Evaluation and Management of Obscure GI Bleeding

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Background
Obscure GI Bleeding (OGIB) is common
The investigation and management of OGIB has changed dramatically over the past decade
New technologies have led to a paradigm shift

Objectives
To understand the presentation of OGIB
To review the current management strategy for OGIB
To understand the role of capsule endoscopy and deep enteroscopy in OGIB
**Definitions of GI Bleeding**

<table>
<thead>
<tr>
<th>Type of GI Bleeding</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overt GIB</td>
<td>Hematemesis, hematochezia, melena, coffee-ground emesis</td>
</tr>
<tr>
<td>Occult GIB</td>
<td>Iron deficiency anemia, + FOBT</td>
</tr>
<tr>
<td>Obscure GIB</td>
<td>Persistent or recurrent bleeding w/o identified source of EGD, colonoscopy, or radiologic testing</td>
</tr>
<tr>
<td>Obscure-occult</td>
<td>Persistent or recurrent +FOBT Unexplained iron deficiency anemia</td>
</tr>
<tr>
<td>Obscure-overt</td>
<td>Persistent or recurrent passage of visible blood without identifiable source</td>
</tr>
</tbody>
</table>

**Obscure GI Bleeding**

**Small Bowel Causes**

Grouped by Age

- **Patients < 25 years old**
  - Meckel's Diverticula
- **Patients between 30 – 50 years old**
  - Tumors
- **Patients > 50 years old**
  - Vascular ectasias

**Small bowel causes of OGIB**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angioectasia</td>
<td>22-55%</td>
</tr>
<tr>
<td>Small bowel tumors</td>
<td>10-20%</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>2-10%</td>
</tr>
<tr>
<td>Meckel’s diverticulum</td>
<td>2-5%</td>
</tr>
<tr>
<td>NSAID enteropathy</td>
<td>5%</td>
</tr>
<tr>
<td>Dieulafoy lesion</td>
<td>1-2%</td>
</tr>
<tr>
<td>Ectopic varices</td>
<td>1-2%</td>
</tr>
<tr>
<td>Portal hypertensive enteropathy</td>
<td>1-2%</td>
</tr>
<tr>
<td>Radiation enteritis</td>
<td>41%</td>
</tr>
<tr>
<td>Hemobilia, H. pancreaticus</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
Small Bowel Bleeding
Causes
By Etiology

- Vascular Lesions
- Neoplasms
- Inflammatory Lesions
- Other

Small Bowel Bleeding
Vascular Lesions

- Most common cause of small bowel bleeding
- Responsible for 70 - 80% of small bowel bleeding

Angioectasias
Telangiectasias
- Hereditary hemorrhagic telangiectasia
- CREST Syndrome
- Osler-Weber-Rendu, Berry aneurysm
- Hereditary hemorrhagic telangiectasia
- Other

Other
- Dieulafoy's lesion
- Aortoenteric fistula
- Small bowel varices

__________________________
Small Bowel Bleeding
Angioectasia

- Dilated tortuous blood vessels with thin walls lined by endothelium with little or no smooth muscle
- Age-related degeneration of vascular integrity

Angioectasia on capsule endoscopy
Small Bowel Bleeding
Tumors

- Second most common cause of bleeding
- One out of ten patients with obscure bleeding will have a small bowel tumor
- Most common cause in persons age 30 – 50 years of age
- Malignant and Benign
  - Adenocarcinoma, carcinoid, lymphoma, leiomyosarcoma,
  - Leiomysarcoma, purpuric (von Recklinghausen, familial polyposis), GIST
- Metastatic
  - Melanoma, breast, renal cell, kaposi’s sarcoma, colon, ovarian

Causes of Small Bowel Bleeding
Diverticula

- Small bowel diverticula
  - At the site of perforating blood vessels
- Meckel’s diverticulum
  - Remnant of vitelline duct in distal ileum
  - Prevalence of 1 – 3%
  - Most common cause of small bowel bleeding in patients under the age of 25
  - Ectopic gastric tissue causes ulceration

