A Review of Laryngopharyngeal Reflux

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Objectives

- To present and discuss a case involving laryngopharyngeal reflux (LPR)
- To review the prevalence and presentation of LPR
- To differentiate between LPR and GERD
- To discuss the diagnosis and management of LPR
- General open discussion
Case Presentation

- 52 yo male with 2 month history of globus sensation worse with coughing or swallowing
- Has periodic heartburn
- No dysphonia
- Smokes cigars occasionally
Case

- Flexible laryngoscopy showed normal cord mobility but hyperfunctioning on videostroboscopy and incomplete closure.
Treatment

• Started on Pantoprazole 40mg po od
• Discussed lifestyle modification
• Lesion persisted so booked for OR
• Microlaryngoscopy and excisional biopsy of lesion done.
Outcome

• Ultimately had excised, base of lesion removed with CO2 laser and then injected with Kenelog.
• Referred for speech therapy
• Placed on Pantoprazole 40mg po bid but poor compliance.
• Now on Nexium od maintenance therapy after a 3 month course of Nexium bid.
Case 2

• 50 yo female presents to the ER with sternal chest pain, persistent cough
• Neck soft Tissue finds free air in the cervical esophagus.
• Pt was kept NPO, started on Clindamycin IV, and subsequently started on Nexium bid.
• Review of past history reveals a long history of a persistent cough for many years despite quitting smoking 2 years previously.
• Patient admits to chronic throat clearing, globus sensation and heartburn, with raspy voice.
• Flexible nasopharyngoscopy found extensive pachyderma, arytenoid erythema, normal mobility of vocal cords.
• After treatment with IV antibiotics and advanced to normal diet, the patient was started on Nexium bid long term with no further symptoms for over a year.
LPR: What is it?

Gastric acid washing up onto the laryngeal and pharyngeal mucosa
Prevalence

- Koufman et al
  - 113 consecutive patients with laryngeal and voice disorders
  - 78/113 (69%) had symptoms and signs of LPR
  - 57/78 (73%) had an abnormal pH study
  - Conclusion: LPR occurs in at least 50% of patients with laryngeal and voice disorders

Otol H&N Surg, Jan 2001
Presentation

- Hoarseness/dysphonia 71%
- Chronic cough 51%
- Globus pharyngeus 47%
- Chronic throat clearing 42%
- Dysphagia 27%
- Heartburn present in 6%-43%

Koufman JA. Laryngoscope 1991 Apr; 101
Current Perspectives on LPR

• Book et al
  – Discern current practices of otolaryngologists
  – Symptoms most related to reflux
    • Throat clearing (98.3%)
    • Persistent cough (96.6%)
    • Globus sensation (94.9%)
    • Dysphonia (94.9%)
  – Most common diagnostic test
    • Fiberoptic laryngoscopy (75.7%)
  – Most common adjunctive test
    • Double pH probe test (37.2%)

Laryngoscope. Aug 2002;112
LPR vs GERD

- As few as 3 episodes of reflux per week can cause damage
- pH of up to 5 considered damaging to the laryngopharynx
- 100 times more sensitive to acid exposure
- No protection from acid exposure.

- Up to 50 episodes of GER/24 hrs considered normal.
- Prolonged exposure of acid, pepsin at pH <4 required for damage
- Bicarbonate, peristalsis, mucosal barrier protect esophagus.
LPR: Common associations

- Asthma
  - 70% of asthmatics exhibit reflux symptoms and abnormal results on pH monitoring
- Subglottic stenosis
- Globus Pharyngeus
- Laryngospasm
- Laryngeal Cancer
- Sinusitis
- Acute otitis media
Prevalence of Reflux in Patients with Chronic Rhinosinusitis

- **Objective:** To determine whether there is a difference in the prevalence of reflux in patients with refractory chronic rhinosinusitis (CRS) compared to controls.

