Core Lecture:
Small Bowel Physiology and Motility Disorders

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Case Presentation

- 43 yr old female presented with multiple hospitalizations for nausea, abdominal distension, vomiting over past 8 years
- Can eat after discharge, but readmitted every month
- Weight loss of 90 lbs over several yrs
- Diarrhea 10-12 x/day
Case Presentation (cont.)

- PMH
  - Polymyositis, dermatomyositis, scleroderma
- Outside work-up
  - Normal EGD
  - Gastroparesis by GET
  - Abd CT no neoplasm
  - No SBO by UGI-SBFT
- Refractory to reglan, tegaserod, erythromycin
- J-tube placed for nutrition
Case Presentation (cont.)

• PE
  – Cachetic 85 lbs, telangectasia, percussion dullness on lung exam, abdominal distension
• NG suction 3.8 liters in 1 day
• Labs
  – Normal CBC
  – CPK 780, TSH 7.1, albumin 1.4, TP 4.3
  – Normal liver tests, PT, PTT, Cosyntropin test
Case Presentation (cont.)
Case Presentation (cont.)
Case Presentation (cont.)
Case Presentation (cont.)

- EGD
  - Loss of duodenal folds
  - Biopsy non-specific inflammation
  - Immunohistochemical stain negative
  - Congo red negative
Case Presentation (cont.)

• In hospital
  – Tolerated J-tube isosource 85cc/hr at night
  – Liquids only, no solid foods by mouth
  – Octreotide 200 μg sc bid
  – Reglan 10 mg liquids q6
Case Presentation (cont.)

• 6 weeks later
  – Diarrhea 6x/day
  – Gained 5 pounds

• To start
  – Cipro 500 mg bid x 21 days
  – Domperidone
  – ↑ Octerotide dose
Core Lecture: Small Bowel Physiology and Motility Disorders

• Case presentation of chronic intestinal pseudo-obstruction
• Normal physiology
• Pathophysiology of small bowel motility disorders
• Clinical manifestation
• Diagnostic evaluation
• Treatment
# Differences in the GI Tract

<table>
<thead>
<tr>
<th>Embryonic origin</th>
<th>ANS dependence</th>
<th>ENS dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharynx to mid duod.</td>
<td>Foregut</td>
<td>+++</td>
</tr>
<tr>
<td>Small bowel to prox. colon</td>
<td>Midgut</td>
<td>++</td>
</tr>
<tr>
<td>Colon to rectum</td>
<td>Hindgut</td>
<td>+</td>
</tr>
</tbody>
</table>

ANS (autonomic nervous system); ENS (enteric nervous system)
Enteric Nervous System

Vagus Nerve

- Mesentery
- Perivascular Sympathetic Nerve
- Muscularis Externa (longitudinal)
- Muscularis Externa (circular)

Submucosal Plexus

Myenteric Plexus

Subepithelial Plexus

- Muscularis Mucosa
- Submucosa
- Villus
- Intestinal Lumen
- Serosa
- Deep Muscular Plexus
Enteric Nervous System

- Most important control in GI motility
- Provided frequency and direction of peristalsis
- Can function independently of CNS
- Output is modulated by CNS, autonomic system, peptides, glucose, etc.
Enteric Nervous System

Excitatory motor neuron (Ach, 5HT)

Interstitial cell of Cajal

Musculature

Inhibitory motor neuron (NO, VIP)
Interstitial Cells of Cajal

Gastric fundus

Small bowel

ICC staining
Slow Wave from Interstitial Cells of Cajal
Electromechanical Association

Food, vagal input, peptides, distension

Spike potentials

Contraction

Action potential threshold

Slow Waves (ICC)

Voltage

Time
Enteric Nervous System Controls GI Electrical Rhythm

**Stomach**
(3/min)

**Small intestine**
(8-12/min)

**Colon**
(3-6/min)

30 sec

-30 mV
-70 mV
-22 mV
-62 mV
-41 mV
-81 mV
Normal Fasting Motor Patterns: Migratory Motor Complex

<table>
<thead>
<tr>
<th>Location</th>
<th>Pattern Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antrum</td>
<td>Irregular</td>
</tr>
<tr>
<td>Duodenum 1</td>
<td>Maximal propulsion</td>
</tr>
<tr>
<td>Duodenum 2</td>
<td>Quiescent</td>
</tr>
<tr>
<td>Jejunum 1</td>
<td>Phase II</td>
</tr>
<tr>
<td>Jejunum 2</td>
<td>Phase III (activity front)</td>
</tr>
<tr>
<td>Jejunum 3</td>
<td>Phase I 10 min.</td>
</tr>
</tbody>
</table>

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Fasting Migratory Motor Complex
“Intestinal Housekeeper”

• Most powerful propulsion
• Maximal electrical-mechanical association at phase 3
• Function of enteric nervous system
• Important for
  – Transit of indigestible solids
  – Prevention of bacterial overgrowth
Normal Postprandial Motor Patterns

- Duodenum 1
- Duodenum 2
- Jejunum 1
- Jejunum 2
- Jejunum 3

Meal

30 min.