Gralnek, Gastroenterology 2005; 128:1424-1430

Small Bowel Bleeding
Inflammatory Lesions

- Crohn’s Disease
- Isolated ulcers
  - Idiopathic ulcers
  - Nonsteroidal antiinflammatory drugs
  - Ischemic
- Other
  - Vasculitis, Celiac disease
Small Bowel Bleeding

Rare Causes

- Hemobilia
  - Neoplasm, vascular aneurysm, liver abscess, trauma, liver biopsy

- Hemosuccus pancreaticus
  - Pancreatic pseudocysts, pancreatitis, neoplasms
  - Erosion into a vessel with communication with PD

Upper GI causes of OGIB

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Percentage of OGIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameron’s erosion</td>
<td>5-15%</td>
</tr>
<tr>
<td>Angioectasia</td>
<td>5-10%</td>
</tr>
<tr>
<td>Varices</td>
<td>1-5%</td>
</tr>
<tr>
<td>Dieulafoy lesion</td>
<td>2-3%</td>
</tr>
<tr>
<td>Gastric antral vascular ectasia (GAVE)</td>
<td>1-2%</td>
</tr>
<tr>
<td>Portal hypertensive gastropathy</td>
<td>1-2%</td>
</tr>
</tbody>
</table>
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Upper GI causes of OGIB: Cameron’s erosion

Slide 20
Upper GI causes of OGIB: Gastric Antral Vascular Ectasia

Slide 21
Lower GI causes of OGIB

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Percentage of OGIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angioectasia</td>
<td>2%</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>1%</td>
</tr>
<tr>
<td>Dieulafoy lesion</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
Case presentation #1

- 71 y/o female with PMH of CAD on ASA
- Presents to PCP c/o melena x 1 week
- Labs: Hematocrit 38 → 23
- Admitted to NWH with BP 90/50, HR 110
- Transfused & volume resuscitated
- Started on IV omeprazole drip
- Aspirin is discontinued
- Cardiac enzymes normal

EGD – esophagus is normal

Stomach – nonhemorrhagic gastritis
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Stomach – normal pylorus

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Duodenum – Dieulafoy lesion

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Dieulafoy lesions

- Large, tortuous submucosal arteriole
- Bleeds through a mucosal defect
- 75% in stomach
- 14% in duodenum
Dieulafoy - clipped and cauterized

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Case #1

- No overt bleeding for one week...
- Melena recurs
  - Hct 31.8 → 27

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Case #1: Repeat EGD
Incidental large polyp found

What next?
- EGD
- Colonoscopy
- Capsule endoscopy
- Push enteroscopy
- Tagged RBC Scan
- Angiography
- Barium small bowel series
- CT
- Balloon-assisted deep enteroscopy

Capsule findings
Actively bleeding distal jejunal angioectasia
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Bleeding jejunal angioectasia

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Cautery of jejunal angioectasia on deep enteroscopy

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Case #1 Follow-up

- No further bleeding events since endoscopic therapy for 4 months
- Normal bowel movements
- Hgb/Hct = 15/45
- FeSO4 discontinued
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Synchronous lesions happen!

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Case #2

- 79 year old woman with PMH of a diverticular bleed and gastritis
- Presents to NWH for large volume hematochezia x 2 days.
- PMH: DVT, PE, Afib, CAD, Chronic kidney disease
- Meds: warfarin and aspirin
- ER: BP 123/80, pulse 78, 100% room air

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Case #2

- Exam: Red blood on rectal exam
- Labs: INR 3.3, Hct 40.9 → 19.9
- Cardiac enzymes, platelets normal
- Admitted to ICU and resuscitated
- PRBCs and FFP given
- Coagulopathy reversed and vitals remain stable
Case #2

- Urgent colonoscopy
  - Red blood all through the colon
  - ? diverticular bleed
  - Terminal ileum revealed red blood as far as the colonoscope was able to be passed

- EGD was normal

What next?

