

Case Report

High-risk jejunal gastrointestinal stromal tumor: case report and comparative review of international guidelines

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ABSTRACT

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, arising from interstitial cells of Cajal. Diagnosis and management have advanced through molecular testing, surgery, and tyrosine kinase inhibitors. Although usually seen in older adults, GISTs may occur in younger patients with atypical symptoms. We report a high-risk jejunal GIST and compare major international guidelines to inform management. A literature review and guideline comparison were conducted using recent recommendations from ACG, AGA, ESMO, BSG, ESGE, NICE, JSCO, and the Royal College of Pathologists. These were correlated with the clinical, imaging, surgical, and histopathological findings of a 40-year-old male patient. The patient presented with abdominal distension, obstructive symptoms, and a palpable mass. CT revealed a 14×13×11 cm well-circumscribed mass in the epigastric/mesogastric region. Surgery identified a jejunal tumor 30 cm distal to the ligament of Treitz, requiring en bloc resection and primary anastomosis. Histopathology confirmed a spindle-cell GIST (CD117+, DOG1+, CD34–, Ki-67: 5/50 HPF) with high-risk features. Postoperative recovery was uneventful. Guidelines consistently recommend R0 resection, immunohistochemical confirmation, mutational profiling, and long-term surveillance. Adjuvant imatinib is advised for high-risk disease. This case underscores the need for early recognition and guideline-based management of GISTs, particularly in patients with nonspecific symptoms and large abdominal masses. International concordance emphasizes imaging, endoscopic ultrasound with biopsy, immunohistochemistry, and molecular testing for risk stratification. Surgery remains the cornerstone of treatment, with adjuvant therapy in high-risk cases. Multidisciplinary care is essential to optimize outcomes.

Keywords: Gastrointestinal stromal tumor, GIST, CD117, DOG1, Surgical resection, Adjuvant therapy, Imatinib, Endoscopic ultrasound, High-risk GIST

INTRODUCTION

GISTs are the most common mesenchymal neoplasms of the gastrointestinal tract, originating from the interstitial cells of Cajal-pacemaker cells responsible for gut motility and are primarily characterized by activating mutations in the KIT or PDGFRA genes, which determine their biologic behavior and therapeutic responsiveness.^{1,2} Despite their relative rarity, with an annual incidence

ranging from 8 to 15 cases per million individuals, improvements in diagnostic imaging and endoscopic techniques have led to increased detection rates, particularly of small, asymptomatic lesions or micro-GISTs discovered incidentally during routine evaluations.^{1–5}

Most GISTs are sporadic; however, genetic syndromes such as neurofibromatosis type 1, Carney–Stratakis syndrome, and germline KIT or PDGFRA mutations have

been implicated as important risk factors.^{2,5} While the stomach remains the most common site of origin (60–65%), followed by the small intestine (20–30%), clinical presentation can vary widely—from incidental findings to overt gastrointestinal bleeding, abdominal pain, or obstructive symptoms, depending on tumor size, location, and malignant potential.^{2,4,5}

A stepwise diagnostic approach is essential and includes clinical assessment, imaging—primarily contrast-enhanced computed tomography (CT)—and tissue diagnosis via endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB), with immunohistochemical confirmation using CD117 and DOG1, and molecular profiling to guide targeted therapy.^{1,2,4-6} Surgical resection with negative margins (R0) remains the cornerstone of treatment for localized disease, while tyrosine kinase inhibitors (TKIs), such as imatinib, represent the mainstay of therapy for advanced, unresectable, or metastatic disease.^{2,5,7,8}

Given the complexity of clinical presentation and therapeutic decision-making, international guidelines from major organizations—including the American College of Gastroenterology (ACG), American Gastroenterological Association (AGA), European Society for Medical Oncology (ESMO), European Society of Gastrointestinal Endoscopy (ESGE), British Sarcoma Group (BSG), Japan Society of Clinical Oncology (JSCO), and NICE—provide critical frameworks for the diagnosis, risk stratification, and management of patients with GIST.¹⁻⁸

CASE REPORT

A 40-year-old male with no history of chronic degenerative diseases or previous surgeries presented to the emergency department with a 3-day history of abdominal distension, associated with 4 days of constipation, nausea with three episodes of vomiting, oral intolerance, and a progressively enlarging epigastric mass noted over the past two months.

Physical examination revealed a distended abdomen with absent peristalsis. On palpation, a firm mass was noted occupying the epigastrium, left hypochondrium, and mesogastrium, without clear delimitation and non-tender on examination. Contrast-enhanced abdominal CT scan demonstrated a well-defined, ovoid, solid mass involving the epigastrium and mesogastrium, measuring 14×13×11 cm. The lesion exerted a mass effect on adjacent intestinal loops and was surrounded by a peripheral vascular network composed of small vessels (Figure 1).

