Mucociliary Clearance
• Neurally mediated responses
  – Sneezing
    – Response to particulate matter or irritants in the nose or nasopharynx
  – Cough
    – Response generated to stimulation of laryngeal or airway receptors
Neurally Mediated Clearance
- Bronchoconstriction
  - Increased lower airway tone in response to receptor stimulation to limit dispersion of inspired particles

Why Cough?
- Larynx
  - Irritant
  - Thermal
- Trachea
  - RARs - Irritant
  - SARs - Facilitate

Why Cough?
- Lower Airways
  - C-Fibers
- Esophagus

What Is a Cough
- Coughing is a physiologic reflex that augments airflow thus enhancing mucociliary clearance and expelling large accumulations of mucous
- Coughing is in effect a normal response to a pathophysiologic state
- Cough can be both reflexive and controlled

How Do We Cough
- Initial inspiration above tidal breathing to a point in IRV but below TLC
- Glotic closure with contraction of abdominal and thoracic muscles raises transpulmonary pressure
- Opening / closing glotis in repetition allows high velocity air flow transients to propel mucous
High Velocity Air Flow Moves Liquids!

Is a Cough Always Bad
- Coughing is a normal and protective physiologic defense
- Chronic coughing represents ongoing response to a pathophysiologic state
- Generally a cough lasting more than four weeks requires further investigation

Is a Cough Always Bad
- A cough that is acutely worsening likewise requires more attention

Cough: Efficient Accurate Diagnosis
- Chronic cough in association with chronic lower airway inflammation results in permanent lung injury
  - Bronchiectasis is permanent and progressive

Cough: Efficient Accurate Diagnosis
- Morbidity and physiologic limitations associated with chronic coughing significantly disrupts daily activity
  - School, sleep, activity, parental concern

So Many Coughs: Where to Start?
- History is the key!
**Characterize It:**

**Types of Cough**

- Clinical descriptors of cough help tremendously
- Character
  - Wet or productive?
  - Dry and hacky?
  - Barking or seal-like?

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**Wet and Productive**

- Generally associated with excessive mucous production, ineffective clearance, and inflammation
  - Asthma: “wet” asthma vs. “dry” asthma
  - Bronchitis: chronic or acute
  - Pneumonia: infectious or non-infectious

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**Dry and Hacky**

- Generally associated with upper airway stimulation
  - Asthma
  - Allergic rhinitis
  - Sinusitis
  - Gastroesophageal reflux
  - Post infectious hypersensitivity
  - Psychogenic

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**Barking or Seal-like**

- Generally not a chronic finding but more a qualitative descriptor – think acute
  - Croup / laryngotrachobronchitis
  - Characteristic of tracheomalacia
  - History of T-E fistula

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**Characterize It:**

**Types of Cough**

- Setting and stimulus
  - During wakefulness or asleep?
  - During exercise or at rest?
  - Following meals or drinking?
  - Continuous or disruptive in nature?
Barking or Seal-like

- External / internal airway compression
- Psychogenic – honking quality

Setting or Stimulus

- Awake or asleep?
  - Pathologic coughing usually continues and disrupts sleep
  - A cough that resolves during sleep and resumes on awakening raises concern of psychogenic etiology
  **diagnosis of exclusion**

Setting or Stimulus

- During exercise or rest
  - Coughing only with exercise represents a physiologic change
  - Asthma, EIB, GERD, environmental factors
  - A cough that occurs at rest is most common in the pathologic state and usually is exacerbated by activity

Setting or Stimulus

- Continuous or disruptive in nature
  - Coughing that is seemingly uncontrollable or disruptive is often psychogenic in nature
  - While this is a diagnosis of exclusion and requires careful assessment, a chronic cough is generally responsive to active suppression

Setting or Stimulus

- Following meals or drinking
  - Generally would be triggered by irritant receptors independently or in association with lower airway disease
  - Think aspiration: vocal cord paralysis, laryngeal clefts, primary aspiration, thermal sensitivity

Setting or Stimulus

- GERD
- Gustatory responses
Evaluation of Chronic Coughing

- History, history, history
- Physical examination
- Routine diagnostic testing
  - What is done by the primary care provider
- Subspecialty evaluation
  - Advanced diagnostics available at tertiary care centers

Physical Exam

- HEENT
  - Chronic OM, sinusitis?
  - Auscultation of the neck?
- Cardiac
  - Cardiac and vascular abnormalities?

