UPPER GASTRO-INTESTINAL BLEEDING IN THE YOUNG - GASTRIC GIST TUMOR OR PEPTIC ULCER DISEASE?

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ABSTRACT

GIST tumors are unusual in the young and middle-aged and a high index of suspicion is needed for its possible diagnosis in young patients who present with upper gastrointestinal bleeding. Appropriate imaging such as a computed tomographic scan (CT scan) may identify this tumor that may easily be misdiagnosed as a bleeding peptic ulcer disease. We present a case of a healthy 38-year-old man with no alcohol use who presented with epigastric pain and melena and subsequent torrential bleeding uncontrolled during endoscopy necessitating an emergency exploratory laparotomy by the general surgery team. The bleeding intraluminal component of the tumor with gross splenic and pancreatic involvement was identified and surgical management consisted of a wedge resection of the greater curvature of the stomach incorporating the tumor and the spleen with successful dissection of the tumor off the tail of the pancreas. Histology was positive for C-KIT and DOG-1 markers. The postoperative course was uneventful, and he is presently on Imatinib mesylate.

KEYWORDS Gastric; gastrointestinal stromal tumor; upper endoscopy; C-KIT, DOG-1; Imatinib

Introduction

The clinical presentation of gastric GIST tumors is gastrointestinal bleeding and discovery on radio-imaging or endoscopy is typical. We present a case of upper GI bleeding initially managed as peptic ulcer disease with subsequent life-threatening hemorrhage uncontrolled by upper endoscopy. The patient was successfully managed by emergency surgical resection of the bleeding tumor. Tumor histology was positive for C-KIT.

Case Report

A healthy 38-year-old active African male immigrant with no medical problems who presented at our facility with a few weeks history of dark, tarry stools and recent onset of hematemesis. He denied a history of recent vomiting or acid peptic disorder. He also denied cigarette smoking, alcohol use or recent weight loss. His vitals on admission was 123/82mmHg, pulse 92/min. His hemoglobin at presentation was 7.0, normal white count, normal coagulation profile and platelet count. Abdominal examination revealed no abdominal tenderness or palpable masses. A nasogastric lavage was done yielded coffee granules. He was admitted to the medical service and floor as a case of upper gastrointestinal bleed - presumably from peptic ulcer disease or gastritis and managed with proton pump inhibitors. His hemoglobin was optimized by multiple packed red blood cell transfusions to 8.0. However, melena persisted.

The gastroenterology team evaluated him on the second day...
which was grossly visualized on gastrotomy. The tumor was unresponsive to endoscopic intervention with epinephrine, and the patient had become hemodynamically unstable. Interventional radiology guided tumor embolization was not immediately available at this time. The patient was emergently intubated and transferred to the OR for emergency surgical exploration.

Emergency exploratory laparotomy revealed a giant tumor with a profusely bleeding intraluminal component of the tumor which was grossly visualized on gastrotomy. The tumor was externally abutting the spleen and the tail of the pancreas in the lesser sac. Cautery and suture ligation were successfully controlled the bleeding. We commenced with a splenectomy to due gross adherence of the tumor to the spleen. We mobilized the gastrophrenic and gastrocolic ligaments and then continued the mobilization of the tumor from the splenic hilum, and we were able to dissect successfully manually the intact spleen from the tumor. Once the spleen was removed, it was easier to mobilize the tumor manually from the tail of the pancreas without breach- ing the tumor capsule. There was no gross evidence of pancreatic tail infiltration or involvement. A wedge resection of the greater curvature and the tumor was then successful done as seen in Fig 1. Gross anatomy revealed a 15.0 x 10 x 9 cm mass that was ulcerated through the gastric mucosa. Gastric pathology showed a gastrointestinal stromal tumor (GIST), spindle cell type. The spleen was negative for GIST. A fibrous capsule surrounded the gastric tumor and with a mitotic rate of Less than five /50 High power field (HPF). The histologic tumor grade was G1 - Low grade with no identifiable areas of necrosis and the surgical margins were negative for GIST. The spindle cell proliferative lesion was positive for CD117 and DOG-1 immunohistochemical stains.

The size of the tumor and associated mucosal ulceration were poor prognostic indices, however, the low tumor grade and low mitotic rate overall put in the tumor in this case in the intermediate risk prognostication. The patient had an uneventful postoperative recovery and was discharged home in a stable condition.

Following discharge, a repeat tomography of the abdomen revealed a splenic bed collection, which was successfully managed with radiography - guided pig-tail catheter drainage. The patient has been commenced on Imatinib by the hematology-oncology team and is being followed by serial abdominopelvic radio-imaging.

Discussion

Gastrointestinal stromal tumors (GIST), albeit uncommon gastrointestinal malignancies, are the most frequent mesenchymal tumors of the GI tract. The average worldwide incidence of these tumors is five to twenty per one million people per year [1, 3]. In the United States, newly discovered cases of GIST tumors are about 3000 - 5000 cases annually [1, 4]). GIST tumors typically express the gain - of - function proto-oncogenes C-KIT (CD-117) (85%) or PDGFRA (5-10%) with activation of receptor tyrosine kinase. They manifest as mutually exclusive sporadic or hereditary mutations [1- 3] or infrequently as wild-types that do not express C- KIT or PDGFRA [1, 5].

GISTs may frequently express CD34, nestin, caldesmon, DOG-1, calponin, vimentin and embryonic smooth muscle myosin. DOG-1 is an immunohistochemical marker for GIST tumor and has applicability in pathologic diagnosis of both C-KIT positive and wild-type GIST tumors. However, its positivity in other gastrointestinal tumors of non-mesenchymal etiology reduces its specificity [6].

