The Role of Capsule Endoscopy Today: It's Not Just for Bleeding Anymore

ACG Annual Course
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October 2012

Capsule Endoscopy-Clinical Applications

- GI bleeding
  - Obscure/Overt
  - Iron def anemia of unknown origin
- Crohn’s disease
  - Suspected
  - Known
- Small bowel tumors/ulcers
- Malabsorption syndromes
  - Celiac disease
    - Evaluation or extent of the disease
Pediatric Applications

- FDA cleared for pediatric use - 10 yrs and older
  - Obscure GI Bleeding
  - Early diagnosis Crohn’s Disease
  - Celiac disease
  - Polyposis syndromes
  - Necrotizing enteritis
  - Peutz Jegher syndrome
  - Malabsorption disorders

What is the question we all ask ourselves when reading a capsule?

- Is this a real finding or is this in my imagination?

- You have to admit there is a great deal of imagination at times that goes in to interpreting a capsule study
Limitations of Capsule Endoscopy

1. No redos
   – Abnormalities may be missed due to:
     • rapid transit of the capsule
     • blurred, uninterpretable images
     • transit is so slow that the capsule examines only part of
       the small intestine before the battery fails
2. Pathology may only be visible on one image
3. Normal mucosa may appear abnormal
4. There is no biopsy confirmation of your finding

Case 1

• 67 year old male with a long standing history of osteoarthritis involving the cervical spine and hands
• In the last 2 years, he has developed intermittent melenic stools and postprandial periumbilical cramping. Labs reveal an iron deficiency anemia.
• EGD and colonoscopy was performed and is negative for a bleeding source. A capsule endoscopy is performed and although the patient is currently asymptomatic, the capsule is not identified entering the colon. Repetitive views of the following image are identified.
What should be the next step in the management of this patient?

a. Start course of corticosteroids.
b. Balloon enteroscopy should be performed.
c. Obtain an abdominal x-ray.
d. Administer prokinetic agent.
Retention

- **Definition**
  - Capsule caught proximal to an intestinal narrowing for at least **TWO WEEKS**
  - Removal requires medical, endoscopic or surgical intervention
  - Can be permanent

The Real Definition of Capsule Retention
Retention

• Causes
  – NSAIDs
  – Crohn’s disease
  – Tumors
  – Radiation enteritis
  – Post surgical

• How often does this occur?
  • Obscure GI bleeding - 1.4% (15/1089)
  • Established IBD--5-13%
  • Suspected IBD--1%
  • Healthy controls--0%
  • Suspected SBO--21%

Patency System

Patency Capsule

Handheld Patency Scanner

TesTag

Dimension - Ø11 x 26 mm
Weight - 3.3gr
12 Month Expiry

Retention

• How do we diagnose it?
  – Capsule images
  – Localization picture
  – Failure to see the colon
Retention

- Suspect by capsule images
  - Clear obstructing lesion
  - Repetitive views
  - Excessive lumenal contents
Retention--Ulcerated Stricture

- If diagnosis is Crohn’s disease:
  - Medical management
    - generally need steroid/IM/biologic trial
  - Surgical--rarely emergent/urgent
  - Endoscopic retrieval

Retention--Mass

- If retention occurs in video with findings suggestive of mass/tumor
  - Cross sectional imaging
  - Endoscopic/Surgical evaluation
Retention in our patient was a…

NSAID-related stricture

• If NSAID/diaphragm stricture suspected
  – d/c nsaid’s and observe
  – endoscopic/surgical intervention if needed

NSAID Enteropathy

• The prevalence of NSAID enteropathy is underestimated.
• Varied findings exist such as small erosions or minor mucosal breaks to more severe stricturing diaphragms
• The risk of capsule retention in diaphragmatic disease is fairly high, although complete obstruction is rare.
• Most patients with capsule retention are asymptomatic.
What should we do with our patient?

- As the patient is asymptomatic, an AXR should be obtained at 2 weeks and followed until capsule passage.
- If obstructive signs/symptoms arise a balloon enteroscopy can be attempted to retrieve capsule and balloon dilate the stricture.

