Longitudinal Case Study of Treatment for Adult-Onset Laryngeal Papillomatosis

Michael Morgan
State University of New York College at Plattsburgh
Miguel Triana
Columbia University Medical Center, NYC
Magdalena Hertel
State University of New York College at Plattsburgh

ASHA 2006

Introduction

Human papillomavirus (HPV) is an oncogenic DNA virus that infects epithelial cells. More than 100 subtypes of HPV exist with subtypes 6 and 11 being associated with the majority of genital and laryngeal lesions. Recurrent respiratory papillomatosis (RRP) is the most common benign laryngeal neoplasm with true vocal folds being the most frequently affected site. Prevalence estimate is 4.3 per 100,000 children and 1.8 per 100,000 adults in the United States. The first sign of disease is usually hoarseness. Clinical course of RRP is unpredictable, but occurs more aggressively in children with an age of onset that peaks at 5 years compared to typically less aggressive adult onset that peaks between 20 and 30 years. Spontaneous regression occurs in some patients, but reoccurrence has been seen as long as 30 to 40 years after remission. Gender ratio of RRP is about equal in juvenile onset, but is more prevalent in males with adult onset (2:1 to 4:1 male-to-female). Aggressive forms of the disease have required multiple surgical procedures over many years for both children and adults.

Before the early 1970s, treatment of RRP involved removal of lesions by cold instrumentation, followed in the early 70s with the introduction of carbon dioxide (CO2) laser surgery. The viral nature of the disease caused surgical treatment to be less than optimal. Complications from CO2 removal of RRP can be soft tissue damage such as scarring, web formation, and airway stenosis. CO2 debulking of lesions has continued to be the most common surgical approach to treating RRP; however, some surgeons have reconsidered this approach in favor of cold instrumentation approaches for more complete removal of diseased tissue.

Other surgical approaches to RRP have included photodynamic therapy (PDT) and pulsed-dye laser (PDL) treatment in an attempt to preserve tissue without active disease. Microdebridement (oscillating blades with suction and irrigation) has been used. Long-term injection of alpha-interferon, as a non-surgical approach, has been successful in remission of disease for some patients. Nutritional supplementation with indole-3-carbinol (found in high concentrations in cruciferous vegetables) has been reported to be effective in controlling growth of new papilloma for some patients.

Since the mid 1990s, intralesional injection of Cidofovir, an antiviral drug that blocks the replication of certain DNA viruses, has been used in the larynx in an attempt to control RRP. Cidofovir has resulted in complete remission of disease for some and increased surgical intervals for others. As with PDT and PDL, Cidofovir only targets active disease and does not eliminate dormant DNA virus within infected tissues; thus, papilloma often returns. Therapeutic response to Cidofovir is, in part, dependent on length of time between injections, concentration levels of injection, and debulking of lesions before injection. Canine models have shown permanent damage including necrosis, atrophy, and fibrosis with higher concentrations (20 and 37.5 mg/ml). More research is needed to determine optimal concentration levels.

Case Study

A 65-year-old cross-country ski/mountain bike instructor was seen initially at the SUNY Plattsburgh Voice Lab with an aggressive form of adult-onset RRP in May of 1999. His original diagnosis by a local ENT followed three months of hoarseness. Treatment over the past 7.5 years is described. All laser surgeries were performed by Dr. Stanley Shapshay. A treatment plan for the immediate future is indicated.
Diagnosis
May 1999
Age 57

3 weeks
Surgery
Cold Instrumentation

4 months
Surgery
Cold Instrumentation

6 months
Surgery
Cold Instrumentation

4 months
Surgery
CO₂ Laser and Pulsed Dye Laser of Anterior Commisure

3 months
Surgery
CO₂ Laser and Injection of Interferon (5mg/ml) into Anterior Commisure

1 year, 5 months
Systemic Interferon: 5 million units 3x/week for 6 weeks and 2.5 million units 3x/week for 3 months, 2 weeks. Dosage reduced due to negative side effects (fatigue, depression).

February 2001

Value | Norm | SD
--- | --- | ---
Fo | 117 | 145 | 23
Jitter % | .32 | .589 | .535
Shim dB | .16 | .219 | .085

Voice: Posterior resonance with significant, habitualized laryngeal tension. Mild-moderate breathiness. Worked on forward focus/oral resonance.

May 2000

Fully Abducted during respiration
Supraglottic tissue vibration

Value | Norm | SD
--- | --- | ---
Fo | 85 | 145 | 23
Jitter % | 2.24 | .589 | .535
Shim dB | .422 | .219 | .085

Voice: low pitch, extreme harshness, severe breathiness, phonation breaks, and limited pitch range. Excessive neck tension during phonation. Vibratory source was primarily supraglottic tissue.
October 2006

CO₂ Laser and Injections of Cidofovir (5mg/ml)

Surgery

Four Laser & Injection treatments
Cidofovir (5mg/ml)

3 Years, 6 Months

Four Laser & Injection treatments
Cidofovir (5mg/ml)

November 2006
3 weeks post surgery

CO₂ Laser and Injections of Cidofovir (20mg/ml). Began Indole-3-Carbinol

Cidofovir Injections (20mg/ml)

Voice: Moderate breathiness, moderate laryngeal tension, higher pitch, and diplonhia.

Treatment Plan:
Three Cidofovir treatments over the next three months

One Vibratory Cycle at 155 Hz, 71 dB

CO₂ Laser and Cidofovir (5mg/ml)

Cidofovir and I3C

Surgery

CO₂ Laser and Injections of Cidofovir (5mg/ml)

Voice: Moderate breathiness. Mild laryngeal tension with posterior resonance. Discussed anterior focus of voice and reduction of habitualized laryngeal tension.

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Norm</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fo</td>
<td>178</td>
<td>145</td>
<td>23</td>
</tr>
<tr>
<td>Jitter %</td>
<td>4.06</td>
<td>.589</td>
<td>.535</td>
</tr>
<tr>
<td>Shim dB</td>
<td>.51</td>
<td>.219</td>
<td>.085</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Norm</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fo</td>
<td>123</td>
<td>145</td>
<td>23</td>
</tr>
<tr>
<td>Jitter %</td>
<td>.356</td>
<td>.589</td>
<td>.535</td>
</tr>
<tr>
<td>Shim dB</td>
<td>.144</td>
<td>.219</td>
<td>.085</td>
</tr>
</tbody>
</table>
Conclusions

- Recurrent respiratory papillomatosis (RRP) is the most common benign laryngeal neoplasm with the true vocal folds being the most frequently affected site. The first sign of the disease is usually hoarseness.
- There currently is not a cure for RRP; however, a number of treatments have been used in recent years including cold-instrumentation surgery, CO2 laser, photodynamic therapy, pulsed dye laser, microdebridement, Interferon, and injections of Cidofovir.
- Aggressive forms of RRP require multiple surgical procedures over many years, which may result in vocal fold scarring.
- Intralesional Cidofovir injections have been reported to reduce papilloma and time between treatments; however, the extent of papilloma in this patient’s larynx has not been amenable to intralesion Cidofovir treatment only. The patient has required repeated laser debulking in addition to injections.
- Speech pathologists provide patient education, vocal hygiene counseling, and voice therapy for patients with RRP. Patient education requires basic understanding of the disease and current surgical/medical treatments. Voice therapy typically targets reduction of compensatory laryngeal muscle tension developed secondary to disease progression and/or treatment related phonotrauma.

References