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CASE REPORT | PATHOLOGY

A Diagnosis of Gastric Inflammatory Myofibroblast Tumor: A Challenge Like No Other!

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ABSTRACT

Inflammatory myofibroblastic tumors (IMTs) are mesenchymal tumors of intermediate malignant potential. Gastric IMTs are rare and commonly affect young adults. They are typically confused with gastrointestinal stromal tumors, inflammatory fibroid polyps, and leiomyosarcomas. The etiology of IMTs remains unclear, but is theorized to be due to hyperinflammatory response to chronic infections. We present a middle-aged woman found to have a gastric mass positive for *Helicobacter pylori*, underwent multiple endoscopies with endoscopic ultrasound, and a definitive diagnosis of gastric IMT was only made after a partial gastrectomy with immunohistochemistry negative for CD-117, S-100, ALK-1, and positive for vimentin and SMA.

KEYWORDS: tumor; gastric tumor; endoscopy; endoscopic ultrasound; pathology

INTRODUCTION

Inflammatory myofibroblast tumors (IMTs) are rare solid tumors of mesenchymal origin with intermediate malignant potential. They are frequently referred to as inflammatory pseudotumors because of the uncertainty as to whether they are inflammatory, infectious, or neoplastic in origin. These tumors may originate in any anatomic site but are often found within the lungs, retroperitoneum, mesentery, and genitourinary tract.[1] IMT arising from the stomach is very rare and predominantly occurs in children with only a few cases reported in adults.[2] Given the rarity of these tumors, their true incidence and prevalence remain unclear. It is reported to have a high local recurrence rate; however, it rarely metastasizes to distant organs.[3] Gastric inflammatory myofibroblast tumor (G-IMT) is often confused or misdiagnosed with other soft-tissue neoplasms such as gastrointestinal stromal tumor (GIST), leiomyoma, leiomyosarcoma, lipoma, lymphoma, fibromatosis, and schwannoma.[4] A thorough combination of histopathologic assessment and immunohistochemistry staining is currently the main key ancillary technique to reach a definite diagnosis of G-IMT. We present a bewildering case of a middle-aged woman with recurrent hospitalizations for melena due to a gastric mass, and despite multiple endoscopies and endoscopic ultrasound (EUS) with biopsies, a definitive diagnosis of G-IMT was not made until a partial gastrectomy with intraoperative esophagogastroduodenoscopy (EGD) was performed.

CASE REPORT

A 42-year-old woman with a history of iron deficiency anemia presented to the emergency department with melena and generalized weakness. Vitals were within normal limits, and a physical examination demonstrated orthostatic hypotension and mucosal pallor. Laboratory findings were significant for hemoglobin 4.9 g/dL (reference range: 12–15 g/dL). A diagnosis of acute blood loss anemia was made, and she was transfused with 3 units of packed red blood cells. Abdominal and pelvic computed tomography revealed a gastric mass (3.1 × 2.9 × 2.4 cm) in the body of the stomach (Figure 1). An upper endoscopy was performed, which showed a 7 × 10 cm ulcerative, necrotic, fungating mass at the fundus extending into the body (Figure 2). Biopsy of the mass reported hyperplastic antral gastric mucosa with ulceration, fibrinopurulent exudate, granulation tissue, severe chronic active gastritis, positivity for *Helicobacter pylori*, and negativity for any malignancy (Figure 3). Immunohistochemistry showed glandular epithelium. Because of the concern for

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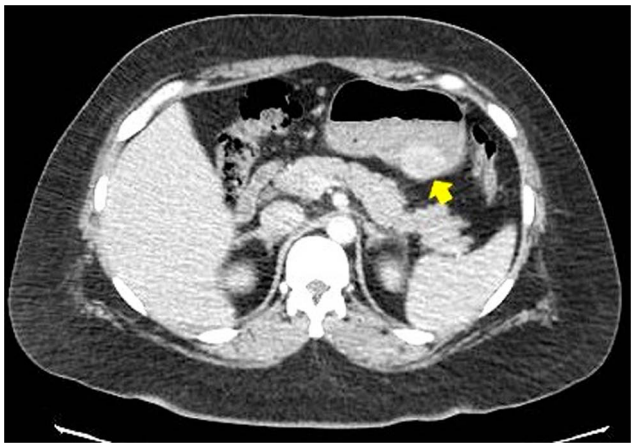