- Balloon-assisted deep enteroscopy

Why?
- Urgency of bleeding
- High likelihood of a positive finding
- Don’t want the delay of capsule
- Patient was prepped

Per-oral balloon-assisted deep enteroscopy

Jejunal polypoid mass
Case #2 - Outcome

- Tubulovillous adenoma on biopsies
- Jejunal resection 3 days later:
  - Tubulovillous adenoma
  - Poorly differentiated adenocarcinoma
  - Nodal sampling was negative
- No further GI bleeding over past week
- Recovering smoothly following surgery

What are the tools of the trade?
Radiology

Upper GI small bowel X-ray series

Pros
- Simple
- Well-tolerated

Cons
- Poor sensitivity for definitive lesion in obscure GI bleed: 0-6%

Zuckerman, Gastroenterology 2000; 118:201-221
Enteroclysis
- Contrast injected into small bowel
- X-rays obtained
- Improved yield over small bowel series
- Yield is poor:
  - 10%-25%

CT Enterography

Technetium-labeled RBC scan
- Infuse technetium-labeled RBC’s
- Nuclear imaging obtained over 60 – 90 min
**Slide 49**

**Technetium-labeled RBC Scan**

- Can detect intermittent bleeding over time
- Sensitive to low bleeding rates
  - Localizes bleeding at rates of 0.1 - 0.4 mL/min
  - Angiography requires rate of > 0.5 mL/min
- Data in OGIB limited
  - 15% false positive
  - 12 – 23% false negative

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**Limitations of tagged RBC scan**

- Diagnostic not therapeutic
- Delay during active, intermittent bleeding leads to missed opportunity to treat
- Overlapping loops of bowel and colon as blood pools

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**Role of Tagged RBC Scan**

- Good test to perform in conjunction with angiography
- In a series of 271 arteriograms, tagged RBC scan prior to angiography increased yield of angiography from 22% to 53%
- If tagged RBC scan without active bleeding, no angiogram performed, and patients spared contrast load
Angiography

Active bleeding  Coil embolization  Post treatment

Kobayashi J Surg Rad 2011 Jan 1; 2 (1)

Pros of Angiography

- Accurate localization of rapid bleeding
  - During active bleeding, angiography has diagnostic yield 27% - 77%.
- Potential to be diagnostic and therapeutic

Zuckerman, Gastroenterology 2000;118:201-221

Cons of Angiography

- Large contrast load = risk for acute renal failure
- When bleeding stops, diagnostic yield falls to ~10%
Endoscopy in OGIB

Challenges presented by the anatomy of the small bowel
- Small bowel length: 5-7 meters
- Small bowel mesentery is floppy
- Vigorous contractility
- Adhesions
- Difficult access by mouth
  - Looping in the stomach
  - Duodenum is a tight C-shape
  - Ileocecal valve is sharply angulated

Push enteroscopy
- Enteroscope up to 240-cm long
- Permits evaluation to 50 – 100 cm beyond Ligament of Treitz
- Diagnostic yield: 26% - 80%

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Capsule endoscopy

- Propelled via peristalsis
- Captures ~ 60,000 images
- Ambulatory office procedure
- Naturally excreted

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History of capsule endoscopy

- Brain child of a senior engineer from Israeli Ministry of Defense
- Goal to create “tiny missile” to visualize the small bowel
- FDA approved capsule in 2001 for obscure GI bleeding

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Technology behind the Pill

1. Optical dome
2. Lens holder
3. Lens
4. LEDs (Light Source)
5. Electronic Chip converts Images to Radio Waves
6. (2) Battery
7. Electronic transmitter
8. Antenna
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Capsule Motion Is Unpredictable

Cave DR, et al. GIE 68,3 : 2008

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Capsule has high sensitivity & specificity in obscure GIB


- 82.6 % Negative predictive value
- 97.0 % Positive predictive value
- 88.9 % Specificity
- 95.0 % Sensitivity

(Analysis of patients with verified final diagnosis, n = 56)

Capsule has high sensitivity & specificity in obscure GIB

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High sensitivity for lesions in OGB is reproducible

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pennazio 2004</td>
<td>88.9</td>
<td>95</td>
<td>97</td>
<td>82.6</td>
</tr>
<tr>
<td>Delvaux 2004</td>
<td></td>
<td></td>
<td>94.4</td>
<td>100</td>
</tr>
<tr>
<td>Botalboge 2005</td>
<td>91.6</td>
<td>98.3</td>
<td>98</td>
<td>90.4</td>
</tr>
<tr>
<td>Hartmann 2005</td>
<td>95</td>
<td>75</td>
<td>95</td>
<td>86</td>
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</tbody>
</table>

