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CASE REPORT | LIVER

Gastrointestinal Stromal Tumor Complicated by Fistula Formation

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ABSTRACT

Gastrointestinal (GI) stromal tumors are mesenchymal tumors that may arise in any portion of the GI tract. Their clinical presentation and complications may vary but do not often present with fistulization. This case is of clinical interest because of the rarity of GI stromal tumor intestinal fistulas.

KEYWORDS: gastrointestinal stromal tumor; GIST; fistula; case report

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors that arise from activating mutations in genes responsible for the expression of receptor tyrosine kinases.[1] Patients are often asymptomatic at the time of presentation. Complications of these tumors include tumor rupture, obstruction, bowel perforation, or bleeding. Fistulization is not a commonly cited complication.[2] We present a case of a metastatic GIST presenting with a proximal small bowel fistula.

CASE REPORT

A 66-year-old woman with a history of GIST of unknown primary with metastasis to the liver, chronic kidney disease, hypertension, and acute ischemic stroke presented to the emergency department after a progressive drop in hemoglobin from 9.1 to 7.1 g/dL of a normocytic distribution over 2 weeks was noted on surveillance laboratory work.

The patient was incidentally diagnosed with GIST with hepatic metastasis 10 years ago in Santo Domingo. Upper endoscopy at that time did not reveal a primary mass, and she underwent liver resection. Four years later after immigrating to the United States, she was found to have recurrence in the liver and underwent a second resection with confirmation of GIST (KIT Exon 11 mutation p.V560D). The patient was started on neoadjuvant imatinib but developed disease progression after 5 years, so she was transitioned to sunitinib with good response. Unfortunately, sunitinib was discontinued 3 months before presentation because of change in insurance status.

On admission, the patient did not endorse abdominal pain, hematochezia, hematemesis, melena, jaundice, or recent nonsteroidal anti-inflammatory drug use. The remainder of the review of systems was negative. Physical examination was within normal limits, and laboratory findings were otherwise unremarkable. Gastroenterology was consulted for the evaluation of anemia of unknown etiology, and the patient underwent an upper endoscopy and colonoscopy to rule out a gastrointestinal (GI) source of anemia. Upper endoscopy did not reveal ulcers or active areas of bleeding, but was notable for open draining fluid in the duodenal bulb (Figure 1). The colonoscopy was unrevealing. Follow-up imaging with an abdominal-pelvic computed tomography scan revealed a $10.4 \times 9.6 \times 8.3$ cm heterogeneous peripherally hyperattenuating and centrally heterogeneously hypoattenuating mass along the right hepatic resection margin in the right upper quadrant with a fluid and gas-filled component difficult to delineate from the adjacent bowel concerning for recurrence of liver metastasis and fistulization with the proximal small bowel (Figure 2). The surgery service recommended close outpatient follow-up. Her hemoglobin remained stable throughout the admission without overt bleeding, and on discharge, hematology/oncology considered her normocytic anemia to be due to low erythropoietin from chronic

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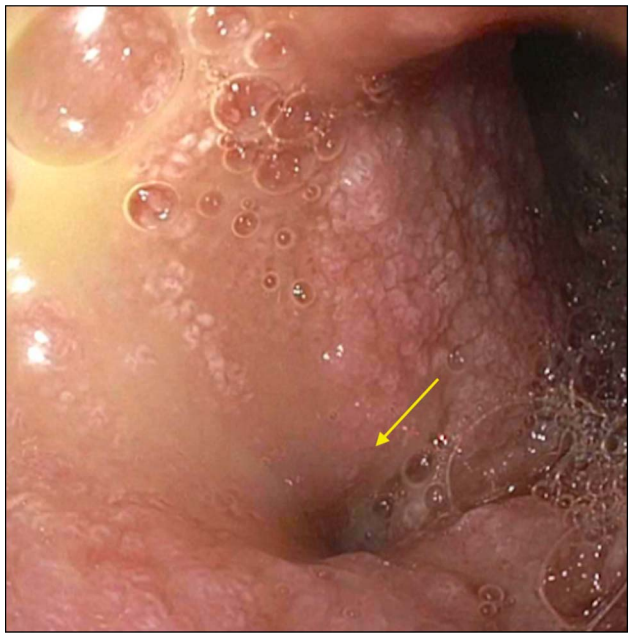

Figure 1. Gross upper endoscopic image of the duodenal bulb with an associated fistula (arrow).

renal failure, which she will be supplemented with in the future. Capsule endoscopy performed after this hospitalization did not reveal the source of the bleeding in the small bowel, nor was it revealing of the location of her primary GIST. Furthermore, her oncologist plans to restart her GIST therapy with sunitinib after successfully obtaining approval from the patient's insurance.