- **Patients:**
  - Study group: 38 patients w/ history of ≥ 1 endoscopic sinus surgery with continued CRS symptoms & mucosal inflammation
  - Control group 1: 10 patients w/ ≥ 1 ESS procedure & no symptoms of CRS or mucosal inflammation
  - Control group 2: 20 subjects w/ no history of CRS or sinus surgery

- **Assessments:** Reflux symptom scales, 20-item sinonasal outcome test, sinusitis symptom scale, nasal endoscopy, 24 hour pH study

Nasopharyngeal Reflux Events in Chronic Rhinosinusitis

*\( p = 0.004 \) vs. controls; **\( p = 0.00003 \) vs. controls

Pathologic Reflux in the Esophagus

- **Non-CRS controls**: 35% with pH < 4 over 4% of study esophagus
- **Successful ESS controls**: 30% with pH < 4 over 4% of study esophagus
- **Chronic rhinosinusitis**: 66% with pH < 4 over 4% of study esophagus

Reflux in Patients with Chronic Rhinosinusitis: Conclusions

- Compared to controls, patients with persistent CRS after ESS have more reflux at:
  - The nasopharynx
  - The upper esophageal sphincter
  - The distal esophagus
- Greatest difference is in nasopharyngeal reflux, especially pH less than 5
- Nasopharyngeal reflux is likely an important causative factor of refractory CRS

LPR: Testing

- Laryngoscopy
- 24 hr ambulatory pH probe monitoring
- Esophagogastroscopy
- Esophageal manometry
- Esophagogastroscopy
- Intraluminal impedance manometry
- Empiric therapy
- Barium Swallow?
Clinical findings on Laryngoscopy

- Erythema/hyperemia
- Vocal fold edema
- Diffuse laryngeal edema
- Posterior commissure hypertrophy
- Ventricular Obliteration
- Granuloma
- Thick endolaryngeal mucus
- Pseudosulcus
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pH probe testing

- Placed by esophageal Manometry or direct visualization.
- 5cm above LES and just above cervical esophagus
- Difficult to place probe in ideal position in the hypopharynx and esophagus
- Debate over correct placement of upper probe
- pH of 5 felt to be damaging to the larynx vs pH 4 for esophagus
- Very brief window of time studied with 24 hour test
- Can be useful to guide therapy
Diagnostic Criteria

- A decrease in the pH to less than 4.0
- Decrease in the pharyngeal pH level immediately following distal esophageal acid exposure
- No decrease in the pH with eating or swallowing
- A rapid and sharp decrease in the proximal pH rather than a gradual change
- Not useful to predict severity of symptoms

» Laryngoscope 2002; 112(12)
LPR: Treatment

- Different than GERD
- Laryngeal mucosa is more susceptible to acid injury than esophageal mucosa
- Acid needs to be suppressed for 24 hours
- Bile and Pepsin also need to be considered
LPR: Management

• Lifestyle Modification
  – Smoking cessation
  – Alcohol cessation
  – Reduction in Caffeine
  – Avoidance of late night meals and liquids
  – Wt loss

• Medications

• Surgical: Nissen Fundoplication
Elevating the head while sleeping?
Role of H2 Blockers

- Only effective in 50% of cases
- Useful for tapering pt’s off PPI therapy
- Not ideal for initial treatment of LPR
Medical Therapy: PPI’s

- Still 10% failure rate reported
- Directly target H+-K+ ATPase, key enzyme for final acid pdn pathway in parietal cell.
- Reduce exposure of damaged tissues to acidic environment
- Reduces activity of Pepsin
- Also result in reduced gastric volume further reducing reflux.
LPR: Duration of Treatment

- Symptoms found to be improved at 2 months of therapy
- Laryngoscopic changes persistent until 4 months
- Recent studies suggest 6 months of therapy with PPI’s and then tapering off medication.
- Lifetime treatment for some.
% of patients with intragastric pH > 4 for > 12 hours

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nexium® 40 mg</td>
<td>65%*</td>
</tr>
<tr>
<td>omeprazole 20 mg</td>
<td>44%†</td>
</tr>
<tr>
<td>lansoprazole 30 mg</td>
<td>41%†</td>
</tr>
<tr>
<td>rabeprazole 20 mg</td>
<td>38%†</td>
</tr>
<tr>
<td>pantoprazole 40 mg</td>
<td>32%†</td>
</tr>
</tbody>
</table>