Laboratory tests were within normal limits. The patient was taken to the operating room for an exploratory laparotomy. A tumor resection was performed with negative margins. The mass originated from the jejunum approximately 30 cm distal to the ligament of Treitz and was adherent to the mesentery and adjacent jejunal loops. The tumor was firm and measured approximately 20 cm in diameter. A 50 cm segment of the jejunum was resected,

followed by a termino-terminal jejunojunctional anastomosis (Figure 2). Histopathological analysis confirmed a GIST of the spindle cell type, classified as high risk for disease progression. Immunohistochemistry was positive for CD117 and DOG1, negative for CD34, with a Ki-67 index of 5 positive cells per 50 high-power fields. Surgical margins were free of tumor (Figure 3). The patient had an uneventful postoperative course, without complications or abnormalities.

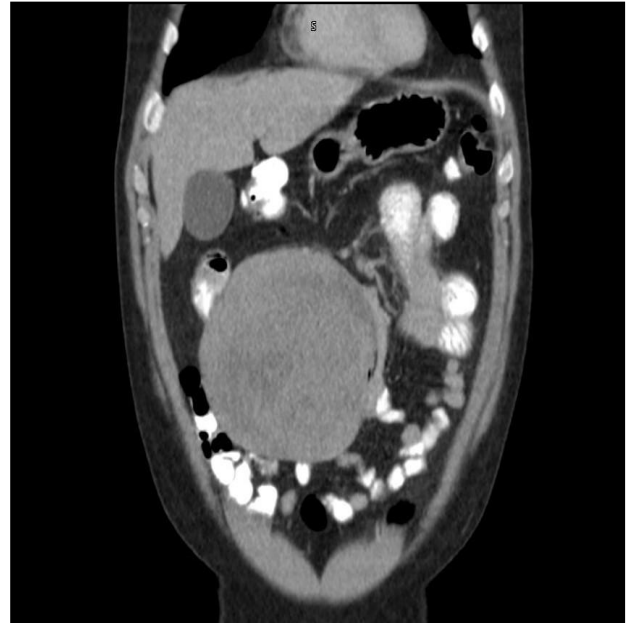


Figure 1: Coronal section of a Contrast-enhanced abdominal CT scan demonstrated a well-defined, ovoid, solid mass involving the epigastrium and mesogastrium, 14×13×11 cm.

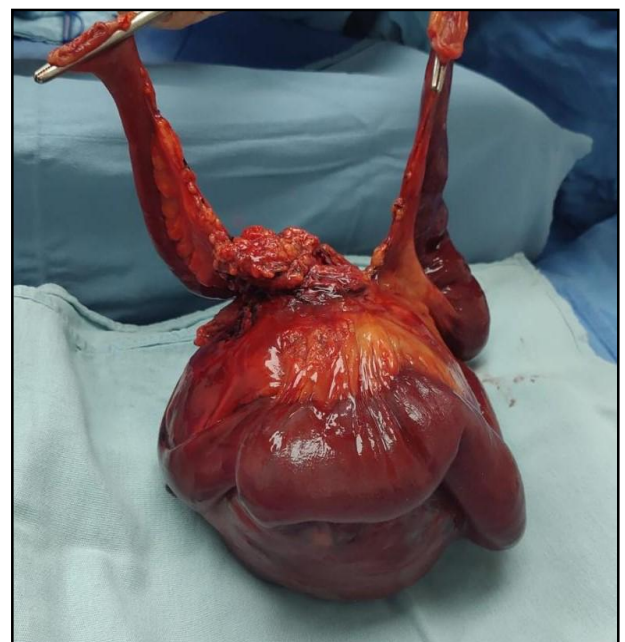


Figure 2: Resection of tumor dependent on the jejunum, approximately 20 cm in diameter.