Case 2

- A 48 year old female with a history of iron deficiency anemia and 3 prior episodes of obscure gastrointestinal bleeding
- Now presents with 3 days of melena
History

• PMH: HTN, GERD
• PSH: Hysterectomy
• Meds: Zocor, Nexium (no NSAIDs)
• All: NKDA
• Soc Hx: No tobacco/etoh/drugs
• Fam Hx: colon cancer (brother)

2007
  – Anemia/Hgb 6.7
  – Colonoscopy: blood seen from terminal ileum to rectum without definite lesion
  – EGD normal

2008
  – Melena
  – EGD: gastritis
  – Colon: no source of bleeding identified

2009
  – Presents with melena
  – Capsule endoscopy
Case 2 (Video 1)

Case 2 (Video 2)
Capsule endoscopy in summary...

- Umbilicated submucosal mass mid ileum
- Large ulcerated mass in distal ileum

Differential Diagnosis

Submucosal Mass/Tumor
- Adenocarcinoma
- Neuroendocrine tumors/Carcinoid
- Lymphoma
- Sarcoma/GIST
- Metastatic lesions

Ulcer
- Crohn’s Disease
- NSAIDs

What would you do?
**What would you do next?**

a) Enteroscopy with biopsy  
b) CTE/MRE  
c) Exploratory laparotomy  
d) Treat for Crohn’s

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**Balloon Enteroscopy**

Retrograde  
- 3 sessile 6-8 mm submucosal nodules in the distal, mid, and proximal ileum (biopsied)
Balloon Enteroscopy

- Retrograde
  - Ulcerated submucosal mass in the mid ileum
  - Distal ileal ulcerated submucosal 1.5 cm polypoid mass

Chromogranin stain
CT Abdomen/Pelvis

2 cm mesenteric mass

Octreotide Scan

Abnormal activity in the pelvic mesentery
Surgery

- Small intestine, appendix, and lymph node resection
  - 6 small intestine carcinoid tumors
    - Invading through the muscularis propria (T3)
    - Lymphatic invasion present
  - 3/22 lymph nodes positive (N1)
  - Negative margins
  - Tumor cells positive for **chromogranin** & **synaptophysin** by immunostain

Small Bowel Neoplasms in Patients Undergoing Video Capsule Endoscopy

- 29 European center
- 5,129 VCE patients – multiple indications
  - 124 (2.4%) small bowel tumors identified
    - 108 (87%) Obscure GI bleeding
    - 112 primary, 12 metastatic
      - GIST 32%
      - Adenocarcinoma 20%
      - Carcinoid 15%

Rondonotti. Endoscopy 2008
Age of Patient is an Important Factor in Bleeding Source

• Less than 50 years old:
  – Think tumors: Leiomyomas, carcinoids, lymphoma, adenocarcinoma
  – Meckels, Dieulafoy’s, Crohn’s
• Over 50 years old:
  – Angiodysplasias


Case 3

• 68-year old female was transferred for evaluation of obscure GI bleeding
• Initial presentation in 2004:
  – Hematochezia and melena
  – Required 8 units of PRBC
  – Patient was taking NSAIDs for osteoarthritis
  – Work-up at that time:
    • EGD: small hiatal hernia
    • Colonoscopy: diverticulosis
  – Bleeding attributed to NSAIDs
    • Patient discharged and sent home
Case 3

- Over next 6 years:
  - 8 separate admissions for GI bleeding despite strict avoidance of NSAIDs
  - Presented with hematochezia and melena at each time of admission
    - Each would spontaneously stop
- Total transfusion requirement >100 units of blood

Case 3

- Extensive work-up:
  - 8 EGDs
  - 6 colonoscopies (at multiple centers)
  - 4 bleeding scans
  - 1 Meckel’s scan
  - 2 angiograms
  - 1 diagnostic laparoscopy with cholecystectomy for incidentally noted cholecystitis
  - 2 push enteroscopies
  - 1 capsule endoscopy
Case 3