* Nexium vs. other PPIs (p < 0.05), n=34
† 5-way crossover study of once daily-dosing for 5 days

Adapted from Miner et al.†

Am J Gastroenterol. Dec 2003;98
Medical Therapy: Role of Nexium

• DelGaudio et al
  – 30 patients treated with 40 mg od x 8 weeks
  – At 4 weeks
    • 8 patients had significant improvement in symptoms
  – At 8 weeks
    • 19 patients had significant improvement in symptoms
  – 4/10 nonresponders improved after increasing their dosage to bid
Surgical Management

• A consideration in patients younger than 40 who require long term therapy
• Surgical experience with laparoscopic technique essential
• 0.05% mortality rate
• Proportion of patients end up back on PPI’s after about 5 years.
Conclusions

- LPR is a clinical diagnosis
- Barium Swallow test is not diagnostic
- Treatment can be protracted
- Maximal treatment benefit is achieved with lifestyle modification and with PPI’s
- Nexium has been shown to have superior acid suppression to other PPI’s.
Case

• 5 year old female presents with ototorhea from left ear to my office.
• Patient otherwise well, no systemic complaints.
• Tubes placed 3 months ago for chronic otitis media.
• Seen recently at a walk in clinic and prescribed Amoxil.
• No improvement noted.
Ideal treatment?

• This patient should have been started on topical antibiotic drops.
• Ciprodex or Cipro HC with no oral antibiotics in this case.

• The Journal of Otolaryngology, Volume 34, Supplement 2, August 2005
Use of Ototopical vs Systemic Antibiotics

- **Ototopical antibiotics**
  - All cases of uncomplicated AOMT

- **Systemic antibiotics**
  - Systemic illness
  - Complicated otitis media (ie mastoiditis)
  - Associated strep pharyngitis
  - Diabetic and immunocompromized patients
  - Failure of topical therapy
Ototoxicity

• No reported ototoxicity in animal or human studies with fluoroquinilones

• All other ototopical agents may be ototoxic in humans.

• Peter s. Roland Et al Consensus Panel on Role of potentially ototoxic antibiotics for topical middle ear use. Otolaryngology-Head and Neck Surgery. 2004; 130:S51-S55
Case
Pathology

• Some atypical dyskeratotic squamous cells present and inflammatory cells
• Referred for opinion from another pathologist in Hamilton; diagnosed with squamous cell carcinoma in-situ.
• Re-biopsied with same results but clinically consistent with Granuloma
Barium Swallow for LPR?

- Useful if patient complains of dysphagia
- Symptoms of regurgitation
- Suspected stricture
- Esophagitis
- Zenker’s diverticulum
- Normal study does not rule out LPR
# LPR: Different from GERD

<table>
<thead>
<tr>
<th>Table. Summary of typical differences between GERD and LPR*</th>
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</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
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<tr>
<td>Heartburn and/or regurgitation</td>
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<tr>
<td>++ +</td>
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<tr>
<td>Hoarseness, cough, dysphagia, globus</td>
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<tr>
<td>+ ++</td>
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<tr>
<td><strong>Findings</strong></td>
</tr>
<tr>
<td>Esophagitis</td>
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<tr>
<td>+++ +</td>
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<tr>
<td>Laryngeal inflammation</td>
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<tr>
<td>+ ++</td>
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<tr>
<td><strong>Test results</strong></td>
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<tr>
<td>Erosive or Barrett’s esophagitis</td>
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<tr>
<td>+++ +</td>
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<tr>
<td>Abnormal esophageal pH monitoring</td>
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<tr>
<td>+++ +</td>
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<tr>
<td>Abnormal pharyngeal pH monitoring</td>
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<tr>
<td>+ ++</td>
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<tr>
<td>Esophageal dysmotility</td>
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<tr>
<td>+++ +</td>
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<tr>
<td>Abnormal esophageal acid clearance</td>
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<tr>
<td>+++ +</td>
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<tr>
<td><strong>Pattern of reflux</strong></td>
</tr>
<tr>
<td>Supine (nocturnal) reflux</td>
</tr>
<tr>
<td>+++ +</td>
</tr>
<tr>
<td>Upright (daytime) reflux</td>
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<tr>
<td>+ ++</td>
</tr>
<tr>
<td>Both</td>
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<tr>
<td>+ ++</td>
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<tr>
<td><strong>Response to treatment</strong></td>
</tr>
<tr>
<td>Effectiveness of dietary and lifestyle modifications</td>
</tr>
<tr>
<td>++ +</td>
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<tr>
<td>Successful treatment with a single-dose PPI†</td>
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<td>+++ +</td>
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<tr>
<td>Successful treatment with a twice-daily PPI</td>
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<td>+++ +</td>
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</tbody>
</table>
Clinical manifestations reported to be related to LPR

