Laryngeal Papillomatosis Associated Dysplasia in the Adult Population: An update on prevalence and HPV subtype

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Disclosures

- None
Introduction

- HPV subtypes most frequently associated with laryngeal papillomatosis include HPV 6, 11, as well as HPV 16, 18, 31, 33, 51.
- High risk HPV subtypes (16/18) are increasingly associated with oropharyngeal carcinoma’s.
- Recent studies cite dysplasia associated with laryngeal papillomatosis to occur with a 22-50% prevalence.
- The association of high risk HPV subtypes have yet to be explored for laryngeal papilloma associated dysplasia.
Objectives

- To determine the prevalence of laryngeal dysplasia in a sample population of adult patients with laryngeal papillomatosis

- To determine if there is an association of high or low risk HPV subtypes with laryngeal papilloma associated dysplasia’s

- To assess pathologic agreement between pathologists when grading dysplasia
Methods

- Institutional IRB approval
- Retrospective review
- Inclusion criteria:
  - Patients over age 18 (both adult and juvenile onset)
  - At least one surgical procedure under GA
  - Pathologic confirmation of laryngeal papillomatosis
Methods – Chart review

- Demographic data
  - Age, sex

- Disease data
  - Onset, duration, number of procedures, presence of dysplasia (initial diagnosis)

- Degree of dysplasia

- HPV sub-typing

- Risk factors
  - GERD/LPR, smoking, head and neck irradiation, carcinogen exposure, immunosuppression
Methods – Pathologic Review

- All pathologic specimens reviewed by a single H&N pathologist (SM)
- Diagnosis (present/absent)
- Grade (WHO classification)

Low Grade Dysplasia  Moderate Grade Dysplasia  High Grade Dysplasia
Methods – Pathologic review

- Specimens identified to be dysplastic were then further tested by ISH for HPV subtype
  - HPV 6/11 or HPV 16/18 DNA probe
  - Presence of punctate or diffuse staining patterns were noted
Results: Patient demographic

- 85 patients
  - 26 female
  - 59 male
- Onset of disease
  - 17 JORRP
  - 68 Adult onset
- 154 total specimens reviewed
## Results – Patient demographics

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Minimum, Maximum</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.6</td>
<td>18,89</td>
<td>16.7</td>
</tr>
<tr>
<td>Duration of disease (years)</td>
<td>12.0</td>
<td>1,70</td>
<td>14.8</td>
</tr>
<tr>
<td>Mean age of onset (years)</td>
<td>35.3</td>
<td>1,89</td>
<td>15.8</td>
</tr>
<tr>
<td>Number pathology specimens per patient</td>
<td>1.8</td>
<td>0.14</td>
<td>2.0</td>
</tr>
</tbody>
</table>
Results: Inter-rater Agreement

- Presence or Absence of Dysplasia
- “Good” agreement (0.73 Cohen’s Kappa)

<table>
<thead>
<tr>
<th></th>
<th>Dysplasia absent (R)</th>
<th>Dysplasia present (R)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysplasia absent (I)</td>
<td>58</td>
<td>6</td>
<td>64</td>
</tr>
<tr>
<td>Dysplasia present (I)</td>
<td>3</td>
<td>18</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>24</td>
<td>85</td>
</tr>
</tbody>
</table>
Results: Inter-rater agreement

- Degree of Dysplasia
- Overall agreement “fair” (0.63 Kappa Value)

<table>
<thead>
<tr>
<th></th>
<th>No dysplasia</th>
<th>Low (R)</th>
<th>Moderate (R)</th>
<th>High (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dysplasia</td>
<td>58</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Low (I)</td>
<td>3</td>
<td>7</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Moderate (I)</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>High (I)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>
Results: HPV subtyping

24 Patients +ve Dysplasia

18 Samples Adequate for ISH

15 Samples undergo ISH

Low Grade (11)

8/11 HPV 6/11

0/11 HPV 16/18

High Grade (7)

7/7 HPV 6/11

0/7 HPV 16/18

6 patients inadequate tissue

3 samples previously subtyped
Results: Risk Factors

- No relation of risk factors to presence or grade of dysplasia
- Smoking
- Reflux
- Adjuvant therapy
  - 6 cidofovir
- Immunosuppression
- XRT
Study limitations

- Single pathologist reviewed slides
  - Un-blinded to original results
- Single institution
  - Tertiary care institution
- Rare disease
Conclusions

- 28% prevalence of laryngeal dysplasia in this sample population
- No association of high risk HPV subtypes with presence or degree of dysplasia associated with laryngeal papillomatosis
- Pathologic inter-rater agreement “good” for the identification of dysplasia, but not for grade of dysplasia
References


THANK YOU