50 mmHg

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Postprandial Motor Patterns

- Contractions of variable frequency, amplitude, propagation
- Depends on caloric content
- Initiated by vagal reflex
- Important for mixing
ENTERIC MOTOR NEURONS ARE FINAL PATHWAYS FROM THE ENTERIC NERVOUS SYSTEM TO THE GASTROINTESTINAL MUSCULATURE

**Inhibitory Motor Neurons**
- VIP (-)
- IJP
- NO (-)

**Excitatory Motor Neurons**
- Sub P (+)
- EJP
- ACh (+)

Muscle
Enteric Nervous System Controls GI Peristalsis

Excitatory Motor Neuron

5-HT₄ Receptors

5-HT

Enterochromaffin Cells

Sensory Neuron

5-HT, NO, Ach receptors (stretch, food, etc.)

Inhibitory Motor Neuron

VIP, NO

Contraction

Relaxation

Ach, 5HT, SP
# Diagnostic Testing for the Small Bowel Motility Disorders

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visualize lumen to exclude other diseases</td>
<td>Enteroscopy, UGI/SBFT, capsule endoscopy</td>
</tr>
<tr>
<td>Vasculature</td>
<td>CT-angiogram</td>
</tr>
<tr>
<td>Look for dilated small bowel</td>
<td>KUB, UGI/SBFT, CT scan</td>
</tr>
<tr>
<td>Small bowel transit</td>
<td>SBFT, small bowel scintigraphy, capsule endoscopy, smart pill</td>
</tr>
<tr>
<td>Bacterial overgrowth</td>
<td>H2 breath test, culture of small bowel aspirate</td>
</tr>
<tr>
<td>Motor patters</td>
<td>Antroduodenal or SB manometry</td>
</tr>
<tr>
<td>Neuromuscular structures</td>
<td>Full thickness biopsy</td>
</tr>
</tbody>
</table>
KUB

- Dilated small bowel
- Air-fluid levels may not be present
UGI/SBFT

- Look for small bowel dilation and diverticulum
- Rule out obstruction
- Segmental involvement
UGI-SBFT (Incomplete Malrotation)
Abdominal CT

- Small bowel dilation
- Neoplasm

Patient with ovarian cancer and radiation
CT-Angiogram
(Celiac Artery Stenosis – Median Arcuate Ligament Syndrome)
H2 Breath Testing with Lactulose

- Stomach
- Small bowel
- Colon

- Bacteria overgrowth
- Normal
- Non-diagnostic

Lactulose given

Time (hrs)

H2 content (ppm)
H2 Breath Testing with Glucose

- Time (hrs): 0, 0.25, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2
- H2 content (ppm): 0, 20, 40, 60, 80, 100

- Stomach
- Small bowel
- Colon

Bacteria overgrowth

Glucose given

Normal
# Accuracy of Tests for Small Intestinal Bacteria Overgrowth

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>Abnormal test</th>
<th>Sensitive*</th>
<th>Specificity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactulose breath test</td>
<td>Double peaks of &gt;20 ppm H₂ above baseline</td>
<td>17 – 68%</td>
<td>70 – 100%</td>
</tr>
<tr>
<td>Glucose breath test</td>
<td>&gt;12 ppm H₂ above baseline</td>
<td>41 – 100%</td>
<td>67 – 98%</td>
</tr>
</tbody>
</table>

*Gold standard: >10⁵ aerobes or anaerobes CFU/ml of jejunal aspirate*
Antroduodenal Manometry
Indication for Small Bowel Manometry

- Refractory nausea and vomiting
- Unexplained nausea and vomiting
- Intolerance of jejunal feeding
- Considering colectomy for colonic inertia
Normal Fasting Antroduodenal Manometry

3x / minute

12x / minute

Migratory Motor Complex
Normal Postprandial SBM
Abnormal Fasting SBM: Intrinsic (Enteric) Neuropathy
Abnormal Postprandial SBM: Extrinsic (Vagal) Neuropathy
Abnormalities Diagnosed by Small Bowel Manometry

- Intrinsic Neuropathy (enteric nervous system)
  - Fasting pattern: abnormal MMC
- Extrinsic Neuropathy (vagal neuropathy)
  - Fed pattern: impaired postprandial response
- Myopathy
  - Low contraction pressures
Smartpill® Wireless Diagnostics Capsule

- Wireless measurements:
  - Pressure
  - pH
  - Temperature
Smartpill® Wireless Pressure and pH Tracing

From University of Louisville
Full-Thickness Biopsy

- H&E for inflammatory infiltrate
- Trichrome stain for fibrosis
- Congo red for amyloidosis
- Silver stain for enteric neurons
- C-kit immunochemical stain for interstitial cells of Cajal
- Viral culture
Scleroderma
Reactive Hyperganglionosis
Myenteric Neuritis of the Enteric Nervous System

De Giorgio et al. Am J Gastroenterol 2002;97:2454
Small Bowel Motility Disorders

- Slow transit
  - Chronic intestinal pseudo-obstruction
  - Bacterial overgrowth
  - Post-surgical dysmotility
- Fast transit
  - Dumping syndrome
  - Post-vagotomy diarrhea
Chronic Intestinal Pseudo-Obstruction (CIP)