• Last capsule endoscopy 2007
  – “Normal” but incomplete luminal visualization due to excessive contents
• On this transfer, patient had 6 units of blood and still had melena and maroon stool
• EGD/colonoscopy at outside hospital: negative
• Colonoscopy: blood in right colon and TI

Case 3

• Differential diagnosis of “really obscure GI bleeding”
  – Missed upper source
    • Cameron ulcers, GAVE, AVM, Dieulafoy, hemosuccus pancreaticus, hemobilia
  – Missed colonic source
    • Neoplasm, diverticulosis, AVM
  – Small bowel source
    • Meckels, AVM, Dieulafoy, IBD, neoplasm
• What would you do next?
  – Repeat EGD/colonoscopy
  – Deep enteroscopy (antegrade/retrograde)
  – Intra-operative enteroscopy
  – Repeat capsule upon discharge
  – Repeat capsule while bleeding

Case 3
Case 3

- Plan was to repeat colonoscopy/retrograde BE, followed by IOE if bleeding continued
- Colonoscopy findings:
  - AVM in cecum immediately behind IC valve, seen initially only on retroflexion in caput
- APC
  - Significant bleeding that took 20 minutes to control
- No other ectasias noted in colon or ileum
Case 3

• Final diagnosis: cecal AVM
  – Patient discharged 2 days after procedure
  – Normalization of hemoglobin with normal iron studies > 1 year after procedure

• Take home points:
  – A second capsule endoscopy can be valuable
  – Maximize yield by performing study as close to bleeding episode as possible
  – Review the entire capsule video

Case 4: Is this the bleeding lesion?
Is this the reason for iron deficiency anemia?

Factors Associated with Identifying AVM at CE

- The most common location for small bowel AVMs is the jejunum.
- Age > 65 and the presence of AVMs on EGD predictive of jejunal AVMs but not ileal AVMs. There were no clinical characteristics predictive of ileal AVMs.
- AVMs on colonoscopy alone are not predictive of small bowel AVMs

Factors That Increase Yield of Finding Bleeding Lesion at CE

1. Obscure overt > Obscure occult bleeding
2. Performing capsule within 2 weeks of bleeding episode
3. Hb < 10g/dl
4. Bleeding for > 6 months
5. > 1 bleeding episode

Bresci G. J. Gastroenterol 2005;40:256-9

Case 5

• A 20 y/o M college student with no PMH presented with dark stools and decreased exercise tolerance.
• Hemoglobin 7.8
• EGD, Colonoscopy, Meckel’s Scan, Capsule Endoscopy, Small Bowel Series –unremarkable
• The patient was stable, did not require transfusion and was discharged.
Case 5 (continued)

- Two months later develops one day of lightheadedness and weakness
- Following day syncopized, found by family in pool of dark red blood per rectum
- On admission, Hb 7.5 with MCV 68; BUN 18, Cr 0.9
- Unremarkable EGD, Tagged RBC Scan, CT A/P with contrast
- Colonoscopy – red blood throughout colon

- Patient had no PMH or PSH
- Took no medications including NSAIDs, ASA or supplements
- No FH of GI cancers or IBD
- Patient admitted to binge drinking on weekends, no smoking, drugs
- PE: stable vital signs
- Well developed young man
- Pale
- No stigmata of liver disease
- Soft abdomen, NT/ND; no HSM
DDx Includes:

- Cameron’s erosions
- Angiodysplasia
- Dieulafoy’s lesion
- Meckel’s diverticulum
- Small bowel tumors/ulcers
- Crohn’s disease

Hospital Course

- Admitted to MICU
- Patient underwent unrevealing push enteroscopy to 120 cm
Normal Meckel’s Scan

Normal Bleeding Scan
Further Workup

- Patient’s bleeding stopped, remained stable
- Decision made to bolus patient with heparin
- Hemoglobin dropped 1 gram on heparin
- While patient was on a heparin drip, a repeat bleeding scan was performed

