Asthma in Children with Sickle Cell Disease

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(presented by Patricia Kavanagh, MD)
Why do we care about Asthma in SCD?

Asthma: most common chronic disease of childhood in the US; disproportionately affects African Americans

Asthma is associated with
- Increased rates of ACS and pain; earlier onset of ACS
- Increased risk of mortality

Many patients with SCD exhibit individual features of asthma in isolation

Knight-Madden JM et al, *Thorax* 2005
Knight-Madden JM, Greenough A, *Paed Resp Rev* 2014
Why do we care about lower airway disease in SCD?

“Asthma”

Hypoventilation [from pain, opioids]

Ventilation-perfusion mismatch → Regional hypoxia → Inflammation Adhesion Vessel Injury → Pain +/- ACS Mortality

Adapted from:
Setty BJ et al, Blood 1999
Glassberg JA et al, Curr Opin Ped 2014
Strunk RC, personal communication
Features of Asthma are Common in SCD

Wheezeing is common (next slide)

Airway obstruction: 10-15% of patients *without* asthma

Airway hyper-responsiveness: 55-77% of children *without* asthma

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Pediatric Pulmonologist extraordinaire
Wheezeing is Common in SCD

Common feature of ACS
26% during hospitalization

Commonly heard on presentation to ED
262 children + adults over 4 years: 19% had > 1 presentation with wheezing

Common among adults
Of 114 adults, 30% reported recurrent wheezing w/ SOB
Not associated with family hx of asthma, eosinophilia, IgE, allergic rhinitis, or eczema
Associated with lower FVC and FEV$_1$: May be a marker of SCD severity

“Recurrent Wheezing in SCD”
Wheezing limited to SCD-specific episodes
Warrant a different approach to therapy

Vichinsky EP et al, NEJM 2000
Glassberg JA, Brit J Haem 2012
Cohen RT et al, Am J Hem 2011
Knight-Madden JM, Paed Resp Rev 2014

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Wheezeing is Common in SCD

- Wheezeing (even without a dx of asthma) is associated with SCD morbidity

<table>
<thead>
<tr>
<th>N=114</th>
<th>Effects of MD dx asthma</th>
<th>Effects of Severe Recurrent Wheezeing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>0.99 (0.6-1.7)</td>
<td>0.46</td>
</tr>
<tr>
<td>Wheezeing</td>
<td>2.0 (1.2-3.4)</td>
<td>0.005</td>
</tr>
<tr>
<td>ACS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>1.3 (0.7-2.6)</td>
<td>0.97</td>
</tr>
<tr>
<td>Wheezeing</td>
<td>2.1 (1.1-4.0)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

HR 4.2 (1.0-17.5), p=0.046

So...which patients with SCD have asthma?

Wheezing Symptoms and Parental Asthma Are Associated with a Physician Diagnosis of Asthma in Children with Sickle Cell Anemia

SAC study: compared 53 children w/ asthma to 134 w/o asthma
Compared parent history, respiratory symptoms, spirometry, BDR, PC\textsubscript{20}, WBC, eosinophils, serum IgE, allergy skin test results, age, sex,
Multivariable model of factors associated with the asthma dx in this cohort: wheezing and parent history of asthma

Adding >2 + skin tests to the model improved it’s predictive power

“Airway obstruction” and bronchodilator responsiveness did not improve the model

Strunk RC et al, J Peds 2014
PFTs – YES in Symptomatic Patients

Children with diagnosis of asthma

As part of **DIAGNOSTIC evaluation** in symptomatic children, including:
- Dyspnea (and rest and with exertion)
- Exercise limitation
- Low daytime oxygen saturation
- History of wheeze during SCD episodes
- Chronic cough
- Recurrent acute chest syndrome
PFTs — ?? in Asymptomatic Patients

2014 NHLBI guidelines: No screening for pulmonary disease with PFT’s for asymptomatic individuals

No trials done to show benefit, none done comparing screening intervals

BUT

Abnormal pulmonary function may be a marker of SCD severity

Recent study began to define phenotypic clusters based on patterns of lung function and biomarkers

Cluster 1: Severe anemia, increased cardiac output, mixed obstructive/restrictive defect
Cluster 2: More severe restrictive lung disease, diffusion defects, older
Cluster 3: Younger, baseline obstruction, BDR, increased LDH

The jury is still out...

Lunt A. et al, Thorax 2018

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