Physical Exam

- Pulmonary
  - Wheezing, crackles, rhonchi, tight / prolonged expiration, auscultation pre / during / post cough
- Neurologic
  - Weakness
- Extremity
  - Clubbing

Routine Diagnostic Testing: Primary Care Setting

- Pulse Oximetry
- CXR
- Office Based Spirometry
- Upper GI
- Baseline Immunologic Evaluation
- Rast Allergy Evaluation

Advanced Diagnostic Evaluation: Subspecialty Setting

- Advanced pulmonary function testing
- HRCT
  - Capability of advanced imaging techniques
- Bronchoscopy and BAL
  - A +/- ENT or GI - Aerodigestive Evaluation

Advanced Diagnostic Evaluation: Subspecialty Setting

- Nasal brushing biopsy - EM
- Genetic testing
- Advanced immunologic evaluation
  - Often done in collaboration with immunology
Summary

• Cough duration > four weeks requires further intervention
• Evaluation and treatment begins in the primary care setting
• Characterization of the cough is highly important in guiding diagnosis

Summary

• Advanced diagnostics and subspecialty evaluation may be necessary
• Primary goal is accurate diagnosis and treatment to prevent morbidity and permanent lung damage

References


References


Case 1

• 7-year-old female presents with cough and chest pain worsened with exercise
• Diagnosed as asthma
• ROS
  – Constipation and abdominal pain
• PMHx
  – Seen by GI and allergist
**Case 1**

- **FAMHx**
  - Negative for childhood disease
- **Social**
  - Outside smoking by parents

**Previous Treatment**

- Allergist diagnosed allergic rhinitis and asthma
- Treated with multiple ICS, nasal steroids without improvement
- Recently increased to ADVAIR 250/50 BID, flonase BID, zyrtec 10mg qd, tessalon pearls 2-4 daily PRN
- Neg CXR by hx but no spirometry

**Cough**

- Dry and barky
- Often associated with clearing of throat
- Occurs at rest and activity
- At times seems worse after eating
- Does not occur at night during sleep

**Cough**

- Chest pain is vague and difficult to characterize
  - Mostly when coughing and it is getting worse

**Exam**

- VSS O2 Sat 99% Ht and Wt at 45%
- General: Well Appearing
- CV: RRR w/o murmur 2+ Pulses
- Chest: Clear BS Bilaterally
- Abdomen: Benign
- Extremities: ? 1+ clubbing and CR <2 sec

**Endoscopy / Bronchoscopy**

- Bronchoscopy and BAL were completely normal
- Upper endoscopy revealed severe esophagitis with white plaques
  - Esophagus: mixed eosinophillic and neutrophillic microascesses with budding yeast and pseudohyphae
  - Dx: invassive candidal esophagitis
Evaluation and Treatment

- Immunologic evaluation was negative
- ICS felt to contribute in the setting of GERD
- All asthma and allergy meds stopped with addition of BID PPI and Diflucan
- At follow up pt was symptom free with no chest pain or cough

Summary

- While asthma is the most common association with cough in children, this cough was NOT completely characteristic of asthma
- Spirometry should be used in the diagnosis of refractory asthma
  - Children as young as 4-5 y/o
- Ultimately escalation of treatment contributed to nosocomial disease

Case 2

- 14 y/o male with coughing, fatigue, shortness of breath and a “racing heart” while walking or climbing stairs
- Increasing exertional dyspnea of the last three weeks
- Cough that worsens with activity and when supine

Nasal congestion and sinusitis
- Tx with Augmentin
- Started on ADVAIR 250/50 2 weeks ago without improvement

ROS

- Neuro / psych
  - Baseline Asperger Syndrome
- CV
  - Racing heart, dyspnea with walking
- Pulm
  - Cough which is worsened supine

