Extra-esophageal manifestations of GERD: GPs at the forefront

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Objectives

- Identify the main extra-esophageal syndromes of gastroesophageal reflux (GER)
- Recognize the diagnostic challenges in these syndromes
- Become familiar and comfortable with best management approach
- Appreciate the important role GPs can play in the management of these problems
GERD - Definition

- GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications.
Typical reflux syndrome

- Heartburn
  - Burning sensation in retrosternal area

- Regurgitation
  - Perception of flow of refluxed gastric contents into mouth or hypopharynx
Main extra-esophageal manifestations of GERD

- Reflux related cough
- Reflux related laryngitis
- Reflux related asthma
- Reflux related non-cardiac chest pain
GERD mechanisms in extra-esophageal manifestations

- **Direct**
  - “high” reflux of gastroduodenal contents
  - direct pharyngeal or laryngeal stimulation/aspiration

- **Indirect**
  - “distal” reflux
  - vagally mediated tracheal/bronchial reflex due to common embryologic origin and neural innervation by the vagus nerve shared by esophagus and bronchial tree
  - cough then causes intra-abdominal pressure gradient, reflux, and then a vicious circle
1. Reflux related cough

- Chronic cough: >8 weeks
- Normal CXR?
- Non-smoker?
- No ACE inhibitor?

Then, 90% related to:
- Postnasal drip syndrome (PNDS)
- Asthma
- Chronic bronchitis
- GERD (10%)
Reflux related cough – diagnostic considerations

- Challenging – up to 75% do not have “typical” heartburn/regurgitation symptoms
- Consider other causes of chronic cough first
- Cough features: primarily during daytime; in upright position; during phonation; when rising from bed; when eating
- No definitive diagnostic test that establishes GER as the cause of chronic cough
Reflux related cough – diagnostic considerations

- OGD can rule out complications: esophagitis; Barrett’s; cancer
  - but most will be normal; only 15% of chronic cough have esophagitis on OGD

- 24-hour pH monitoring: not useful, low specificity

- Laryngoscopy: might be useful if mechanism is “high reflux” and laryngitis is evident (but see more later)
Reflux related cough and empiric PPI

- 80% of chronic cough due to GER can be diagnosed AND treated with empiric PPI

- Superior cost-effectiveness to other diagnostic modalities, e.g. 24-hour pH probe

- Usually bd initial dosing; however, once daily may be similar
Reflux related cough: best management

- Evaluation should begin for other causes (CXR; ACE-inhibitor; smoking)

- Then rule out PNDS and asthma

- If reflux related cough is diagnosis: PPI bd for 12-16 weeks
  - this will identify and treat the majority of patients

- If unresponsive: consider other tests to rule out large mechanical defects (e.g. hernia causing volume regurgitation) and evaluation for other lung-related issues
2. Reflux related laryngitis

- Called laryngopharyngeal reflux (LPR) by ENT

- Symptoms: hoarseness, throat pain, sensation of lump in throat, cough, repetitive throat clearing, excessive phlegm, difficulty swallowing, pain with swallowing, voice fatigue

- Non-specific symptoms; also seen in postnasal drip, allergies, exposure to irritants such as smoke

- Reflux often implicated because of chronicity and laryngeal findings of edema/and erythema
Laryngoscopy most common

Findings uncertain, non-specific

- High prevalence of similar findings in normal volunteers
- High level of variability in diagnosing subjective signs (erythema and edema of the larynx)
- Therefore, LPR is often over-diagnosed in patients with chronic throat symptoms

24-hour pH monitoring

- Up to 45% of healthy volunteers have pharyngeal reflux
- Best done off PPI
LPR and PPI

- PPI is the standard of care if chronic throat symptoms are suspected to be due to GER

- Disappointing results in studies – why?
  - “Dilution effect” – many patients did not have the disease for which they were randomized
  - ENT makes the diagnosis based on non-specific symptoms and signs

- Those not responsive to PPI may have non-reflux related disease

- Note placebo response rate of 40% in LPR
Reflux related laryngitis: best management

- Suspected LPR patients with no warning signs or symptoms should be treated empirically with PPI for 1-2 months.
- If symptoms improve, may prolong therapy for up to 6 months to allow healing of laryngeal tissue.
- Then, taper PPI dose to minimal acid suppression resulting in continued response.