Positive Bleeding Scan
Capsule Endoscopy

- Colorectal surgery consulted, requested further localization
- Right hemicolectomy vs. ileocecal resection
- Capsule Endoscopy was performed
- Patient pre-medicated with Zelnorm and remained mobile
- Capsule spent 2 hours in stomach, battery died in jejunum
- No blood seen

Colonoscopy

- Colonoscopy performed while patient on heparin
- Old blood seen throughout colon, ileum normal without any blood seen
- Capsule found in cecum
Repeat Capsule Study

- Repeat EGD with capsule placement in last attempt to localize source prior to surgery
- Capsule endoscopically placed in to duodenum
- Heparin drip continued during capsule exam

Capsule Image

Active bleeding with suggestion of false lumen with ulcer in ileum
Surgical Exploration

• Patient taken immediately to OR for laparoscopic exploration

Diverticulectomy
Ectopic gastric mucosa with histopathologic features of Meckel's diverticulum
Post-op Course

• Post-op: uneventful recovery, discharged home post-op day 3.
• No recurrence of bleeding following surgery

Case 6

• 25 y/o male with 8 month history of diarrhea 5-6 times per day, crampy abdominal pain, iron def anemia, elevated sedimentation rate at 32 and 15lb weight loss. Denies NSAID use.
• Normal EGD, colonoscopy, duodenal biopsies and random colon biopsies. Capsule endoscopy to evaluate for possible Crohn's disease.
Case 6


Case 7

Is this IBD?

Unfortunately NOT

Is there a universal standard in diagnosing Crohn’s at CE?

Unfortunately NOT
How reliably do we diagnose Crohn’s disease by CE?

- There is no standard criteria for the diagnosis of Crohn’s disease with CE
  - Cut off of three ulcers of any size to establish a diagnosis of Crohn’s disease\(^1\) (most commonly used diagnostic criterion)
  - 4 or more ulcers, erosions, or a region with clear exudate and mucosal hyperemia and edema\(^2\)
  - Metaanalysis for CE in Crohn’s recognized the lack of a uniform method of categorizing findings\(^3\)

\(^3\)Triester SL. Am J Gastroenterol 2006;101:954-964

Sensitivity for Active SB CD

Differences did not reach statistical significance.

P > 0.05 CE compared with other tests

GIE 2008:68(2):255-66

ACG 2012 Postgraduate Course • October 20-21, 2012
Specificity for Active SB CD

In contrast to sensitivity, the specificity of CE compared to the other tests was significantly lower
P < 0.05 CE compared with other tests

GIE 2008:68(2);255-66

Can CE Predict Patients at High Risk of Postoperative Recurrence?

• Over 70% of patients with ileal resections for CD will have endoscopically visible recurrence within a year postoperatively.

• Inflammatory changes in the neoterminal ileum seen at ileocolonoscopy 3 months after surgery may be predictive of the likelihood of recurrence

Case 8

- 37 yo female with history of Crohn’s disease
- S/P ileocolonic resection for long segment stricturing disease 2 years ago
- Now presents with abdominal pain, frequent loss bowel movements and intermittent low grade fevers
Can CE Predict Patients at High Risk of Postoperative Recurrence?

Two series comparing CE to ileocolonoscopy (ILscopy) in pts s/p resection for CD

1. 32 pts 3-6 months post-op. ILscopy had sensitivity 90% and specificity 100%. CE sensitivity 70% and specificity 95%. CE did detect lesions proximal to reach of colonoscope in 2/3 pts.

2. 23 pts CE detected neoterminal recurrence in 62% whereas ILscopy detected only 25%.

   – All pts had side-to-side anastomosis -? Limits visualization


Can CE Predict Patients at High Risk of Postoperative Recurrence?

• Conflicting results regarding the value of CE in detecting postoperative recurrence compared with ileocolonoscopy

• However the clinical relevance of lesions proximal to the neoterminal ileum seen only by CE needs to be elucidated
“Garbage in = Garbage out”

Defining “suspected CD”

Whom do we test?

