29 *Obscure GI Bleeding—Role of Endoscopy and Other Modalities in Diagnosis and Management*

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Abstract: Obscure Gastrointestinal Bleed (OGIB) is defined as GI bleeding that persists or recurs without any obvious etiology, after a negative routine upper GI endoscopy and colonoscopy. It accounts for 5% of patients with GI bleed. OGIB can be overt or occult. Vascular lesions, the commonest causes of OGIB, are seen in 40% of patients. The majority of these lesions are present in the small intestine. Visualization of the entire small intestine is a challenge and newer technologies are directed towards this goal. Barium meal follow through, enteroclysis, angiography and nuclear scan have all been used in the diagnosis and management of OGIB but have limitations. A re-look routine Upper GI endoscopy surprisingly yields good results and is justified while evaluating patients of OGIB. Push enteroscopy remains the "work horse" of OGIB both for diagnosis and therapy. Capsule endoscopy is a noninvasive tool, convenient and reproducible with a yield of 50-70% in diagnosing OGIB and offers a positive outcome in management. The newly developed double balloon enteroscope offers visualization of the entire small bowel with therapeutic potentialities. Outcome studies with double balloon enteroscopy are eagerly awaited. Intraoperative enteroscopy is considered the "gold standard " in OGIB and resorted to when other modalities fail to achieve results. With newer technologies developing, visualization and treatment of lesions in the small bowel should become easier.

INTRODUCTION

Obscure Gastrointestinal Bleeding (OGIB) continues to pose diagnostic and therapeutic challenges despite the advances made in the field of endoscopy, imaging and surgery. OGIB is defined as gastrointestinal bleeding that persists or recurs without any obvious etiology, after negative standard endoscopic procedures, i.e. routine upper gastrointestinal endoscopy and colonoscopy.[1] It represents 5% of patients of GI bleed.[2,3] OGIB can be categorized into the following two groups.

a. *Obscure occult GI bleed:* This is defined as persistently positive fecal occult blood without any frank blood loss recognizable to the patient or physician. It may present with or without iron deficiency anemia.
b. *Obscure overt GI bleed:* This is clinically evident bleeding that persists or recurs and is not identifiable after routine upper GI endoscopy and colonoscopic examination.

Normally 0.5 to 1.5 ml of blood is lost from the GI tract daily and this blood loss is not detectable by occult blood tests.[4] It takes more than 5 ml of daily blood loss in the GIT for the occult blood test is positive. Patients with blood loss up to 100 ml per day may have normally

appearing stools.[5] Bleeding above this volume presents as visible GI bleed. Therefore, patients with daily GI blood loss between 5 to 100 ml would generally fall in the category of obscure occult GI bleed while those with blood loss of >100 to 150 ml per day have visible blood loss and are labeled as obscure overt GI bleeders.

Causes of OGIB

Table 29.1 lists out the common causes of OGIB, while Table 29.2, lists the causes GI bleed that are commonly missed on routine upper GI endoscopy.[6]

Table 29.1: Common causes of OGIB (lesions mostly in the small intestine) (From Carey and Fleischer[6])

- Angiodysplasia
- Dieulafoy's lesions
- Erosions/ulcers
- Crohn's disease
- Small bowel varices
- Tumors
- NSAID enteropathy
- Radiation enteritis
- Small bowel diverticulosis
- Small bowel polyps
- Aortoenteric fistula
- Meckel's diverticulum

Table 29.2: Lesions commonly missed on upper GI endoscopy (From Carey and Fleischer[6])

- Cameron's erosions
- Gastric varices
- Dieulafoy's lesion
- Angiodysplasia
- Esophagitis
- Portal hypertensive gastropathy
- Gastric antral vascular ectasia.

Age is an important factor in identifying the etiology of the OGIB.[7] Patients who are younger than 40 years are more likely to suffer from tumors, carcinoids, Dieulafoys lesions and from polyps. Patients over 40 years are more prone to bleed from vascular ectasias. Vascular lesions account for over 40% of all causes of OGIB.[3] The small intestine is often the site of bleed in patients with OGIB.

In this article we will list out the various diagnostic modalities useful in identifying the etiology in OGIB and briefly mention their limitations. The role of endoscopic techniques in the diagnosis will be discussed in greater detail.