(In unresponsive patients, may consider pH monitoring and/or impedance study to rule out reflux as the cause and to move forward with considering other causes for patient’s continued symptoms.)
3. Reflux related asthma

- Strong association between asthma and GER (based on epidemiologic studies and physiologic testing)

- The two induce each other

- Asthma meds (beta-agonists, steroids, theophylline) can reduce LES pressure

- Possible clues for GER related asthma: symptoms worse after meals, non-responders to traditional asthma meds, history of heartburn/reflux before asthma onset
Reflux related asthma – benefit of acid suppression treatment

- Controversy with mixed results

- Different endpoints in studies

- A study showed that 75% of patients who had Nissen fundoplication had improvement in asthma exacerbations compared to 9% and 4% (ranitidine and control) – but no improvement in PFT or use of meds

- The issue of asthma control by treating reflux is not yet clear
Reflux related asthma: best management

- Similar approach to chronic cough and laryngitis
- Initial empiric PPI bd for 2-3 months
- In responders, taper to minimal dose necessary to control symptoms
- In non-responders, testing for reflux may be needed to measure for continued reflux of acid or non-acid material that could be responsible for asthma exacerbation (24-hour pH probe and/or impedance pH monitoring)
4. Reflux related non-cardiac chest pain (NCCP)

- NCCP: recurring angina-like retrosternal chest pain in patients with negative cardiac evaluation
- GER is the most common underlying cause
- Diagnosis is difficult
  - Esophageal and cardiac chest pain often similar
  - May improve with similar treatment (e.g. nitroglycerin)
  - Reflux can be worsened with exercise
  - GER and CAD can co-exist
Reflux related NCCP

- Possible clues for reflux-related: post-prandial, lasting hours, no radiation, disturbs sleep, relieved with antacids
- Likely caused by vagal stimulation triggered by stomach contents in contact with esophageal mucosa
- If no response to GERD treatment, next step is motility testing (diffuse esophageal spasm, nutcracker esophagus)

REMINDER/WARNING: By definition, non-cardiac chest pain implies that cardiac causes have been ruled out
Reflux related NCCP – diagnostic tests for GER

- 24-hr pH monitoring: insufficient; has the capability to detect reflux but may not establish a link between chest pain episodes and reflux events
- OGD: Limited role; only 10-25% of these patients have endoscopic evidence of esophagitis
- Empiric trial with PPI therapy: has emerged as the first-line diagnostic tool in the evaluation of non-cardiac chest pain once cardiac etiology has been ruled out
  - 81-95% shown to improve with PPI bd
  - Empiric PPI approach is cost effective and results in cost savings ($454 per patient)
Reflux-related NCCP: best management

- In patients without warning symptoms (weight loss, anemia, dysphagia), use an empiric course of PPI until symptoms remit, and then taper to lowest dose that controls symptoms.

- Other diagnostic testing (manometry, pH monitoring/impedance) reserved for those who continue to be symptomatic despite initial empiric trial of PPI therapy.
GER is a common condition affecting many patients in different parts of the world

- Usually presents with classic symptoms: heartburn, reflux
- In some, it can also present with extra-esophageal manifestations: chronic cough; laryngitis; asthma; chest pain
- Commonly used tests (OGD, pH/impedance studies) are not very useful due to poor sensitivity and specificity
- In contrast, empiric PPI trials are effective and cost-effective
- However, patients may require long-term treatment to establish effectiveness
- Poor response to PPI may be an important indicator for non-GER causes of symptoms and should initiate search for other causes
Summary & Conclusions

- Effective diagnosis & management of extra-esophageal GERD does not usually require an Endoscopy Unit or a Motility Lab
- GPs at the forefront
- Gastroenterology can help