• Prefer to avoid working up every “IBS” patient for small bowel CD
• Presence of “hard data”
  – Anemia, weight loss, peri-anal disease, +Fhx, fevers, elevated ESR/CRP
  – children--growth failure
• Know the patient’s history – NSAID usage
What role does CE play in the Crohn’s disease patient?

1. Evaluates patients with clinical and/or biological suspicion of CD, who have normal results of radiological and traditional endoscopic procedures
2. Determines presence of small bowel involvement in patient with known colonic Crohn’s disease
3. Monitors for recurrence in patients s/p ileocolonic resection
4. Subclassifies patients with previously diagnosed “indeterminant colitis”

Case 9

• 22 year old female
• Medical history:
  – Recurrent episodes of colicky abdominal pain for several years
• Presentation:
  – Black tarry stools for one day
  – Physical examination significant for dark brown pigmented macules on lips
  – No family history of gastrointestinal malignancies, IBD, polyps
Case 9

• Work-up:
  – Upper endoscopy demonstrated a Schatzki’s ring and a hiatal hernia, but no source of bleeding
  – Colonoscopy to 20 cm of terminal ileum:
    • No active bleeding was identified
    • Questionable arterio-venous malformation in descending colon was cauterized with argon plasma coagulation
    • 3 mm polyp in descending colon

What would you do next?

a) Deep enteroscopy
b) Small bowel series
c) CTE/MRE
d) Capsule Endoscopy
Radiologic Evaluation

• Upper GI series with small bowel follow-through:
  – Normal jejunal and ileal mucosa

Case 9

video
Case 9

video

Case 9
Enteroscopy

• Push enteroscopy yielded successful removal of the lesions identified on VCE

Histopathology

• Hamartomatous Polyp
Final Diagnosis

- Peutz-Jeghers syndrome, spontaneous mutation

Peutz-Jeghers Syndrome (PJS)

- Autosomal dominant disorder characterized by intestinal hamartomatous polyposis and mucocutaneous melanin deposition
- PJS gene mapped to chromosome 19p13.3
- Encodes serine threonine kinase LKB1 or STK11
- Functions as a tumor suppressor gene
- Mutations of LKB1 detected in 50-65% of cases

PJS Clinical Features

Mucocutaneous Pigmentation

- Lips and perioral region: 94%
- Hands: 74%
- Buccal Mucosa: 66%
- Feet: 62%

Gastrointestinal Polyps

- Small Intestine: 64%
- Colon: 64%
- Stomach: 49%
- Rectum: 32%

PJS Malignant Potential

- Hamartomatous polyps benign but represent premalignant condition
- Overall relative risk of developing cancer 15.2
- Relative risk of small bowel cancer within PJS
  - 118.6 per 100,000 (0.7 per 100,000 general population)
  - Relative risk 520
- Relative risk of pancreatic malignancy: 132
- Extraintestinal tumors
  - Females: ovarian, cervical, uterine, bilateral breast
  - Males: Sertoli cell testicular

### PJS Malignant Potential

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<th>Site</th>
<th>RR</th>
<th>95% CI</th>
<th>p-value</th>
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<tr>
<td>Esophagus</td>
<td>57</td>
<td>2.5-557</td>
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<td>96-368</td>
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<td>Colon</td>
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<td>Pancreas</td>
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<tr>
<td>Ovary</td>
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<td>Cervix</td>
<td>1.5</td>
<td>0.31-4.4</td>
<td>0.63</td>
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### PJS Surveillance

- Colonoscopy:
  - 3 year intervals beginning at age 18
- Upper endoscopy and small bowel series (or capsule endoscopy):
  - Beginning at age 10 every 2-3 years
- Endoscopic ultrasound:
  - Beginning at age 25 every 1-2 years for pancreatic malignancy
- Mammogram, transvaginal ultrasound and CA-125:
  - Annually
- No recommendations on genetic testing, but newly diagnosed patients and family members may benefit