Diagnostic Modalities for Patients of OGIB

Barium Meal Follow Through (BMFT)

BMFT has often been used for the diagnosis of OGIB. The diagnostic yield is questionable and in a large series the probable diagnosis was picked up in 5.6% of 215 patients.[8] It is useful in identifying tumors, Crohn's disease and small bowel diverticulosis. In todays practice BMFT has little role in the evaluation of OGIB.[3]

Enteroclysis

Enteroclysis offers better visualization of the small bowel because of the double contrast of barium and air. The infusion of water under high pressure distends the bowel and this provides

for good visualization of the mucosal folds. It is superior to BMFT and a diagnostic yield of 10-20% is seen in patients with OGIB.[9]

Technetium Labelled Nuclear Scan

Technetium tagged red blood cell scan detects active bleed at the rate of 0.1 ml per minute. It can only yield positive results in an actively bleeding patient. The pickup rates of these nuclear scans varies between 15-70%.[3,10] The limitations are: a) high false localization rates; b) useful only in actively bleeding patients; c) localization is only to a region and not to any particular site; d) etiologies cannot be identified; and e) no therapeutic options are available. Therefore, radionuclear scans have a limited role in the evaluation of OGIB.

Angiography

As a primary diagnostic modality, angiography is useful in patients who bleed actively (> 1 ml per minute).[11] It also identifies non-bleeding vascular lesions from their vascular patterns. Yields between 40-80% have been reported.[3,12] It has the added advantage of offering therapy. Pharmacological agents can be injected directly or embolization can be carried out using coils or beads. Its limitations are the need of a specialized center, presence of trained interventional radiologists as well as the complications associated with the procedure.

Others

Meckels scan using technetium pertechnetate can identify a bleeding ectopic gastric mucosa in cases of Meckels diverticulum. Helical CT angiogram identifies the source of bleed if the active bleed is greater than 6 ml per minute. Evidence of bleed was found in 13 out of 18 patients (72%) with helical CT as compared to 11 out of 18 patients with conventional angiography.[13] Although still under evaluation, helical CT promises to be an important non-invasive tool for OGIB.[3]

Role of Endoscopy in OGIB

As the majority of the causes of OGIB are located in the small intestine (see Table 29.1) proper visualization of this part of gastrointestinal tract is imperative. Small bowel examination however is problematic, technically difficult and offers a great challenge to the clinician investigating patients with OGIB. Limitations of small bowel examination are because of its length, its contractibility and intraperitoneal location which makes endoscopic passage difficult.[3] Newer modalities have been directed towards this "last frontier" in luminal endoscopy. Therapy in OGIB depends on etiology and the description of individual therapeutic techniques is beyond the scope of this article.

Endoscopic modalities that have been utilized in evaluating the small bowel in patients of OGIB will be discussed as follows:

1. Re-look routine upper GI endoscopy and colonoscopy.
2. Sonde enteroscopy.
3. Push enteroscopy (PE).
4. Double balloon enteroscopy (DBE).
5. Capsule endoscopy (CE).
6. Intraoperative enteroscopy.

Re-look UGI Endoscopy and Colonoscopy

Lesions responsible for OGIB often fall in the reach of a routine upper GI endoscope and are missed. A repeat routine UGI endoscopy, with a previously negative report, has a surprisingly high yield ranging from 25 to 64%.[14,15] The lesions most commonly missed and yet in the reach of the upper GI endoscope are listed in Table 2. Repeat colonoscopy is relatively less useful with a

yield of around 6%.[16] It is, therefore, justified to repeat an upper GI endoscopy when evaluating patients of OGIB.

Sonde Enteroscopy

Sonde enteroscopy was the first successful effort to evaluate the small bowel. The scope was introduced trans nasally and advanced into the small bowel by peristalsis. Examination was done 6 to 8 hours later and the mucosa visualized on withdrawal.[17] Its limitations were the cumbersome procedure, the long time taken and the absence of a working channel in the scope which precluded therapeutic interventions or biopsies. It is now a procedure of historical interest.

Push Enteroscopy

Push enteroscopy (PE) or small bowel enteroscopy is an important tool in the management of OGIB—especially, if proximal small bowel lesions are suspected. It was first introduced in 1973[18] and improvement in technology has resulted in the availability of longer instruments with better visualization. The diagnostic yield of PE is between 30-50% and its therapeutic impact on the management is between 50-55%.[19,20] Limitations include the failure to visualize beyond the mid jejunum. Complications are seen in 1% of patients.[21] An overtube has earlier been used to prevent the coiling of the enteroscope in the stomach and improve the depth of insertion. However, this was withdrawn as a result of various complications induced by the overtube.[22] Its obvious advantage is its availability, operator friendliness needing no additional endoscopic skills, excellent visualization and therapeutic capability.[6] PE has rightly been called the "workhorse" for investigating OGIB.

