Pathology of the GI Tract: Esophagus

MHD Course
Tuesday, 1/2/2018 - 9:30 am
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Lecture Objectives

- Review and understand the function and histology of the normal esophagus
- Know and understand the clinical features of Atresia (congenital abnormality of the esophagus) and its associations/complications
- Know and understand the clinical and pathologic features of the following entities:
  - Achalasia, Scleroderma, Pomeroy-Vinson Syndrome, Mallory-Weiss Tear, Boerhaave Syndrome
  - Know and understand the clinical and pathologic features of Hiatal hernias and esophageal varices
- Know and understand the clinical and pathologic features of esophagitis and its various underlying etiologies:
  - GERD, Esophagitis, Infectious esophagitis (Candida, Herpes, CMV), Chemical/Ph esophagitis
- Know and understand the clinical and pathologic features of Barrett's Esophagus, including endoscopic and histological criteria for diagnosis
- Know and understand the two most common types of malignancies associated with the esophagus, as well as the pathology and risk factors associated with them:
  - Squamous cell carcinoma
  - Adenocarcinoma

“The Food Tube”

- Hollow muscular tube/conduit promoting the transfer of food and liquid from the oral cavity to the stomach via peristalsis (and gravity assist)
- Lined by squamous mucosa that effectively acts as a barrier to “passive” absorption of nutrients into the blood before reaching the stomach
- LES prevents reflux of gastric contents/acid back into the esophagus

http://www.meddean.luc.edu/lumen
The esophagus can be bypassed via either a nasogastric tube or a PEG tube.

Normal Gross Morphology
Clinical-Pathological Entities of the Esophagus

Atresia and Tracheoesophageal Fistula

- Atresia is a rare congenital defect affecting up to 1/4500 US births
  - It is composed of a discontinuous segment of esophagus associated with a terminal blind pouch proximally and a lower blind pouch leading to the stomach distally
  - Can be either short gap or long gap discontinuity (short gap is easier to treat surgically)
  - Typically associated with a fistula between the trachea and the lower discontinuous segment
- About 1/3 of afflicted babies exhibit other congenital abnormalities
  - Cardiac, GI, GU and Neurological anomalies
- Regurgitation shortly after birth with poor feeding
  - Complications include aspiration pneumonia, paroxysmal suffocation and fluid/electrolyte disturbances
  - Can be life-threatening if not immediately recognized
Achalasia

- Failure of the LES "to relax" due to degeneration of the myenteric plexus with muscle denervation and increased LES resting tone
  - Odynophagia as a result of swallowing against a closed LES
  - Impaired peristalsis with progressive dysphagia
  - Barium swallow study shows dilatation of the esophagus with "Bird’s beak deformity"
  - Unknown etiology
    - Autoimmune or viral etiologies are suspected
  - Nocturnal regurgitation that can lead to aspiration pneumonia
  - Increased risk of carcinoma (especially squamous cell carcinoma)
  - Secondary achalasia
    - Trypanosoma cruzi infection (Chagas disease)
    - Mass effect from extrathoracic tumors
    - Diabetes, sarcoidosis, amyloidosis etc…

Scleroderma

- Autoimmune mediated chronic connective tissue disease
  - Rare disease more common in middle aged women
  - Localized or systemic involvement
    - Systemic is further divided into a limited form (CREST) or widely diffuse form (systemic sclerosis)
  - Inflammatory damage of skin, connective tissue and blood vessels with subsequent progressive fibrosis (hardening)
  - Organ involvement occurs in the systemic form
    -GI involvement is often present with the esophagus being the most common site
    - Progressive dysphagia due to damage of esophageal tissues and fibrosis
    - Acid reflux
    - Secondary Barrett’s can occur in long term
    - Aspiration
Plummer-Vinson Syndrome

- Rare and typically affects middle aged women
- Triad of “dysphagia, iron deficiency anemia, and esophageal webs”
- May or may not be associated with glossitis and stomatitis/angular cheilitis
- Web like fibrous structures in the esophagus
- Increased risk of squamous cell carcinoma
- Balloon dilation of webs for relief of dysphagia

Hiatal Hernia

- Occurs as a result of separation/widening of the diaphragmatic crura leading to herniation of the GEJ and/or proximal stomach into the chest cavity
- Exact cause unknown
  - Thought to be associated with increased abdominal pressure
    - Obesity
    - Pregnancy
- 2 main types
  - Sliding
  - Rolling (Paraesophageal)
- Complications
  - Strangulation/obstruction with or without perforation, bleeding
  - GERD