DISCUSSION

We describe a rare case of fistula formation in the setting of a GIST. Although GISTs are rare in incidence, they are the most common mesenchymal tumor of the GI tract and are believed to arise from the interstitial cells of Cajal, which are a complex cellular network that function as the pacemaker cells of the GI tract regulating peristalsis.[1] GISTs arise from activating mutations in genes responsible for the expression of receptor tyrosine kinases: *KIT* or platelet-derived growth factor alpha (*PDGFA*). GISTs often present as solitary masses in the subepithelial layer of the intestinal lining.[2] They can arise anywhere along the GI tract but are predominantly located in the stomach (60%) and small intestine (30%) and commonly metastasize to the liver, omentum, and peritoneum.[3] Most patients, such as the one described in this report, may be asymptomatic at the time of presentation, with the GIST detected incidentally during palpation, imaging, surgery, or autopsy. Occasionally, tumors may grow to a size that may cause ulceration because of mucosal irritation or pressure. Tumors of this size may present as tumor rupture, obstruction, bowel perforation, or bleeding, but fistulization between tracts and structures is rare.[2]

Although there have been isolated case reports of GISTs presenting with enterocolic or vesicocutaneous fistulas, these patients often presented with overt clinical signs or symptoms as mentioned.[4] By contrast, our patient's fistula was found incidentally during workup for an unrelated anemia. Radiographic evidence of fistulization may include the presence of air fluid levels within the suspected mass.[5] Despite being clinically asymptomatic, fistulization between the GIST and the intestinal lumen is important to recognize because it may serve as a conduit for bacterial translocation, leading to infectious complications.

The management of GISTs depends on the degree of disease extension. Localized disease greater than 2 cm warrants surgical excision of the tumor.[6] Depending on the size and location of the tumor, preoperative imatinib may be considered for tumor shrinkage and to reduce the unwanted resection of surrounding organs before surgery. Adjuvant imatinib, a tyrosine kinase inhibitor (TKI), is usually initiated after surgery to reduce the chance of recurrence.[7] There are many stratification models that exist to predict the potential of recurrence. Tumor characteristics that factor into these models include size, mitotic rate, location of the primary site, tumor rupture, or lymph node involvement.[8] Contrarily, metastatic GISTs are treated initially

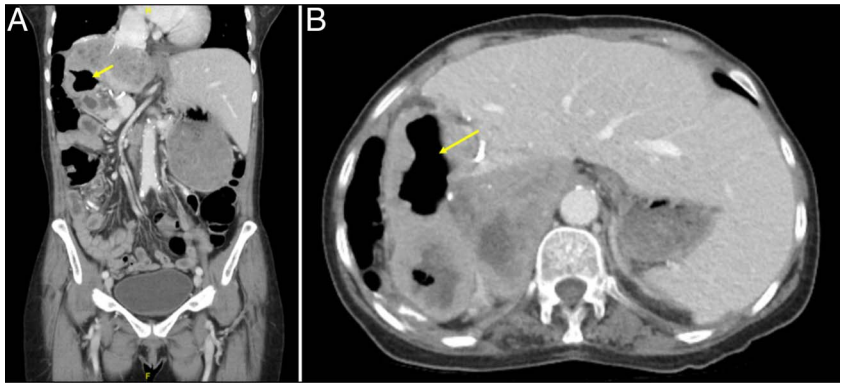

Figure 2. (A) Coronal view of an abdominal-pelvic computed tomography (CT) scan demonstrating fluid and gas-filled component at the expected location of the right hepatic lobe concerning for fistulization with the proximal small bowel (arrow). (B) Axonal view of the abdominal-pelvic CT scan demonstrating fluid and gas-filled component at the expected location of the right hepatic lobe concerning for fistulization with the proximal small bowel (arrow).

with systemic imatinib, which has been shown to prolong progression-free survival.[9] Some patients, as the one described in this report, may experience treatment failure with imatinib because of acquired resistance. In these cases, second-line therapy is with a different TKI, sunitinib. The role of surgical resection in patients who are on TKI therapy is currently unclear and remains to be studied.[10] Similarly, there is minimal literature on the management of fistulas from GISTs given their rarity. However, 1 case report did demonstrate success with treatment of a gastrocutaneous fistula with imatinib, which aligns with our oncology service's recommendation to treat the hepatoduodenal fistula with a TKI.[11] In summary, although rare, a GIST should be on the differential for any tumor found in the GI and hepatobiliary tracts. Moreover, clinicians should be aware that fistulization can occasionally arise as a complication of GISTs and may even present without symptoms, as in the case of our patient. Further research is needed to better elucidate the pathophysiology of fistula formation from GISTs to offer more targeted preventative and therapeutic options.

DISCLOSURES

Author contributions: N. Sunkara performed background research and drafted the article and is the article guarantor. T. Selig and Y. Elfanagely proofread and critically revised the article for important intellectual content. T.E. Sepe provided final approval of the article.

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