Occult and Overt
Obscure Gastrointestinal Bleeding

Scan, Scope or Surgery?

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Case Study

• 49 yr old woman
  • Intermittent mild iron-deficiency anemia for 2 yr
  • 3 mo transfusion-dependent anemia
    • Hg 4.7 g/dl, 5.7 g/dl, 7.6 g/dl
  • Dark formed stool on iron
  • EGD, push enteroscopy, colonoscopy, SBFT normal

What next?
Obscure Gastrointestinal Bleeding (OGIB)

**Definition**

- Obscure bleeding - bleeding of unknown origin that persists or recurs
  - Obscure overt (visible blood)
  - Obscure occult (positive FOBT or IDA)
- Normal upper and lower endoscopy

**Historical Challenges Related to the Evaluation of “Obscure GI Bleeding”**

- High miss rate for lesions on initial upper and lower endoscopy
- The need for invasive intra-operative enteroscopy and exploratory laparotomy to adequately examine the small bowel
- Limited capacity of older diagnostic modalities to adequately examine the small bowel
- Finding a lesion in the small bowel doesn’t always mean that it is the source of the problem
The Challenge.....
Is this the cause of bleeding?

Uncertainty whether angiodysplasia detection and ablation affect long-term outcome because most angiodysplasia not actively bleeding when detected.

Bleeding source found in up to 80%, but rebleeding occurs in as many as 30%.

Small Intestine (SI) Bleeding

Dieulafoy's lesion
Diagnostic Approach in Patients with “Obscure GI Bleeding”

- Document objective evidence of gastrointestinal bleeding
  - Exclude hematologic causes for anemia
  - Exclude malabsorption
- Sufficiently rule out an upper and lower gastrointestinal tract bleeding source with second-look endoscopy as indicated
- Then proceed with a small bowel evaluation

Etiology of Obscure GI Bleeding

**Vascular**
- Angiodysplasia
- Hemangioma
- Dieulafoy lesion
- Portal hypertensive enteropathy
- Varices
- Radiation enteritis

**Inflammatory**
- Inflammatory bowel disease
- NSAID enteropathy
- Celiac disease
- Autoimmune enteropathy

**Neoplastic**
- Carcinoid
- GIST
- Adenocarcinoma
- Lymphoma
- Metastases

**Truly Obscure Etiologies**
- Hemobilia
- Hemosuccus pancreaticus
- Vasculitis

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Etiology of Suspected SI Bleeding

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Management of Suspected SI Bleeding

The Olden Days – circa 2000

Obscure GI Bleeding

↓

Repeat EGD and colonoscopy

↓

Push enteroscopy
small bowel x-ray or enteroclysis

↓

Angiogram

Intraoperative Endoscopy

Zuckerman et al: AGA position statement and review, Gastroenterology 2000; 118:197, 201
Management of Suspected SI Bleeding

The Olden Days – circa 2000

- Obscure GI bleeding
- Capsule endoscopy 2001
- Push enteroscopy 2002
- Balloon-assisted enteroscopy 2004
- Angiogram
- Intraoperative endoscopy
- Small bowel x-ray or enteroclysis


Middle GI Tract Bleeding

The Olden Days circa 2000

- Upper GI
- Lower GI

Today

- Upper GI
- Middle GI
- Lower GI

Ell et al: Endoscopy 2006; 38: 73; Raju et al: Gastroenterology 2007; 133: 1697
Our Case: Suspected SI Bleeding
49 yo female with transfusion dependent recurrent IDA

- Single bleeding nodule
- 30% of small bowel transit

What Next?

Case Study

Antegrad Deep Enteroscopy
- 200cm beyond pylorus
- Mid to distal jejunum
- Bleeding nodule: hemangioma?
- APC hemostasis
Capsule Endoscopy

Yield of CE Compared to Other Modalities

- Range: 45-83%
- Entire small bowel seen in 80-90%
- CE had an incremental yield of 30% and 36% compared to Push Enteroscopy and SBFT, respectively
- Main utility of CE lies in its high positive predictive value (94-97%) and its high negative predictive value (83-100%)
- It can identify a bleeding lesion and help direct further therapeutic intervention and/or surgery
"Deep Enteroscopy"
Tube or Balloon Assisted Enteroscopy

- **Double-Balloon Enteroscopy (DBE)**
- **Single-Balloon Enteroscopy (SBE)**
- **Spiral Overtube Enteroscopy**

**Forcep channel allows biopsy and therapy**

**Deep Enteroscopy**

- Overall diagnostic yield: ~ 60% (41%-80%)
- Channel allows therapeutic interventions
- Total enteroscopy is possible using both routes in ~ 50-70% of cases
- More invasive and often requires anesthesia with MAC or general endotracheal
- Resource utilization is high with procedure duration >60min and need for assistants, anesthesia, fluoroscopy
- Complications low at 1-3% but do occur

Gerson: Clin Gastr Hep 2009;7:828
Ragu et al: Gastro 2007;133;1697
Comparing Deep Enteroscopy Methods

- All are useful techniques
  - Similar yield, safety, learning curve
  - Spiral may allow faster intubation
- Overtubes and balloons
  - DBE has latex (allergy); others don’t
  - Overtubes: one-time use, similar cost
- Altered anatomy (Billroth, gastric bypass)
  - All can reach bypassed stomach
  - All allow successful ERCP

Meta-Analysis of CE vs DBE

8 Studies

- No difference in overall yield between CE and DBE (OR 1.21 [95%CI:0.64-2.29])
- However, CE had a higher yield compared to DBE using a single approach (OR 1.61 [95%CI:1.07-2.43])
- But CE had a significantly lower yield compared to DBE using a combined approach (OR 0.12 [95%CI:0.03-0.52])

