Post Traumatic Airway Stenosis in Patients with Myhre/LAPS Syndrome

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Abstract

Myhre/LAPS syndrome is a rare condition with approximately 60 patients carrying the diagnosis (1,2). The underlying genetic defect in MLS patients is an SMAD4 mutation which affects the codon for Ile500 which in turn alters the signal transduction pathway of TGF-beta and Bone morphogenetic protein (BMP) (3). The downstream pathophysiologic effects of this genetic alteration is that extracellular matrix (ECM) homeostasis is altered which leads to ECM disorganization.

Clinically this results in systemic tissue fibrosis secondary to ECM dysfunction. Patients characteristically have short stature, arthopathy, facial dysmorphism, progynathism and can develop airway stenosis as well as pericardial thickening.

Study Aim

To investigate the role intubation and airway manipulation in airway stenosis in these patients and review four patients with MLS related airway pathology.

Methods

• Retrospective review was performed on all patients diagnosed with either Myhre or LAPS syndrome from 1981-2014 at a single tertiary care center
• Systematic literature review was performed for all patients with MLS and airway pathology.

Table 1: Systematic Review of MLS associated Airway Pathology

<table>
<thead>
<tr>
<th>Study</th>
<th>Age at Airway Symptoms Onset</th>
<th>Symptoms</th>
<th>Work-up and Initial Diagnosis</th>
<th>Age at diagnosis of Airway Stenosis</th>
<th>Method of Diagnosis</th>
<th>Prior Intubation (Y or N)</th>
<th>Number of Airway Interventions</th>
<th>Surgical Complications</th>
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</thead>
<tbody>
<tr>
<td>Hopkins et al 1998</td>
<td>28F</td>
<td>22</td>
<td>Wheezing</td>
<td>Asthma, GPA</td>
<td>23</td>
<td>Unknown</td>
<td>N</td>
<td>4 Tracheotomy placements, 2 LTRs, multiple endoscopic treatments</td>
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<td>Hopkins et al 1998</td>
<td>24F</td>
<td>22</td>
<td>Post operative</td>
<td>Asthma, GPA</td>
<td>25</td>
<td>Unknown</td>
<td>Y</td>
<td>Multiple dilations / Laser treatments</td>
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<td>Hopkins et al 1998</td>
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<td>Dysspnea on exertion</td>
<td>Asthma</td>
<td>23</td>
<td>Bronchoscopy</td>
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<td>None</td>
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<tr>
<td>McGowan et al 2011</td>
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<td>Dysspnea on exertion</td>
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Discussion

• MLS has late onset of airway stenosis that is highly resistant to surgical therapy secondary to a robust scarring response
• Surgical intervention often results in rapid recurrence and should be pursued with caution
• Endotracheal intubation may play a role in the development of airway stenosis in these patients

Conclusions

• MLS is a genetic disorder caused by a mutation in the SMAD4 pathway which results in a wide range of clinical signs and symptoms.
• A subset of these patients develops progressive laryngotracheal stenosis that is refractory to traditional treatment modalities and often results in long term tracheostomy dependence.
• Surgical intervention should be approached with caution in these patients and re-stenosis after intervention should be expected.

References