Giardello FM. Clinical Gastro and Hep 2006;4:408-415
Case 10

- 54-year old post-menopausal female presents for evaluation of slowly progressive iron deficiency anemia
- No overt bleeding
- No GI symptoms
- Past history:
  - Osteopenia
  - Diet-controlled HTN
- No FHx of GI disease
- No NSAIDs/ASA

Case 10

- EGD with duodenal biopsies/colon 2 years ago while still menstruating: normal
  - Patient had erratic but heavy menses from age 45-53, but menopausal for 1 year with progression of iron deficiency
- Stools repeatedly guaiac negative
- Patient’s daughter:
  - Internist who is convinced patient has cancer
• What should be the next step in this patient’s work-up?
  – Repeat EGD/colonoscopy
  – Barium small bowel series
  – CT enterography/MR enterography
  – Capsule endoscopy
  – Close clinical observation with oral iron replacement

Case 10

video

video
Case 10

• What is your diagnosis?
  – AVM
  – Crohn’s
  – Small bowel tumor
  – Celiac sprue
Case 10

• Celiac serologies:
  – Normal one year ago, but gene positive!
• Detailed history:
  – Daughter empirically placed patient on gluten-free diet when diagnosed with osteopenia
  – Patient was initially adherent but then liberalized diet
  – Was on strict diet at time of last EGD and celiac panel
• Patient placed on unrestricted diet
• Endoscopy repeated

Case 10

• Final diagnosis: celiac sprue!
  – Patient placed on strict gluten-free diet
    • Anemia resolved
• Take home points:
  – Always look closely at duodenum for changes consistent with celiac
  – Pathologic changes can be patchy and therefore missed on random duodenal biopsies
Case 11

• 48-year old male presents with 2 episodes of melena 8 years apart

• Patient history:
  – HTN
  – COPD
  – Morbid obesity
  – CAD s/p CABG
  – s/p open cholecystectomy in 2006

Case 11

• Initial episode in 2001:
  – Hospitalized, 5 units PRBC
  – EGD: negative
  – Colonoscopy: 2 small polyps and diverticulosis
  – Bleeding scan: normal
    • Bleeding stopped spontaneously
  – Discharged on iron
    • Patient has been taking iron since that hospitalization
    • Hb ~11.5
Case 11

• 2009: similar episode with abrupt onset melena requiring 3 units PRBC
  – EGD: gastritis
  – Colonoscopy: diverticulosis
  – Bleeding scan: negative
  – Patient placed on PPI and told to stop aspirin

• What should be the next step in this patient’s work-up?
  – CT enterography/MR enterography
  – Repeat EGD/colonoscopy
  – Enteroscopy
  – Capsule endoscopy
  – Close clinical observation off aspirin with oral iron replacement
• What would you do next?
  – Deep enteroscopy
  – Observation on iron
  – CTE/MRE
  – Dx Laparoscopy

Case 11
• Work-up:
  – CTE: normal
  – Per-oral DBE and per-rectal DBE: normal
  – Laparotomy: 3.5 cm ulcerated tumor in mid-ileum

Image courtesy of Peter Legnani, MD
Case 11

- Final diagnosis: GIST tumor
  - Very low mitotic index
- Patient is back on aspirin and plavix
- Hb stable

The Role of Capsule Endoscopy Today:

Final Thoughts

1. Everything that is ulcerated is not Crohn’s disease.
2. Although contrary to common belief, in the world of small bowel capsule — young bleeding patients are more likely to have tumors than older patients
3. If you have performed a capsule endoscopy and the patient continues to bleed consider repeating it (close to the time of bleeding)
4. If you have performed multiple small bowel capsules for GI bleeding accept the fact it is negative and consider another source (it may even still be in the upper or lower tract)
The Role of Capsule Endoscopy Today: Final Thoughts

5. Always question the patient about obstructive-like symptoms and then BELIEVE them
6. Every red dot is not a angioectasia
7. If the patient smells like, looks like and sounds like a celiac patient the negative duodenal biopsies may be wrong
8. Don’t assume your patient knows how to swallow a pill