- Rare in adults
- Symptoms and signs of intestinal obstruction
- No mechanical obstruction
- Primary disorder of small bowel, but can involve anywhere in the GI tract
Primary CIP

• Familial
  – Familial visceral myopathies
    • type 1 (AD) megaduodenum & urinary involvement
    • type 2 (AR) mitochondrial defect, ophthalmoplegia & peripheral neuropathy
    • type 3 (AR) diffuse GI involvement
  – Familial visceral neuropathies
• Sporadic
  – Visceral myopathies
  – Visceral neuropathies
    • Localized Hirschsprung’s disease

Secondary (Acquired) CIP

• Connective tissue disorders
  – Scleroderma, MCTD, SLE, polymyositis, dermatomyositis

• Neuromuscular disorders
  – Paraneoplastic
  – Amyloidosis
  – Muscular dystrophies (myotonic, Duchenne, and oculopharyngeal muscular dystrophies)

Secondary (Acquired) CIP

• Endocrine disorders
  – Hypothyroidism, hypoparathyroidism
• Infections
  – Trypanosoma cruzi, CMV, EBV
• Myenteric ganglionitis
• Radiation
• Paraneoplastic
• Miscellaneous
  – Medications (opiates, tricyclic antidepressants, antiparkinson medications, anticholinergics)

Paraneoplastic GI Motility Syndrome

• Cancer antigens mimicking neuronal tissues.
• Myenteric plexus infiltrated by lymphocytes and plasma cells.
• Cancers
  – Small cell lung cancer (80%), breast, ovarian, multiple myeloma, Hodgkin’s lymphoma.
• GI symptoms can precede diagnosis of cancer.
Paraneoplastic GI Motility Syndrome: Anti-Hu Antibody* Against Enteric Neurons

*Antinuclear neuronal antibodies (ANNA)
Clinical Manifestations of CIP
Depends on Primary GI Involvement

• Small bowel: SBO, bacteria overgrowth
  – nausea, vomiting, high-output NG suction, abdominal distension, diarrhea, weight loss
• Stomach: gastroparesis
  – nausea and vomiting
• Esophagus: achalasia
  – dysphagia, regurgitation
• Colon: colonic inertia
  – constipation
Management Goals for CIP

• Confirm the diagnosis
• Identify the etiology
• Look for coexisting motility dysfunction
• Restore proper nutrition and fluid balance
• Relieve symptoms and improve motility
Diagnostic Criteria for CIP

- No uniform criteria in adult CIP
- Suggested criteria
  1. Recurrent symptoms of SBO
  2. Dilated small bowel
  3. No mechanical obstruction
- Diagnosis should not be based solely by manometry
Small Bowel Manometry

- Alternative test for vagal neuropathy
- Should not diagnose CIP solely by SBM
Treatment for CIP

- Nutrition
- Pharmacologic
- Surgical
- Intestinal transplant
Nutritional Support for CIP

- Similar to gastroparesis
- Behavior modification for aerophagia
- Enteral nutrition
  - Nasojejunal feeding before percutaneous
  - Isosmotic, low in fat, low in fiber
  - Nocturnal enteric feed
- Parenteral nutrition
Complications of TPN

• Line infections
• Selenium and chromium deficiencies
• Hepatotoxicity
  – Biliary sludge
  – Steatosis
  – Cholestasis
  – Cirrhosis
Pharmacologic Therapy for CIP

- Anti-emetic
- Prokinetics
  - Anti-dopaminergic (metoclopramide, domperidone)
  - Acetylcholine agents (bethanechol, and neostigmine)
  - Motilin agonists (erythromycin)
  - 5HT4 agonists (tegaserod)
- Antibiotics for bacteria overgrowth
Octreotide for Scleroderma

• 6 normal subjects
  – Octreotide (10 μg sc) increased # of MMC from 1.5 to 4.1 over 3 hrs

• 5 patients with scleroderma + bacterial overgrowth
  – Octreotide (100 μg sc) increased # MMC from 0 to 3.6 over 3 hrs
  – Octreotide (50 μg sc qhs) improved bacteria overgrowth by H2 breath test
  – ↓ nausea, bloating, and abdominal pain

Soudah et al. NEJM 1991;325:1461.
Surgical Intervention

• Full-thickness biopsy
• Enteral feeding tube
• Resection of dilated segments is controversial
Intestinal Transplantation

- Treatment of last resort
- Indications
  - TPN failure
  - Loss of vascular access
  - TPN associated hepatotoxicity
- 61% of transplant are <18 yrs old
Intestinal Transplantation

- Transplant organ
  - Isolated intestines (41%)
  - Intestines with other viscera, such as liver or pancreas (59%)
- At 3 yrs
  - Graft survival 71%
  - Patient survival 88%
- Survival without TPN 81-96%
Conclusion for CIP

- Rare in adults
- Diagnostic criteria
  - Symptoms of SBO
  - Dilated small bowel
  - Exclude mechanical obstruction
- Look for etiology and coexisting dysmotility
- Management
  - Restore proper nutrition and fluid balance
  - Relieve symptoms
  - Improve motility
  - Treat complications