Small Intestinal (SI) Bleeding: Not Obscure Anymore

-A Case Based Approach-

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Clinical Case Study

72 yr old man

- Cardiac stent placed 2 months ago – started ASA and clopidogrel
- 1 month ago
  - Melena, hemoglobin 8, transfused 2u
  - EGD and colonoscopy negative
- Now
  - Recurrent melena, Hg 9.1
  - EGD and colonoscopy again negative

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 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 75%, but rebleeding occurs in as many as 30%.

Ragu et al: Gastro 2007;133;1697
Gerson: GIE 2008;68:920

SI Bleeding

Dieulafoy's lesion
Diagnostic Approach in Patients with Suspected SI 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

Management of Suspected SI Bleeding

The Olden Days – circa 2000

- Capsule Endoscopy 2001
- Balloon-Assisted Enteroscopy 2004
- Push enteroscopy
- Small bowel x-ray enteroclysis
- Intraoperative Endoscopy
- Angiogram

Zuckerman et al: AGA position statement and review, Gastroenterology 2000; 118:197, 201
Middle GI Tract Bleeding

The Olden Days circa 2000

Upper GI

Middle GI

Lower GI

Today

Upper GI

Middle GI

Lower GI

Etiology of Suspected SI 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
Our Case: Suspected SI Bleeding

72 yr old man

- Recurrent melena, negative EGD/Colonoscopy x2
- Capsule endoscopy: multiple small bowel AVMs in first third of small bowel transit time
- Bleeding stopped, anemia resolved
- 12 months later anemia returned and required more interventions

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

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**


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**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

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

Outcomes with CE

- Diagnostic yield 38-83% with PPV of 94-97% and NPV of 83-100% in OGIB
- Findings lead to a change in management in 37-87% of patients
- 50-66% of these patients remain transfusion free
- The rebleeding rate is low (5.6-11%) in patients with a negative CE

References:
- Pennazio M et al: Gastro 2004;126:643-53
Long-Term Outcome with DBE in SI Bleeding

- 129 patients with SI vascular lesions treated successfully with APC.

- 98 patients followed for 22.6 months (1-52)
  - Rebleeding rate 46% at 36 months
  - Factors associated with rebleeding
    - Total # of lesions
    - Valvular/arrhythmic cardiac disease
  - Complication rate: 2.3%

What If Bleeding Recurs?

- Next steps are not completely evidence-based

- Limited data, and clinical experience, suggests benefit for intervention

- Don’t forget second-look endoscopy
Importance of Second Look Endoscopy

65 yo female with recurrent iron deficiency anemia: colonoscopy negative and upper endoscopy showed “antral erythema”

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 SB 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 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
Case Study

- 70 yo male with overt OGIB for 5 years
- SI source suspected
- Two negative capsule studies
- Patient referred for Deep Enteroscopy
- CTE performed first
Hamartomatous Polyp

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

Positive Capsule
Suggests Vascular Lesion
Treat Those in Reach with Push Enteroscopy even if not bleeding
Deep Enteroscopy if Symptoms Persist
For Mild Anemia, few angiodysplasia, observe with iron therapy, stop antiplatelet therapy if possible

Negative Capsule
Mild Anemia or Low Suspicion – Observe with Iron Therapy
If Serious Problem or Suspicion High, then proceed with Deep Enteroscopy and/or Cross sectional Imaging

Suggests Tumor or Inflammation
Consider Push Enteroscopy or colonoscopy if in reach
Cross-Sectional Imaging is considered complimentary and often very helpful
Otherwise proceed with Deep Enteroscopy if findings might prevent surgery

Endoscopy 2007;39:895-909
Important Points to Remember

- Source identified in ~75% of suspected SB bleeding, usually angiodysplasia
- 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