Figure 1. Abdominal and pelvic computed tomography with intravenous contrast: 3.1 × 2.9 × 2.4 cm in size, intraluminal, lobulated density along the greater curve of the body of the stomach (yellow arrow).

a malignant mass, the patient underwent diagnostic laparoscopy for staging that reported enlarged perigastric lymph nodes without any evidence of peritoneal implants. A surgical biopsy of the lymph node was negative for malignant cells. The patient was diagnosed with severe gastritis secondary to *H. pylori* and was discharged on triple-antibiotic therapy for 2 weeks.

One month later, she presented to the emergency department with melena. A repeat abdominal and pelvic computed tomography revealed an increase in the size of the gastric mass measuring 5.2 × 5.2 × 5.4 cm (Figure 4). A repeat EGD redemonstrated the friable mass with large ulcers in the stomach and body without any change in size or endoscopic appearance despite successful eradication of *H. pylori* (as repeat biopsy was negative for bacteria and intestinal metaplasia). An EUS demonstrated a homogeneous, hypoechoic, 4.5 × 3.5 cm gastric mass that originated from the muscularis propria (Figure 5). Multiple deep biopsies of the mass demonstrated findings consistent with inflammatory gastritis while core fine-needle biopsy demonstrated myofibroblastic tissue with lymphoplasmacytic infiltrate. Immunohistochemistry was negative for CD 117, S-100, and anaplastic lymphoma kinase-1; however, it was positive for SMA, desmin, and vimentin, suggesting the mesenchymal origin of the tumor vasculature, fibroblasts, and lymphoid cells (Figure 3). Hospital course was complicated by recurrent episodes of melena, and she received a total of 32 units of packed red blood cells. After stabilization, the patient underwent a robotic partial gastrectomy with intraoperative EGD, which unveiled an ulcerated gastric mass in the posterior wall. Surgical pathology reported a spindle cell lesion admixed with dominant lymphoplasmacytic component without perivascular cuffing favoring the diagnosis of a G-IMT. She was then discharged without any further complications. On 6-month follow-up, she was symptom-free and repeat radiographic studies did not show any concern for tumor recurrence.

DISCUSSION

Inflammatory myofibroblastic tumors (IMTs) are rare soft-tissue neoplasms with unclear etiology and variable biological behaviors ranging from benign lesions to more aggressive variants.[3] In decreasing order of frequency, intra-abdominal IMTs have been reported to occur in the omentum, mesentery, liver, stomach, bowel wall, and spleen.[3] G-IMT typically affects children and younger adults and has marked female preponderance with a female-to-male ratio of 4:1.[5] The exact etiopathogenesis of these tumors remains unclear. However, various mechanisms of tumor development consist of a reactive inflammatory response to infections by organisms such as *H. pylori*, *Escherichia coli*, and Epstein-Barr virus, among others, have been proposed.[6] It may also occur as a secondary response to recent stress from surgery,

