An unusual cause for upper gastrointestinal bleeding

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Abstract: A variety of GI disorders present commonly as upper GI bleeding. A 30 year old male presented with abdominal pain and hematemesis. UGI scopy revealed extraneous impression over antrum of stomach. CECT Abdomen revealed ulcerated exophytic mass from gastric wall. Histopathological examination after subtotal gastrectomy showed monomorphic spindle cells in muscular layer suggestive of GIST. IHC was strongly and diffusely positive for CD-117. This case is reported here as a rare cause for UGI bleed.

Keywords: UGI Bleed, GIST, IHC, CD117

A 30 year old male, smoker and alcoholic, presented with history of epigastric pain of two weeks duration and 4 episodes of hematemesis - 400-500 ml during each episode and frank bleeding per rectum. History of binge alcohol intake 20 days prior to hematemesis was present. There was no history of melena, jaundice, fever, abdominal distension, loss of appetite and loss of weight or any other medical or surgical comorbidities in the past or present. On examination patient was dehydrated, anemic, hypotensive with rapid thready low volume pulse of 112/min.

Resuscitation was started immediately with IV crystalloids and blood component transfusion adequately. Hemodynamic status of patient was restored. On further examination, patient had no signs of liver cell failure. Abdominal examination revealed tenderness in epigastrium, no mass or organomegaly palpable. Per rectal examination-blood/fecal staining+, no mass palpable and normal sphincter tone.

Routine investigations –Total bilirubin 1 mg/dl, ALP 84 U/l, Total protein 6.2g/dl, Albumin 3.4g/dl, INR 1.16. Bleeding time 2 min, Clotting time 4 min, Total count 7800/cu.mm, Direct count P60 L38 E2, ESR 36 mm/hr, Hb 9 gm/dl, PCV 30 %, Platelets 1.10 lakhs/cu.mm, Blood sugar 94mg/dl, Urea 28 mg/dl, Creatinine 1.0 mg/dl, Na 146meq/l, K 4.3 meq/l. UGI endoscopy revealed extraneous impression over pyloric antrum. USG Abdomen showed hypo-echoic lesion of 11x11cm to the left of gastric wall suggesting exoenteric mass.

CECT Abdomen- 10x12 cm heterodensely enhancing mass lesion noted in lesser sac

Evidence of contrast tracing from gastric wall into the substance of tumor

We proceeded with CECT Abdomen which revealed 10x12 cm heterodensely enhancing mass lesion noted in the lesser sac, compressing body and tail of pancreas with evidence of contrast tracing from gastric wall into the substance of the lumen suggestive of ulcerated exophytic mass from gastric wall. Patient was taken up for surgery. Intra operative findings revealed was taken up for surgery. Intra operative findings revealed exophytic growth arising from posterior wall of stomach. Subtotal gastrectomy was done.

HPE showed submucosal neoplasm with monomorphic spindle cells in muscularis propria, mild nuclear atypia and mitotic figures less than 5 per 10 hpf suggestive of low grade GIST. IHC was strongly and diffusely positive for CD117 confirming GIST. Patient is now started on imatinib and is responding well.
mutations in receptor protein tyrosine kinases like KIT (CD117) or platelet derived growth factor alpha (PDGFRA).

GISTs are the most common mesenchymal tumors of intestinal tract. It results most commonly due to activating mutations in receptor protein tyrosine kinases like KIT (CD117) or platelet derived growth factor alpha (PDGFRA).

**Types of GIST:**
- **Spindle type**
- **Epithelioid type**
- **Mixed type**

Epithelioid GISTs are usually seen in diffuse or nested architecture. Spindle cell GISTs are arranged in short fascicles or whorls. Stroma is usually scanty, hyalinised to myxoid. Extensively myxoid GISTs are rare. Most spindle cell GISTs have uniform cytology with fibriillary eosinophilic cytoplasm and nuclei containing fine chromat and inconspicuous nucleoli. In epithelioid GISTs, there is evidence of binucleation/multinucleation, more significant nuclear atypia compared with spindle cell counterpart. Features in subset of cases include prominent paranuclear vacuoles (gastric lesions), hyaline eosinophilic material known as skeinoid fibers (small bowel lesions), and extensive nuclear palisading.