Mallory-Weiss Tear and Boerhaave Syndrome

- Can be very painful
- Hematemesis (which may be massive)

**Mallory-Weiss Tear**:
- Often seen in alcoholics and bulimics
- Longitudinal mucosal lacerations/tears occurring at the GEJ in association with severe retching and vomiting
- Generally does not require major surgery unless associated with significant bleeding
- Hiatal hernia is thought to be a possible predisposing factor
**Boerhaave Syndrome:**

- Distal esophageal transmural rupture in association with violent retching
  - Pneumomediastinum
  - Surgical emergency
  - Catastrophic/fatal if not treated promptly

**Esophageal Varices**

- Common in cirrhotic patients (portal hypertension with hepatosplenomegaly)
- Portal hypertension leads to diversion of portal blood flow through the veins of the stomach and into the plexus of the lower esophageal veins
  - Leads to dilated submucosal veins in the lower 1/3 of the esophagus, GEJ and proximal stomach
  - Appear as mucosal “bumps” on endoscopy
- Can become markedly dilated
  - Usually asymptomatic until rupture occurs
  - May lead to life threatening massive bleeding episode with up to 50% mortality during the 1st bleed
  - Survivors will likely develop subsequent bleeding episodes
- Surveillance EGD’s

**Esophageal Varices**

- [Image of varices]

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[Image of CT scan showing Boerhaave Syndrome]

[Image of esophageal varices with endoscopy images]

[Image of endoscopy showing esophageal varices]

[Image of portal hypertension and hepatosplenomegaly]

[Image of varices in the stomach and lower esophagus]

[Image of mucosal “bumps” on endoscopy]
Esophagitis

- Inflammation of the esophageal mucosa
  - Secondary to a physical, chemical or biological causes
    - GERD
    - Infectious etiologies (Fungal, HSV, CMV)
    - Eosinophilic Esophagitis
    - Others (ingestion of caustics, pills/medications/chemotherapy)
  - Variable hyperemia/erythema on EGD

General Symptoms

- Chest pain/heartburn (retrosternal burning pain)
  - Crucial to r/o cardiac causes of chest pain in the acute setting
- Dysphagia (difficulty swallowing)
- Odynophagia (Pain with swallowing)
- Hematemesis
- Coughing and hoarseness

Reflux Esophagitis (GERD)

- Reflux of gastric acidic contents into the esophagus
  - Causes:
    - Incompetent LES (decreased tone)
    - Hiatal hernia
    - Delayed gastric emptying/increased gastric volume
    - Increased pressure with forced regurgitation through LES
  - Mucosal inflammation/injury
  - Complications
    - Ulceration and bleeding
    - Barrett’s Esophagus
Variable inflammation:
- Lymphocytes
- Plasma cells
- Neutrophils
- Scattered eosinophils
- Basal cell hyperplasia
- Elongation of vascular papillae

Infectious Esophagitis

Fungal Esophagitis (Candida)

- White mucosal plaques containing fungal structures, neutrophils and squamous debris
Herpes (HSV) Esophagitis

- Punched out ulcers/craters seen on EGD
- Multinucleated cells with viral nuclear inclusions (nuclear molding and nuclear chromatin margination)

Cytomegalovirus (CMV) Esophagitis

- Linear ulcers on EGD
- Viral "owl eye nuclear inclusions" +/- smaller cytoplasmic inclusions

Eosinophilic Esophagitis

- Increasing in incidence
- Usually associated with some type of food allergen exposure
- Occurs in adults and children (often atopic patients)
  - Dysphagia
  - Food impaction (meat common)
  - +/− GERD like symptoms
  - Infants/toddlers often display feeding intolerance
- EGD
  - Esophageal rings/linear furrows +/- white mucosal discolorations present
  - Chronic inflammatory injury with scarring and narrowing of the esophageal lumen
- Treatment
  - Dietary restrictions to prevent exposure to underlying food allergens (if identified)
  - Steroids for severe/recalcitrant cases
  - Typically unresponsive to GERD therapy alone (PPI's etc.)
Chemical/Pill Esophagitis