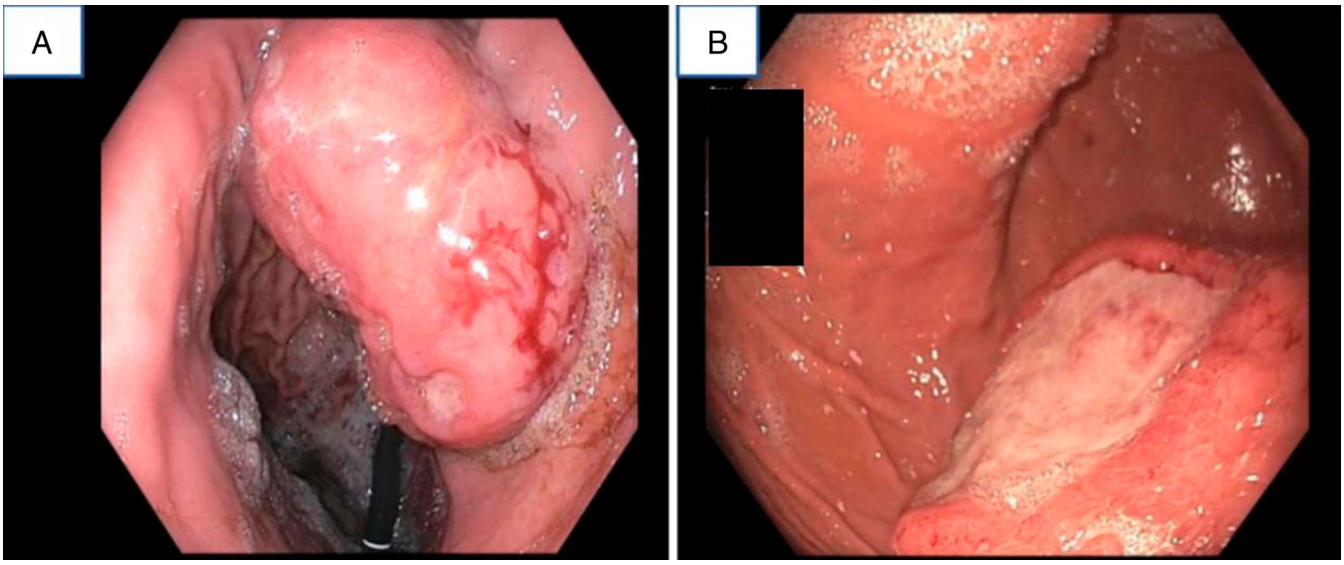

Figure 2. Endoscopic views of the 7 × 10 cm, large friable, ulcerated, necrotic, fungating mass that originates at the fundus (A) and extends into the body (B).