**DISCUSSION:**
The term GIST was first described by Mazur and Clark in 1983 to define intra abdominal tumors that were non-epithelial in origin, and that did not exhibit features of smooth muscle or nerve cells. Now, it is widely accepted that GIST cells originate from stem cells within gut wall which differentiates towards Interstitial Cells of Cajal phenotype. GISTs are the most common mesenchymal tumors of gastrointestinal tract. It results most commonly due to activating mutations in receptor protein tyrosine kinases like KIT (CD117) or platelet derived growth factor alpha (PDGFRA).

**Location of GIST (in descending order of frequency)**
1. Stomach,
2. Small intestine,
3. Esophagus and Recto-anal canal

It rarely develops outside gastrointestinal tract in mesentery, omentum or retroperitoneum. Extra gastrointestinal soft tissue stromal tumors are similar to their gastrointestinal counterpart histologically and immunophenotypically, but have aggressive course similar to small intestinal rather than gastric stromal tumors. Recurrence after resection is predominantly intraabdominal. Liver is the most common site of recurrence in patients with primary presentation than those with metastatic disease at presentation. Lymph node metastasis and spread to lungs or extraabdominal locations are rare.

Nearly 20% remain asymptomatic, while 50% present with abdominal pain and GI bleed. 10-30% present with symptoms of obstruction. Tumors less than 2 cms do not produce symptoms and are detected incidentally during abdominal exploration, endoscopy, radiological imaging or autopsy.

Most GISTs present as single well circumscribed nodule. Cut surface is fleshy, may show areas of cystic degeneration, necrosis or hemorrhage. Ulceration of mucosa leads to gastrointestinal bleeding. Satellite nodules can be seen in peritoneal surface. Two separate GISTs can be seen in 2 different locations in gastrointestinal tract.

Gross specimen: Exophytic nodular and fleshy growth HPE: Monomorphic spindle cells in muscularis propria

**Imaging modalities include Endoscopic USG, CT Abdomen/ pelvis, MRI, PET scan.** Most GISTs appear to take up 18FDG avidly and thus PET represents a very sensitive tool, capable of demonstrating the presence of metastatic disease that is not visible on CT. PET scan will also provide a rapid means of determining the responsiveness of the tumour to imatinib showing response much earlier than the response seen on CT.

Surgery is the mainstay of therapy in patients with primary GIST with no evidence of metastasis. Preoperative biopsy may not be necessary and may lead to hemorrhage and tumor dissemination. GISTs should be handled with care to avoid tumor rupture. The goal is to resect completely with an intact pseudocapsule and negative...
microscopic margins. Abdomen should be thoroughly explored during laparotomy with careful inspection of peritoneal surfaces particularly lesser sac in gastric GIST, rectovaginal or vesical location and liver to identify metastasis. Segmental resection of the stomach or intestine should be performed, with the goal of achieving negative microscopic margins. Lymphadenectomy is usually unnecessary because lymph node metastasis is rare. Laparoscopic resection is a reasonably safe and feasible procedure for patients with low risk smaller GISTs.

Medical therapy primarily involves Tyrosine Kinase Inhibitor (TKI) therapy. IMATINIB is the principal drug used both preoperatively as well as post operatively depending on the scenario. In large localized GISTs and poorly positioned small GISTs, imatinib is used to downstage the tumor prior to surgery. It is also useful in unresectable tumors, organ preserving surgery and function preserving surgery as in sphincter sparing surgery (rectal GIST) and in esophagus sparing surgery (gastroesophageal junction GISTs). Imatinib is also given as postoperative therapy after resection of KIT positive GIST for atleast 12 months in the dosage of 400 mg per day. Apart from imatinib, other drugs used include sunitinib, dasatinib and nilotinib.

Treatment for advanced GISTs has shown marked results with the invent of IMATINIB. Imatinib dramatically decreases the tumor recurrence. 3 clinical categories of disease response to TKI therapy were defined.
1. Stable disease - radiographically stable or responding to TKI therapy and for which all sites of progression could be resected.
2. Limited (localized) disease progression - progression on TKI therapy at one or a few sites of disease. In these patients, all sites of progressing disease could be resected, and other sites of stable disease were resected if the associated morbidity was relatively low.
3. Generalized disease progression - disease progressing in multiple sites for which TKI therapy and complete resection not possible. In metastatic GISTs, omentectomy or peritoneal striping and liver resection becomes necessary. Radiofrequency ablation, hepatic artery embolisation and liver transplantation are alternative options for treating liver metastasis.

References: