**CLINICAL VIGNETTE**

# Gastrointestinal Stromal Tumors – Two Cases and Review

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***Abstract***

Gastrointestinal stromal tumors (GISTs) are rare gastrointestinal tumors. In this report, two cases with completely different presentations of the same disease are discussed. The first patient presented with incidental finding of a sub mucosal nodule on a routine endoscopy; while the second patient, with small bowel tumor, presented emergently with a small bowel obstruction and perforation after mimicking diverticulitis with rectal bleeding, fever and LLQ pain. The stomach GIST was seen as a sub mucosal nodule and was confirmed on FNA. Due to low mitotic rate and size less than 2 cm, watchful waiting was preferred by the patient in lieu of resection. In the second case, CT finding confirmed small bowel tumor and perforation of the viscus. Her tumor was resected and 3 years of adjuvant therapy with Imatinib was recommended due to high mitotic rate of 10 and size >5cm, along with surveillance imaging every 3-6 months. A brief overview of this rare gastrointestinal neoplasm is presented to be used as a learning objective to keep GIST as part of the differential diagnosis.

***Background***

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal smooth muscle neoplasms that can arise anywhere within the gastrointestinal tract. Approximately 60-70% are located in the stomach, followed by small bowel and then colon. The majority of GISTs (approximately 95%) express the CD117 antigen (KIT), a proto-oncogene product. GISTs can be asymptomatic and incidentally found during examination for other pathologies or at autopsy. The most common symptoms of GISTs are abdominal pain, anemia, and bleeding, although emergent presentations with obstruction and perforation may occur as well. Diagnostic work up consists of cross-sectional imaging studies and may require endosonography for further delineation and biopsy. Surgery remains the first-line treatment for localized gastric GISTs, greater than 2 cm, as well as "the gold standard." Both open and laparoscopic operations have been shown to reduce recurrence rates and improve long-term survival. The use of small-molecule selective tyrosine kinase receptor inhibitors, Imatinib, as both adjuvant and pre-op therapy has revolutionized the treatment of advanced GISTs and increased the rate of survival by decreasing rate of recurrence.

***Case 1***

A 78-year-old male with history of hypertension and hyperlipidemia was referred to Gastroenterology with a new onset of rectal bleeding. The bleeding lasted 2 days was associated with some rectal urgency, but no abdominal or rectal pain. He reported 5 bowel movements with clots as well as frank blood. He took Ibuprofen and ASA a few hours prior to the onset of bleeding. Physical exam was unremarkable with normal vital signs; patient deferred a rectal exam. Initial labs included normal hemoglobin with a slight drop from 14.3 to 13.2 but overall normal blood count and comprehensive metabolic panel. Endoscopy and colonoscopywere advised, but due to cessation of symptoms after 2 days and lack of supplemental insurance, he declined a more urgent procedure. A week later, patient returned with a new onset of LLQ pain and chills. Pain was described as cramp-like without radiation and not associated with any change in bowel habits. Stools were described as formed and non-bloody. Pain did not improve with defecation, and no other aggravating factors were noted. He started on Levofloxacin and Metronidazole for suspected diverticulitis. However, after 4 days there was no improvement, and his pain worsened to 10/10 in the LLQ. He also developed anorexia and low-grade fevers but denied melena, rectal bleeding, or change in bowel habits. He was referred to ER, where CT of the abdomen and pelvis demonstrated dilated loops of small bowel with air fluid levels consistent with small bowel obstruction. Patient also had small pockets of extra luminal gas in the peritoneum consistent with a perforated viscus. There was 7.5 cm x 5.6 cm inflammatory soft tissue mass within the upper portion of the pelvis.

He underwent an emergent laparotomy with small bowel resection. A small bowel tumor with necrosis

and partial obstruction was removed. Pathology was consistent with a 7 cm GIST with mixed spindle and epithelial cell types. The margins were negative for tumor; however, the histologic grad was high with greater than 10 mitoses per high-powered field as well as 5% necrosis. The tumor was staged T2NxMx and was positive for CD117 (c-kit). Adjuvant Imatinib at 400mg daily for 3 years was recommended by oncology.

***Case 2***

A 62-year-old Caucasian female presented with a new onset of epigastric discomfort and heartburn of 1 week duration. Patient noted burping but otherwise no nausea, vomiting, dysphagia, or odynophagia. Patient denied melena, rectal bleeding, changes in bowel habits, or weight loss. TUMS did not provide any relief. Pain was described as 5/10, gnawning and radiating around to the back. No pertinent additional PMx or PSx history. Endoscopy demonstrated normal GE Junction located at 38 cm, mild erythema in the antrum as well as a submucocal nodule located in the antrum along the posterior gastric wall. Biopsy was non diagnostic. Subsequent endoscopic ultrasound (EUS) showed a 1.7 cm x 1.4 cm hypoechoic mass arising from the muscularis propria layer of the gastric wall, and FNA was consistent with GIST. CD117 positive and ki67 proliferative index less than 1%. The tumor was less than 2 cm, and patient chose not to have it resected but rather followed with EUS and additional imaging every 6-12 months.

***Discussion***

Gastrointestinal stromal tumors (GISTs) are neoplasms that arise from the non-epithelial, mesenchymal tissue of the gastrointestinal tract, and constitute 1% of all primary GI cancers.[1] Previously labeled as a soft tissue sarcomas, incidence in the U.S. is 7 per million per year. They are found most commonly in the stomach (60-70%), followed by small intestine (30%), less frequently in the rectum and colon (5%), and esophagus (<1%).[2] The spectrum of presentation varies from small benign tumors to overt metastases in up to 20% to the liver, omentum, peritoneum, and other intra-abdominal sites. More than 80% of cases occur in patients older than 50 years with similar gender distribution. Most are sporadic with no established risk factors.[3] They are understood as originating from the interstitial cells of Cajal or their stem cell precursors. Up to 25% are noted incidentally during imaging, or surgery, with 5% found during autopsy. Most frequent symptoms are bleeding, anemia, abdominal pain, and weight loss. Some can present emergently with bowel perforation, obstruction, tumor rupture (the thin pseudocapsule surrounding GISTs tumor can rupture even during surgery), and hemorrhage.[4]

Diagnosis is based on biopsy and may require additional imaging such as endoscopic ultrasound with FNA especially for the extra gastric extensions. CT or MRI will identify presence of metastasis. Morphological patterns of spindle cells, epitheliod and mixed cell types are seen. Immuno histochemical stains are used as other tumors can contain similar cells with 95% of GISTs positive for KIT (cd117).

All GISTs are considered potentially malignant. Therefore, they are stratified according to risk of recurrence and metastasis. The NIH 2002 consensus criteria includes tumor size, tumor mitotic rate, site, and rupture at or prior to surgery as prognostic factors. Prognostic performance has been validated and our two patients were risk stratified for GIST recurrence based on the above methods.[5] In a large series of 1,765 cases of gastric GIST, tumor related mortality was 17%, and only 2% of tumors were smaller than 10 cm with fewer than 5 mitoses/50HPF metastasized. If tumors were greater than 10 cm, and greater than 5 mitoses/50 HPF then 86% metastasized.[6] On the other hand, for small bowel GIST, mortality from tumor was higher at 39%.

The National Comprehensive Cancer Network has recommended an algorithmic approach to management of gastric GISTs but not for other sites in the GI tract with recommendation that all GIST greater than 2cm be resected.[7]

Since GISTs are rare neoplasm, the recurrence free survival and tumor related mortality has been difficult to ascertain. Overall, 5 year survival was between 40-65% even after complete resection.[8] Introduction of adjuvant Imatinib, tyrosine kinase inhibitor, has improved recurrence free survival and median survival with recurrent or metastatic disease.[9] Adjuvant therapy is generally offered for patients at intermediate or high risk of recurrence for at least 3 years after surgery for high-risk patients. Additional follow up with CT or MRI of abdomen and pelvis is usually done every 3-6 months for the first 2 years, although optimal intervals are still being studied.

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