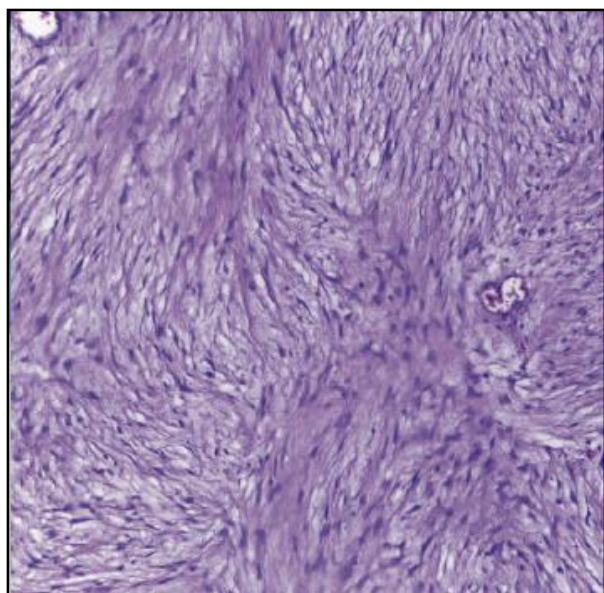


Figure 3: Histopathological analysis confirmed a gastrointestinal stromal tumor (GIST) of the spindle cell type, classified as high risk for disease progression. Surgical margins were free of tumor.

DISCUSSION

GISTs are the most common mesenchymal neoplasms of the digestive tract, though their overall incidence remains low. They arise from interstitial cells of Cajal-gastrointestinal pacemaker cells-and are typified by activating mutations in genes such as KIT or PDGFRA, which influence their biologic behavior and therapeutic response. According to the American College of Gastroenterology (ACG, 2023) clinical practice guideline, the annual incidence of GIST in the general population ranges from 10 to 15 cases per million, although autopsy studies have identified micro-GISTs-subclinical lesions-that suggest the true prevalence may be higher.¹ This estimate aligns with data from the ESMO–EURACAN–GENTURIS guidelines (2022), which report an incidence of 8 to 15 cases per million per year, with slightly higher rates in European and Asian countries.²

Within the context of diagnostic endoscopy, the American Gastroenterological Association (AGA, 2022) and the European Society of Gastrointestinal Endoscopy (ESGE, 2022) state that GISTs account for approximately 5% of all subepithelial lesions detected during routine procedures. This underscores their increasing detection due to improved imaging accessibility and endoscopic surveillance.^{3,4} The mean age at diagnosis is between 60 and 70 years, with a slight male predominance, though large population-based studies show no significant sex difference.^{2,4} The Japan Society of Clinical Oncology (JSCO, 2024) reports similar incidence rates in Japan, with a mean age at diagnosis of 58 years, and highlights a substantial prevalence of gastric micro-GISTs incidentally found via gastroscopy in asymptomatic patients.⁵ Most GISTs are sporadic, without known familial or

environmental associations. However, clinical guidelines consistently identify several genetic and syndromic risk factors. According to ESMO and JSCO, these include: Germline mutations in KIT or PDGFRA, particularly in familial GIST syndromes.^{2,5} Neurofibromatosis type 1 (NF1), which predisposes patients-especially with CD117/DOG1-negative tumors-to multiple intestinal GISTs, Succinate dehydrogenase (SDH) deficiency, particularly in young women, associated with Carney–Stratakis syndrome and KIT/PDGFRA wild-type gastric tumors.^{2,5} Detection of micro-GISTs alongside gastric cancer, possibly representing a latent or precursor form of the disease.⁵ Non-genetic risk factors remain unclear. Some retrospective cohort studies have suggested increased incidence in patients with a history of chronic pancreatitis, abdominal radiotherapy, or exposure to gastrointestinal carcinogens, though these are not recognized as primary risk factors in current guidelines.^{1,2}

GISTs can occur anywhere along the gastrointestinal tract, most commonly in the stomach (60–65%), followed by the small intestine (20–30%), and less frequently in the colon, rectum, or esophagus. A significant proportion of cases are asymptomatic and discovered incidentally during endoscopic or imaging studies conducted for unrelated reasons.^{1,2} When symptomatic, clinical presentation varies depending on tumor location, size, and aggressiveness. The ACG and AGA guidelines list common manifestations including Gastrointestinal bleeding (overt or occult), abdominal pain or palpable mass, nausea, vomiting, or early satiety, notably with large gastric tumors, obstructive symptoms when located in the intestine, weight loss, especially in advanced disease.^{1,3}

European and Japanese guidelines note that small tumors (<2 cm) are usually asymptomatic, whereas larger GISTs may cause complications such as perforation, tumor necrosis, or peritoneal or hepatic metastases.^{2,5} The diagnostic approach to GIST is stepwise, incorporating clinical evaluation, advanced imaging, tissue sampling with immunohistochemistry, and molecular profiling for risk stratification and treatment planning. Endoscopic evaluation may reveal a subepithelial mass with intact or ulcerated mucosa but does not assess lesion depth or origin. Endoscopic ultrasound (EUS) is considered essential by ACG, AGA, and ESGE for lesion characterization.^{1,3,4}