- **Laryngeal**
  - Reflux laryngitis
  - Subglottic and tracheal stenosis
  - Carcinoma of the Larynx
  - Endotracheal intubation injury
  - Contact ulcers and granulomas
  - Arytenoid fixation
  - Paroxysmal laryngospasm
  - Vocal fold Nodules
  - Polypoid degeneration
  - Larayngomalacia
  - Recurrent respiratory papillomas
  - Pachydermia laryngis
  - Recurrent leukoplakia

- **Pharyngeal**
  - Globus pharyngeus
  - Chronic Sore throat
  - Dysphagia
  - Zenker’s Diverticulum

- **Pulmonary**
  - Chronic cough
  - Exacerbation of asthma/COPD
  - Bronchiectasis
  - Aspiration pneumonia

- **Miscellaneous**
  - Sudden infant death syndrome
  - Sinusitis
  - AOM
  - Dental erosions
  - OSAS
Dietary Modification

• Behavioral dietary modifications shown to be most effective
  – Avoidance of food and liquid before sleep
  – Elevation of head of bed (only for about 20% is this helpful)
  – Type of foods had little effect on reflux

Ann Otol Rhinol Laryngol 112;2003
Compliance

- Giacchi RJ et al did a prospective survey on 30 patients with symptoms and findings consistent with LPR
- Followed for 4 months
- Looked at survey and medication renewal from pharmacies
- 80% improved but only 50% took medications as prescribed
- Degree of symptomatic improvement significantly correlated with medication and behavioral compliance.
Medical Therapy: Placebo Effect

• Noordzij et al
  – 53 patients with >1 LPR symptom were recruited and underwent pH study
  – 30 patients with >4 episodes LPR events enrolled
  – 15 patients received 40 mg Losec bid, 15 received placebo for 2 months
  – Symptoms of hoarseness/throat pain/globus/clearing/cough/dysphagia and odynophagia were monitored
  – Both groups improved in most symptoms with hoarseness and throat clearing improving more in the treatment group
LPR: Treatment Regimen

- Start with twice daily dosing
  - AM dose before breakfast
  - PM dose before evening meal
- Reevaluate at 2-3 months
- Repeat laryngoscopy at 4-6 months
  - If failing arrange for pH monitoring
- Minimum length of therapy is at 6 months
- At 6 months replace with H2 blocker first at night and then in the morning alternatively may reduce PPI dosing to once daily
Treatment

Reduce acid exposure for 24 hours
pH > 5 ideal for LPR
Reduce reflux of stomach contents
Bile
Pepsin
Acid
Pathologic Reflux at the Upper Esophageal Sphincter

* $p = 0.006$ vs. controls; ** $p = 0.007$ vs. controls

Symptom and Examination Scores in CRS vs. Controls

- Reflux symptom score: 13.26 (CRS), 5.20 (Successful ESS controls), 4.40 (Non CRS controls)
- SNOT-20: 45.08 (CRS), 20.30 (Successful ESS controls), 14.15 (Non CRS controls)
- Sinus severity score: 42.13 (CRS), 14.50 (Successful ESS controls), 9.15 (Non CRS controls)
- Examination score: 7.79 (CRS), 1.80 (Successful ESS controls), 0.15 (Non CRS controls)

$p < 0.01$ for all comparisons