GIST tumors are most often solitary as seen in 60 – 70 percent of cases [7]. When they occur in a young individual or discovered to be multifocal on surgical resection may be an indicator of a familial etiology [8]. Scarpa et al. reviewed forty-six observational studies with a total of 4,534 adult patients and the conclusion was that gastrointestinal bleeding was the most frequent clinical complaint at presentation [9]. GIST tumors are very uncommon in children and young adults, and the most frequent clinical picture is chronic gastrointestinal bleeding [8, 10]. GIST tumor invasion may be submucosal, intramural or may extend beyond the serosal lining while Locally advanced GIST tumors have been described as infiltrative, pseudo-infiltrative or extensive [11].

GIST tumors could occur anywhere in the gastrointestinal tract, but approximately 60% of all most frequently arise from the stomach [7, 11]. Gastric GIST tumors are frequent in individuals over the age of 60 with no racial or environmental predilection [12]. Miettenen et al. analyzed 1765 cases of gastric GIST and found a male preponderance with less than 10% of all cases occurring at below 40 years of age [12]. Discovery of GIST could be on incidental on routine imaging or the following imaging after presentation with dyspeptic symptoms or gastrointestinal hemorrhage [10, 13]. No imaging modality is gold-standard for diagnosing GISTs, and the only reliable method is biopsy - biopsies are typically reserved for unresectable tumors that might benefit from neoadjuvant tyrosine kinase inhibitors. The diagnosis tends to be missed when young individuals present with dyspeptic symptoms since the etiology is often attributed to acid peptic disorder.

Massive life-threatening hematemesis from Gastric GIST tumor may be arterial from bleeding submucosal vessels that may be visualized as a Dieulafoy-type vascular lesion on endoscopy. It might occur from tumor ulceration [1, 14] or hemorrhagic tumor necrosis [5 – 8]. Massive hematemesis from tumor mucosal ulceration is probably the etiology of bleed in the case presented.
Table 1 Risk stratification of primary GISTs based on mitotic index, tumor site and size. The table was adapted from Miettinen M and Lasota RJ. Gastrointestinal Stromal Tumors pathology and prognosis at different sites [3].

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<th>Tumour parameters</th>
<th>Risk of progressive disease</th>
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<td>Mitotic Index</td>
<td>Stomach</td>
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<tr>
<td>Size (cm)</td>
<td>None</td>
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<td>&gt;5 per 50 high power field (HPF)</td>
<td>&gt;2 &lt;5</td>
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above.

Gastric GIST tumor size is highly variable, and sizes ranging from half a centimeter to 40 centimeters has been reported [1]. Gastric GISTs are the most frequently occurring tumors in the GI tract (approx. 58%). They have a lower recurrence risk as compared to GIST tumors elsewhere in the GI tract with identical mitotic count and tumor dimensions [3,11]. Fundal or gastro-esophageal tumor location of gastric GISTs is regarded as unfavorable as opposed to antral tumors [12].

GIST Tumor risk stratification (see Table 1) stratifies the prognosis and recurrence potential of primary GIST tumors [3, 11, 15]. All GIST tumors are considered to have varying degrees of malignant potential. They are useful for identifying tumors that will benefit from tyrosine kinase inhibitors either as adjuvant or neo-adjuvant treatment. Risk classifications were initially ranked based on size and mitotic index as described by Fletcher et al. in the NIH consensus criteria [15]. The Mietenen and Lasota classification is a newer risk stratification [3, 7]. It included tumor location in combination to criteria above to classify the likelihood of recurrence of primary GIST tumors after resection into very low, low, intermediate and high-risk [Table 1]. Other important independent risk factors for gastric GIST tumor recurrence include C-KIT mutations with an exon 11 point mutation or insertion conferring a better response to Imatinib and reduced the likelihood of recurrence [3, 11,12]. Also that tumor location (with small bowel tumor location of GIST tumors conferring a worse prognosis) and positive resection margins [7].

The significance of tumor rupture in predicting tumor recurrence and prognosis was detailed by Oladeji et al. who identified close to 100% risk of recurrence following tumor perforation or rupture into the abdominal cavity either spontaneously or during operative handling. Oladeji et al. recommended adjuvant treatment in cases of tumor rupture regardless of tumor size or mitotic index [16].

Adverse prognostic indicators identified in our case such as the advanced nature of the tumor (despite tumor’s primary gastric origin), resection morbidity and resection tumor width over of 10cm and tumor perforation with life-threatening hemorrhage [1, 17].

These indicators may serve as adverse indicators for neo-

adjuvant treatment with tyrosine kinase inhibitor regardless of tumor size or mitotic index. The tyrosine kinase inhibitor, Imatinib serves as the first line drug of choice for the processing of all KIT-expressing GISTs regardless of tumor resectability or mutation status. Following tumor resection, patients with localized tumors may benefit from postoperative Imatinib therapy that has been shown to improve long-term tumor recurrence-free rate [1, 11].

Conclusion
The case above describes an unusual etiology for upper gastrointestinal bleeding in a young man. In young healthy individuals with no risk factors for peptic ulcer disease or Upper GI bleed, abdominal imaging is indicated to rule out a bleeding gastric GIST tumor that could be surgically resected and potentially managed with tyrosine kinase inhibitors.

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Competing Interests
The authors declare no conflict of interest.

References