- Chemical/Mucosal irritants
  - Alcohols
  - Corrosives
  - Excessive hot fluid consumption
  - Smoking

- Pill/Medication
  - Typically occurs in patients that take their pills with little water and go to bed shortly thereafter
  - Awakens with sudden onset of odynophagia
  - EGD with shallow ulceration present presumably where pill was in resting contact with the mucosa
  - Increased risk with esophageal motility disorders
  - Typical culprits: NSAIDs, Bisphosphonates, Antibiotics, Potassium

Barrett’s Esophagus

- Complication of long-standing GERD
  - Occurs in ~10% of symptomatic patients 40-60 years old, M>F
  - Chronic acid reflux injury leads to “intestinal metaplasia”
    - Squamous epithelium is replaced by “salmon” colored metaplastic epithelium on EGD
  - Long segment > greater than 3 cm
  - Short segment < less than 3 cm
  - Diagnosis requires both endoscopic evidence of “salmon colored mucosa” and histological evidence of “intestinal metaplasia/goblet cell metaplasia”
  - Considered a pre-malignant condition and is the single most important risk factor for adenocarcinoma
  - Etiology of BE is unclear and it is thought to be secondary to alteration of stem cell differentiation

Endoscopic appearance of Barrett’s Esophagus

- Normal GEJ
- Barrett’s esophagus
Barrett's Esophagus Histology

- Clonal proliferation with associated cytological and architectural changes
- Some patients with newly diagnosed HGD may already have an adjacent occult adenocarcinoma and thus treatment for HG dysplasia is more aggressive (EMR)

Barrett's Esophagus with Dysplasia

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Esophageal Neoplasms and Tumors

- Benign Tumors
  - Most common: leiomyoma
  - Benign smooth muscle proliferation forming a nodule
  - Fibroma, Lipoma, Hemangioma
  - Squamous papilloma/condyloma

- Malignant Tumors
  - Squamous cell carcinoma
  - Adenocarcinoma
  - Others…derived from underlying neoplastic cell type (as above)
Squamous Cell Carcinoma

- More common worldwide than adenocarcinoma
- M:F ratio varies in different areas of the world (2-20:1)
- African-Americans > Caucasian Americans
- More common in rural and underdeveloped areas
- Associated risk factors:
  - Diet and lifestyle
    - Hot tea, alcohol, smoking
  - Underlying Esophageal disorders
    - Plummer-Vinson Syndrome
    - Achalasia
- Often insidious onset
  - Proximal 2/3 of esophagus with progressive dysphagia and weight loss
  - Often advanced at initial diagnosis with 9% overall 5-year survival

Associated molecular abnormalities
- P53 point mutations
- P16/INK4a mutation
- Stepwise acquisition and accumulation of genetic alterations (advancement of dysplasia to malignancy)

EGD and Resection: Squamous Cell Carcinoma
Squamous Cell Carcinoma: Histology

- Infiltrating islands of malignant squamous cells
- Can be well to poorly differentiated
  - More well differentiated variants tend to show squamous islands with abnormal keratinization and “keratin pearls”

Adenocarcinoma

- Malignant epithelial tumor with glandular differentiation
- Marked rise in number of cases over the past few decades (especially in Western countries)
  - Currently approximately 1/3 of esophageal cancers diagnosed in United States
  - < 3% of esophageal cancers before 1970
  - More common in Caucasian men; >40
  - BE (increased risk) with dysplasia (significantly increased risk)
  - Occurs in lower 1/3 of esophagus/GEJ
  - Long latency period with accumulated genetic changes
    - Dysplasia is a very important step in progression to malignancy
    - Once present, requires close clinical follow-up
    - Serial EGDs with targeted biopsies
- Prognosis
  - < 25% overall 5-year survival (more advanced disease at presentation)
  - 80% if diagnosed early and confined to the mucosa/submucosa

PS3 - present at early stages
  - Amplification of c-ERB-B2, cyclin D1, cyclin E
  - Mutation of retinoblastoma tumor suppressor gene
  - Allelic loss of the cyclin dependent kinase inhibitor p16/INK4a
  - Hypermethylation of p16/INK4a
  - Increased epithelial expression of tumor necrosis factor (TNF) and nuclear factor (NF)-κB dependent genes
EGD and Resection specimen: Esophageal Adenocarcinoma

Histology: Esophageal Adenocarcinoma

Questions?