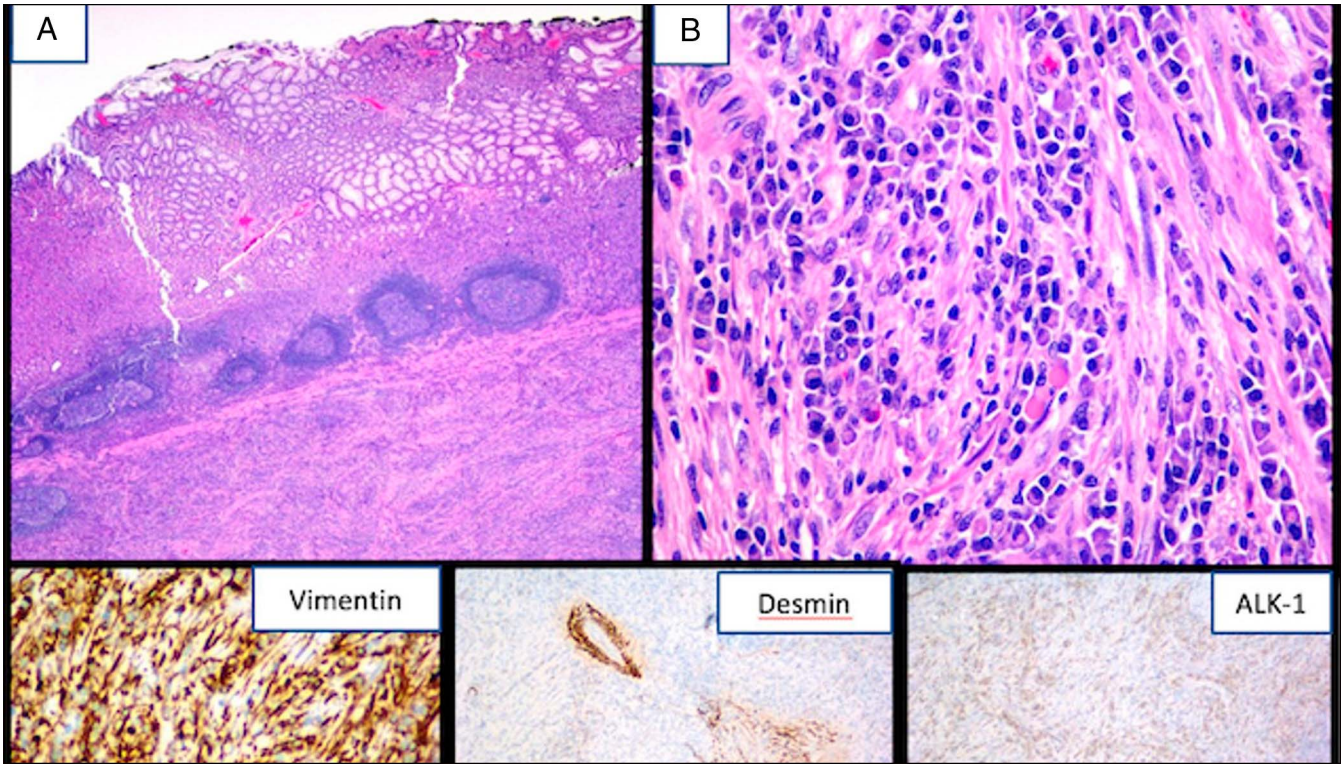

Figure 3. (A) H&E stain (20×) of a gastric mass with gastric mucosa and prominent lymphoid aggregates. (B) H&E stain under high power view (400×) showing spindle cell lesion with dominant lymphoplasmacytic infiltrate and without perivascular cuffing consistent with a diagnosis of a gastric inflammatory myofibroblastic tumor. Immunohistochemical stains show vimentin and desmin positivity along with anaplastic lymphoma kinase-1 negativity. H&E, hematoxylin and eosin.

trauma, radiation, or steroid use.[7] G-IMT has no specific clinical manifestations but often presents with abdominal pain, weight loss, fever, hematemesis, melena, or palpable abdominal mass. Laboratory abnormalities such as anemia, elevated erythrocyte sedimentation rate, and thrombocytosis are common manifestations.[6] These features tend to abate after complete surgical resection and reappear if the tumor recurs.

Our patient was found to have an abdominal mass concerning for malignancy. She underwent an EGD and was diagnosed with chronic untreated *H. pylori* ulcer surrounding the mass, possibly indicating a chronic inflammatory response that may have contributed to the development of the G-IMT. G-IMT manifests with nonspecific symptoms and signs as mentioned above, with iron deficiency anemia being a consistent finding.[7] Even with a thorough diagnostic workup, which included computed tomography (CT) scan, laboratory analyses, and EUS with biopsies, it was difficult to make an accurate preoperative tissue diagnosis. In most cases, G-IMT features mimic malignancy on endoscopy and radiological imaging. As the clinical and radiological features are nonspecific, the diagnosis of G-IMT comes to light only after

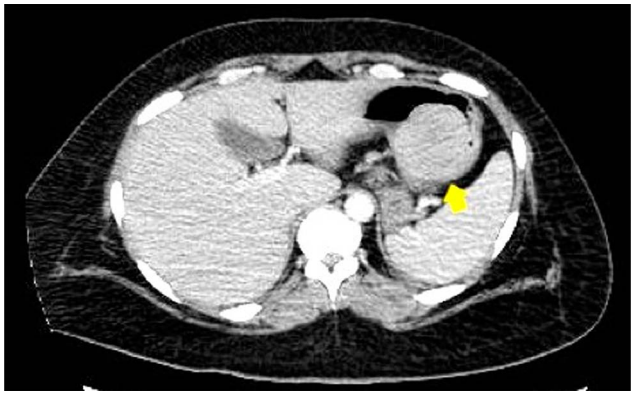

Figure 4. Abdominal and pelvic computed tomography with intravenous contrast (repeated): Increased size of the gastric mass is noted, then measuring 5.2 × 5.2 × 5.4 cm (yellow arrow).