This reinforces the importance of total enteroscopy with DBE in patients with a high clinical suspicion for a SI lesion

Case Study

35 yr old man

• Acute GI hemorrhage
  • Maroon stools, 6 units transfusion
• Negative EGD, push enteroscopy, colonoscopy, SBFT, CT, Meckel’s scan

Capsule endoscopy

• Blood in mid small intestine, source not seen
• Nodular mucosa: unsure if normal lymphoid tissue (vs lesion)

Antegrade DBE performed and negative

Case Study

Lower DBE: 100 cm proximal to ileocecal valve

Meckel’s Diverticulum with Ulcer
Case Study
Meckel’s Diverticulum with Ulcer

View inside diverticulum; light, raised mucosa was gastric-type mucosa on biopsy

Opening of diverticulum with healing ulcer

Newer Radiologic Procedures

Cross-sectional imaging (CTE, CTA, MRE)
- May identify SI angiodysplasia, tumors, inflammation
- Diagnostic yield 10-40% (vs 50-80% CE)
- Consider before capsule if concern for obstruction
- Consider if ongoing bleeding despite negative capsule or deep enteroscopy, especially if IBD or tumor suspected

Gerson: GIE 2008;68:920
CE Compared to Angiography for Acute Overt Obscure GI Bleeding

- 60 patients with melena or hematochezia and nondiagnostic upper and lower endoscopy
- Randomized to CE vs Angiography and then followed for up to 5 years
- Results:
  - Diagnostic yield CE vs Angio: 53.3% vs 20.0%, p=0.016
  - Rebleeding risk CE vs Angio: 33.3% vs 16.7%, p=0.10
  - Long-term outcomes no different

Leung WK et al. AJG 2012;107:1370-1376

CE as a Screening Tool Prior to Deep Enteroscopy

- CE transit times are useful:
  - Antegrade approach for lesions within the proximal 75% based on transit time
  - Retrograde for more distal lesions
- Increases both the diagnostic (73-93%) and therapeutic (57-73%) yield
- A negative CE allows for the avoidance of Deep Enteroscopy in patients with a low pre-test probability for SI findings

Hendel JW et al: Scan J Gastro 2008;43:363-7
62 yo male presented with a hemoglobin of 2: colonoscopy negative and upper endoscopy showed angioectasia in the stomach.

CE-Guided Deep Enteroscopy May Not Always Be Applicable

- CE has been found to have a false negative rate of 11% for all SI findings and 19% for neoplasms
- There are reports of neoplasms missed on CE and diagnosed on Deep Enteroscopy
- Therefore, in patients with a negative CE but a high clinical suspicion, CTE and/or total enteroscopy should be pursued

Jones BH et al: Am J Gastro 2005;100:1058-64
Postgate A et al: GIE 2008;68:1209-14
Surgery for Suspected SI Bleeding

- In most cases, can be avoided except for tumor resection
- Indicated for patients who continue to bleed and have had negative endoscopic and radiologic workups, and are operative candidates.
- Laparoscopy combined with deep enteroscopy may be helpful in a subset of patients


Reasonable Approach to SI Bleeding

- Individualize based on clinical presentation
  - Intermittent overt/occult (CE)
  - Acute ongoing overt (BAE)
  - Obstructive symptoms (CTE/MRE)
- Controlled prospective clinical studies are needed to substantiate these recommendations

Case Study

• 73 yo female with end stage liver disease presents with hematochezia. History of esophageal varices without stigmata of bleeding.

• Two EGDs, two colonoscopies, nuclear RBC scan negative.

• At Mayo, SB enteroscopy negative and bleeding continued.

• Retrograde BAE performed….

Retrograde BAE 150cm Proximal to IC Valve

Jejunal Varix
What To Do In Clinical Practice

Bringing it together

Integrating Capsule and Deep Enteroscopy in suspected SI bleeding

Perform Capsule Endoscopy after Negative EGD and Colonoscopy (and perhaps second look endoscopy)

Review of Capsule Endoscopy
Are findings equivocal and clinical suspicion low?

Consider repeat CE vs Cross-Sectional Imaging vs Observation
Perform Capsule Endoscopy after Negative EGD and Colonoscopy
(and perhaps second look endoscopy)

Review of Capsule Endoscopy
Definite submucosal tumor with bleeding

Should patient go directly to surgery?
If not, then Deep Enteroscopy should be planned

If Surgery Not Planned, Review of Capsule Endoscopy
Estimate Location to Plan Deep Enteroscopy Approach

0% Small Bowel Transit

0% - 75%
Start with Oral Approach

75% - 100%
Start with Anal Approach
Approach to Possible SI Lesion

Positive Capsule

- Suggests Vascular Lesion
  - Treat Those in Reach with Push Enteroscopy even if not bleeding
  - Deep Enteroscopy if Symptoms Persist

Suggests Tumor or Inflammation

Negative Capsule

- Mild Anemia or Low Suspicion – Observe with Iron Therapy

Consider Push Enteroscopy or colonoscopy if in reach

Cross-Sectional Imaging is considered complimentary and often very helpful

For Mild Anemia, few angiodysplasia, observe with iron therapy, stop antiplatelet therapy if possible

Suspected SI Bleeding

Important Points to Remember

- Using CE and Deep Enteroscopy, diagnostic yield is 40-80%
- Overlooked upper or lower GI source common; consider second look endoscopy
- Capsule Endoscopy is next best test - Yield higher if done soon after overt bleeding
- Deep Enteroscopy and cross-sectional imaging are complimentary for detecting bleeding, tumors or inflammation
- Evaluate patient as close to bleeding episode as possible