Double Balloon Enteroscopy (DBE)

Yamamoto and colleagues, first described the technique for visualization of the small bowel in 2001 using a double balloon enteroscope.[23] The scope provides for visualization of the entire small intestine without advancing an excessive length of the scope into the patient. Visualization of the bowel can be done by the antegrade method (per oral route) or in combination with the retrograde route (via the colon). Its unique capability lies in providing both diagnostic as well as therapeutic capability for the entire small bowel. The procedure requires specialized endoscopic skills and may require 75-90 minutes to complete – even in experienced hands.[6] Yamamoto identified the source of bleed in 76% of 66 patients with OGIB. A successful therapeutic procedure was performed in 12 cases. Complications in the entire series of 178 patients were limited to 1.1%.[24] Larger, multicentric trials are needed to establish the role of DBE in OGIB and also its comparison with the other modalities available. Outcome studies with DBE in management of patients of OGIB are also awaited. DBE, today, is considered a very useful procedure in patients with OGIB, with both diagnostic and therapeutic capabilities.

Capsule Endoscopy (CE)

Paul Swain, a gastroenterologist and Gavriel Iddan, a scientist, first developed the capsule endoscope in 1998.[25] It contained a pill-sized camera and batteries to image the entire small bowel. The first commercially available capsule endoscope was introduced by the Given Diagnostic Imaging System (Given Imaging, Yoqneam Israel). The capsule measures 26 × 11 mm, weighs around 4 grams and has a battery life of 8 hours providing two images per second. The diagnostic yield of CE in OGIB ranges from 45 to 66%.[26-28] A meta-analysis comparing CE with PE found a yield of 62% for CE as compared to 29% for PE.[28] Comparison of CE with intraoperative endoscopy reported a sensitivity of 83% in both procedures in 42 patients of OGIB.[29] A positive influence of the clinical outcome was reported in 12 out of 18 patients as a specific intervention was done based on the results of CE.[30] The advantages of CE are its non-

invasive nature, ability to review or share images, safety profile, patient preferences, the clarity of images and the capability to visualize the entire small bowel.[2] The most important limitation is the absence of any therapeutic potential of the present day capsule endoscopes. Capsule entrapment in the GIT is seen in 0.75 to 5% of patients and is defined as failure to expel the capsule after two weeks of the procedure.[31,32] This mostly occurs at the site of the small bowel pathology and can be asymptomatic for long periods. The use of patency capsule which spontaneously disintegrates after two weeks may minimize this problem in the future. Small bowel strictures, diverticula and fistulae are contraindications for CE as the chances of capsule retention and subsequent need for surgery are higher in this group of patients. The experience from our institute, the first reported large series from India, suggests a positive yield of 77% in patients with overt OGIB and 27% with occult OGIB. CE helped in planning further management in 79% of patients with overt OGIB and 26% of those with occult OGIB.[33]

Intraoperative Enteroscopy

The final option in the evaluation of OGIB is surgery. It is resorted to, when all the earlier mentioned modalities fail to achieve the desired results. Explorative laparotomy is combined with intraoperative enteroscopy and this approach is superior to explorative laparotomy alone.[3] A push enteroscope or an upper GI endoscope can be utilized to visualize the entire small bowel during surgery. The diagnostic yield in patients of OGIB is between 50 to 100%.[34-36]

The procedure is to be handled as any major surgical operation and severe complications of up to 12% with a mortality of 8% have been reported.[37] Following the diagnosis a successful therapeutic end result is the additional advantage of the combined surgical and endoscopic approach. Intraoperative enteroscopy is considered as the "Gold standard" in the diagnosis and management of OGIB.

SUMMARY

Patients with OGIB present a difficult and often frustrating challenge both for evaluation of the etiology and its management. Visualization of the entire small bowel has been a major obstacle in this direction. The advances in endoscopic technology have provided better instrumentations in the form of double balloon enteroscopes and capsule endoscopes—both capable of visualizing the entire small bowel. Outcome studies with DBE are awaited, while those with CE have shown positive results. DBE offers the unique opportunity of treating lesions anywhere in the small bowel without resorting to surgery. Capsule endoscopes with therapeutic potential are a distinct possibility in the future and will further strengthen the hands of the endoscopists dealing with OGIB. The future appears promising and to the next generation of gastroenterologists small bowel bleeding need not be obscure.[6]

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