Cough

- Improves with rest and sitting up
- Cannot lie supine
  - Immediately starts coughing
- Cough is harsh and honking
- Activity also causes the cough to worsen but not like lying down
<table>
<thead>
<tr>
<th>PMHx</th>
<th>PMHx</th>
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<tbody>
<tr>
<td>• Asthma: since childhood</td>
<td>• Asperger syndrome</td>
</tr>
<tr>
<td>• Recurrent hemolytic anemia and thrombocytopenia</td>
<td>– Learning disability</td>
</tr>
<tr>
<td>• Multiple cutaneous and hepatic hemangiomata</td>
<td>• Verbal and reading IQ 70</td>
</tr>
<tr>
<td>– Involuted at 13 months</td>
<td>• Overall IQ 85</td>
</tr>
<tr>
<td>• Resolved VSD</td>
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<table>
<thead>
<tr>
<th>PSHx</th>
<th>BHx</th>
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<tbody>
<tr>
<td>• Bilateral inguinal hernia – 1991</td>
<td>• Term delivery: 5lb, 14oz</td>
</tr>
<tr>
<td>• Left leg cellulitis w/debridement - 1996</td>
<td>• Hemolytic anemia and thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td>• VSD</td>
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<thead>
<tr>
<th>FHx</th>
<th>SHx</th>
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<tr>
<td>• Asthma in 9 y/o sibling</td>
<td>• Lives with mother, father, and sibling</td>
</tr>
<tr>
<td>• HTN in adults</td>
<td>• Lives in the city</td>
</tr>
<tr>
<td>• No anemia</td>
<td>• Italian descent</td>
</tr>
<tr>
<td>• No other cardiopulmonary disease</td>
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**Feeding Hx**
- Breast fed for eight months
- Tolerated addition of fruits and vegetables
- Developed vomiting and diarrhea with addition of cow milk and table food which resolved after several months and after trying soy milk

**Feeding Hx**
- Doesn’t eat much meat or dairy products
- Prefers corn, potatoes, cookies, and chips

**Exam**
- VS
  - Hr 125, r 18, bp 110/48 o2 96% ra
- Gen
  - Alert without distress
  - Thin habitus
- HEENT
  - Scleral icterus

**Exam**
- CV
  - S1 with loud single s2 and a 3/6 blowing diastolic murmur 2+ peripheral pulses
- Lungs
  - Clear BS but coughing with deep inspiration and supine position

**Exam**
- AB
  - Soft and NT /ND
  - No hepatomegaly with spleen tip down 3 cm
- Ext
  - Cr 2 seconds and no clubbing

**Evaluation**
- ECHO: Pulmonary HTN
  - Predicted pulmonary artery pressure of 125 systolic and 55 diastolic
  - RVH and LVH with diastolic pulmonary valve insufficiency otherwise normal intracardiac anatomy
**Evaluation**

- Spirometry
  - Moderate obstructive and restrictive disease
  - Patient had difficulty performing the test

**Problem List**

- Severe pulmonary hypertension
- Chronic hemolytic anemia and thrombocytopenia
- Low-normal IQ and learning disability
- History of multiple hemangiomata
- Questionable dietary aversion to protein

**DD**

- Idiopathic pulmonary hypertension
- Metabolic disease
  - Lysinuric protein intolerance, gaucher, etc.
- Hereditary hemorrhagic telangiectasia
- Hemoglobinopathies

**DD**

- PVOD
- Thrombosis (chronic)
- Collagen vascular disease
- Arterial-venous shunting

**Hematologic Evaluation**

- WBC 9, HgB 10 and PLT 50s
- Smear microangiopathic hemolysis
- INR 1.7
  - All coagulation factors slightly low except fibrinogen and factor VII activity
- LDH 1500s

**Hematologic Evaluation**

- Historical evaluation of immune and non-immune hemolysis negative
**Metabolic Evaluation**

- Fasting ammonia: 39
- Post-prandial ammonia: 90-120
- Urine amino and organic acids: normal
- Serum amino acids: normal
- Metabolic storage diseases: normal
- Acylcarnitine profile: normal

**Hepatic Evaluation**

- AST, ALT, GGT and AlkP: normal
- Albumin: 2.0
- Prealbumin: 5
- TB: 3-4 (unconjugated)
- Normal electrolytes

**Congenital Extrahepatic Portocaval Shunts**

- The Abernathy Malformation – 1793
  - Type 1
    - End to side anastomosis and congenital absence of the portal vein
    - Associated with dextrocardia, transposition, and polysplenia
  - Type 2
    - Side to side
    - Not associated with other anomalies but associated with encephalopathy


**Summary**

- Coughing, even as the presenting CC can be a distracter and delay diagnosis
- Coughing is not specific to lung disease

**Summary**

- Focusing on basic history and adhering to the concept that pediatric disease is most frequently of common primary etiology
- Always listen and hear parental instincts