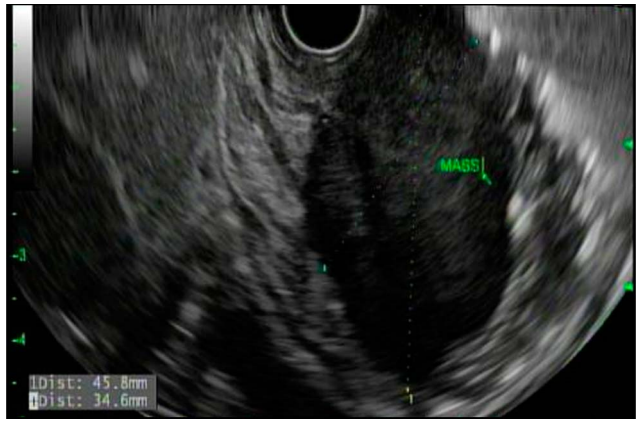

Figure 5. Endoscopic ultrasound views of a 4.5 × 3.5 cm mass with an ulcerated friable surface that originates from the muscularis propria. The mass appears hypoechoic and homogeneous.

a histopathological examination of the excised specimen.[8] Owing to the submucosal location of the tumor, endoscopic biopsies frequently reveal only normal or inflamed gastric mucosa, eluding preoperative diagnosis.[9]

Predominantly, tumor cells are immune-positive for vimentin, smooth muscle antibody (SMA), muscle-specific actin, and desmin or could focally exhibit a positive stain for creatine kinase and Klotho-derived peptide 1.[5] They are negative for S-100, CD117, and estrogen receptors.[5] Approximately 60% of IMTs overexpress ALK proteins, which are detected by immunohistochemistry and are used as a specific prognostic marker if found positive.[5] Coffin et al (1995) reported that older patients often had ALK-negative tumors and such tumors were more likely to show atypical histological features.[5] ALK-positive IMTs occurred more frequently in younger patients with a favorable prognosis but with a higher propensity for local recurrence.[5]

The primary occurrence of G-IMT is extremely rare and closely resembles GIST. A definitive diagnosis of G-IMT is only made postoperatively with histopathology and immunohistochemistry stains that demonstrate positivity for SMA and vimentin.[10] Most GISTs are positive for CD117, DOG1 expression, CD34, and S100 expression, which are negative in G-IMT.[11]

In our patient, microscopically, the tumor revealed prominent lymphoid aggregates and typical spindle cells with dominant lymphoplasmacytic infiltrate and without perivascular cuffing (Figure 3). Immunohistochemistry was negative for CD 117, S-100, and ALK-1 and positive for SMA, with an abundance of myofibroblasts along with expression of desmin and vimentin, suggesting smooth muscle of the vasculature, fibroblasts, and lymphoid cells (Figure 3). In this case, postoperative pathology and immunohistochemistry analysis were key in establishing a diagnosis of primary G-IMT.

Complete surgical resection is the most effective treatment method and will confirm the diagnosis of G-IMT by histopathological examination.[12] In cases where complete resection is not possible, radiotherapy and chemotherapy consisting of cisplatin, doxorubicin, and methotrexate should be considered.[12] Because of a significant local recurrence rate, unpredictable nature of the disease, and lack of well-defined prognostic criteria, long-term follow-up is highly recommended.[13] Recurrence rates after resection have been reported to be as high as 25% and is most commonly caused by positive surgical margins.[13,14] There are no established guidelines for long-term follow-up of G-IMT as the disease is rare; however, most cases have reported using periodic CT imaging, EGD, or EUS.[13,14]

Primary G-IMT is an extremely rare disease that closely resembles GIST. A definitive diagnosis is made postoperatively with histopathology and immunohistochemistry stains that demonstrate positivity for SMA and vimentin. When completely resected, the prognosis is favorable unless there is incomplete resection, in which case the recurrence rate is high. Hence, it is emphasized that G-IMT should be considered as a key differential in cases of exophytic growth arising from the stomach, especially from the muscularis layer.

DISCLOSURES

Author contributions: D. Chukkalore: writing the manuscript, data gathering, and literature review; J. Loeffler: writing, editing, and revision of the manuscript; H. Rabah and S. Amarnath: conceptual design, data analysis, and manuscript review; H. Al Moussawi and L. Deeb: review and revision of the manuscript. D. Chukkalore is the article guarantor.

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