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Positive findings in sub-categories of OGIB

- Ongoing overt bleeding: 62.7%
- Previous overt bleeding: 17.5%
- Quiescent intestinal bleeding and iron deficiency anemia: 19.8%


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Capsule in obscure GI Bleeding

- Capsule endoscopy results led to treatments resolving the bleeding in 86.9% of patients undergoing the procedure while actively bleeding
- (12 – 25 month follow up)


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Small Bowel Bleeding
Lesions seen on capsule endoscopy

- Vascular Lesions
  - Angioectasias
- Neoplasms
- Inflammatory Lesions
  - Ulcers, Crohn’s Disease
- Other
  - Diverticula, varices
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Normal small bowel

Graphic of jejunal concentric folds
Concentric folds of jejunum
Lush villi of jejunum

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Capsule endoscopy:
Normal small bowel

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Capsule endoscopy:
Vascular Lesions
Capsule endoscopy
Video of small bowel ulcers

Capsule endoscopy:
Polyps and Masses

Capsule endoscopy:
Diverticula
Wireless Capsule Endoscopy
Summary

- Time efficient, patient friendly, sensitive method to visualize the small bowel
- Disadvantages
  - No therapeutics
  - Unable to control movement
  - Unable to clear bubbles and debris

Balloon Enteroscopy

- Also called “push-pull enteroscopy”
- First described in 2001
- Allows the diagnosis and treatment of disease along the entire length of the small bowel
- Advance scope through mouth or anus
- Patient Prep
  - transoral: NPO 6-8 hrs
  - transanal: Colonoscopy prep
Yield of Small Bowel Imaging Modalities in Obscure GI Bleeding

<table>
<thead>
<tr>
<th>Length of Insertion</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon enteroscopy</td>
<td>Up to 100%</td>
</tr>
<tr>
<td>Push enteroscopy</td>
<td>50 – 100 cm</td>
</tr>
<tr>
<td>Capsule</td>
<td>100% SB</td>
</tr>
<tr>
<td>Intraoperative</td>
<td>Up to 100%</td>
</tr>
<tr>
<td>Radiology</td>
<td>100%</td>
</tr>
</tbody>
</table>

GIE 2005, 61:6:709-714

Deep enteroscopy or capsule?

<table>
<thead>
<tr>
<th>Study</th>
<th>Capsule</th>
<th>Double balloon enteroscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total enteroscopy</td>
<td>84%*</td>
<td>29%*</td>
</tr>
<tr>
<td>Endoscopic therapy</td>
<td>--</td>
<td>27-57%</td>
</tr>
<tr>
<td>Biopsies</td>
<td>--</td>
<td>27%</td>
</tr>
</tbody>
</table>

*Liao, GIE 2010; 71: 280-6
**Raju, Gastroenterology 2007; 133: 1697-17
Capsule and balloon-assisted deep enteroscopy are complementary:
- The inability of capsule endoscopy to obtain biopsies or administer therapy is made possible with deep enteroscopy.
- The low rates of achieving total enteroscopy in patients during balloon enteroscopy is remedied by capsule which has complete examination rates of 84% in OGIB.

Factors favoring capsule first:
- Total enteroscopy
- Non-invasive
- Stable patient without overt bleeding

Factors favoring deep enteroscopy first:
- If delay of capsule will impact care
- Massive overt bleeding
- Clear need for rapid therapeutic intervention
Obscure occult GI Bleeding
Evaluation
Repeat EGD and Colonoscopy (~35% yield)
Negative
Capsule Endoscopy (~60–70% yield)
Negative
Repeat Capsule Endoscopy (~35% yield)
Negative
Balloon-assisted deep enteroscopy (~40% yield)
Negative
Intraoperative Enteroscopy in selected cases

GIE 2004;60:5:711-713
The Future
Robotics

The Future?

Summary
- Capsule endoscopy and balloon-assisted deep enteroscopy have transformed the approach to the evaluation and management of obscure GI bleeding
- Older diagnostic modalities still play a complementary, but increasingly selective role
Summary

- < 25 y/o
  - Meckel's diverticulum
- 30 – 50 y/o
  - SB Tumor
- > 50 y/o
  - Angioectasia