EUS allows for determination of origin from the muscularis propria (fourth layer), Measurement of size, borders, echotexture, and suspicious features (e.g., heterogeneity, irregular margins, internal cystic spaces) and Guidance of biopsy sampling via fine-needle biopsy or aspiration (EUS-FNB/FNA), strongly recommended for lesions >2 cm or those exhibiting high-risk features.^{3,4} Contrast-enhanced computed tomography (CT) is the imaging modality of choice for local and systemic staging, and is advised for lesions >2 cm, suspected metastases, or preoperative planning. PET–CT may be indicated for assessing treatment response or metastatic disease in select

cases.^{2,5} Pathological diagnosis, as recommended by Royal College of Pathologists, ESMO, and JSCO, should include sample acquisition via EUS-FNB or excised specimen, especially for lesions >2 cm or with aggressive characteristics.^{2,5,6} Diagnostic criteria include: CD117 (c-KIT) and DOG1 immunohistochemistry (both positive in >95% of GISTs), Mitotic index (mitoses per 5 mm² or 50 high-power fields), Tumor size and Resection margin status (R0 vs. R1).^{2,5}

Molecular profiling for mutations in KIT (exons 9, 11, 13, 17) and PDGFRA (exons 12, 14, 18) is crucial to guide imatinib sensitivity and prognostication. Evaluation for SDH, BRAF, or NTRK alterations is recommended for wild-type tumors.^{2,5} Complete surgical resection (R0) is the treatment of choice for localized, resectable gastrointestinal stromal tumors (GISTs), as endorsed by all major clinical guidelines.^{1,4,6,7} The European Society for Medical Oncology (ESMO) and the British Sarcoma Group (BSG) recommend resection without capsular rupture or preoperative biopsy when the diagnosis is clear.^{2,7} The Japanese Society of Clinical Oncology (JSCO) and NICE advocate for minimally invasive techniques, such as laparoscopic resection or endoscopic full-thickness resection (EFTR), particularly in small (<2–3 cm), low-risk gastric lesions.^{6,8} The European Society of Gastrointestinal Endoscopy (ESGE) advises that endoscopic resection with EUS guidance be performed exclusively in specialized centers and only for small, well-defined lesions.⁴

Imatinib is the standard adjuvant therapy for patients with KIT or PDGFRA-mutant GISTs at intermediate or high risk of recurrence, recommended for a minimum of three years, as supported by ESMO, JSCO, and BSG.^{2,5,7} In cases harbouring specific mutations, such as PDGFRA D842V, avapritinib is recommended, given the ineffectiveness of imatinib against this mutation.² Neoadjuvant imatinib is indicated for locally advanced tumors or when tumor downsizing is needed to facilitate surgery in anatomically challenging locations such as the duodenum, esophagus, or rectum.^{2,5}

In the metastatic setting, imatinib remains the first-line therapy and should be continued until disease progression or unacceptable toxicity. Upon progression, sunitinib is recommended as second-line treatment, regorafenib as third-line, and ripretinib—which has received regulatory approval—is advised as fourth-line therapy by both ESMO and JSCO.^{2,5}

Post-treatment surveillance is guided by the estimated risk of recurrence, based on tumor size, mitotic index, and anatomical location, using validated models such as Miettinen–Lasota or AFIP criteria.^{2,6,7} For low-risk GISTs (<2 cm, low mitotic index), AGA, ESGE, and JSCO recommend endoscopic or CT surveillance every 6–12 months.^{2,4,5} For intermediate- or high-risk tumors, regardless of adjuvant therapy status, ESMO, BSG, and JSCO recommend contrast-enhanced CT of the chest,

abdomen, and pelvis every 3–6 months for the first 3 years, followed by imaging every 6–12 months until completing 5 years of follow-up.^{2,5,7} The BSG suggests extending follow-up up to 10 years in high-risk or recurrent cases.⁷

For metastatic or unresectable GISTs, imaging should be performed every 2–3 months during treatment with tyrosine kinase inhibitors (TKIs). PET–CT may be considered in select cases for early assessment of therapeutic response.^{2,5}

CONCLUSION

Gastrointestinal stromal tumors (GISTs) represent a rare but clinically significant subset of gastrointestinal neoplasms. Early recognition and accurate diagnosis are critical, particularly in patients presenting with nonspecific abdominal symptoms and a palpable mass, as illustrated by the case of a 40-year-old male with a large jejunal GIST manifesting as progressive abdominal distension and obstructive symptoms. Cross-sectional imaging and intraoperative findings confirmed a sizable, well-vascularized mass originating from the jejunum, requiring segmental resection and primary anastomosis.

Histopathological evaluation remains essential for confirming the diagnosis and assessing malignant potential through immunohistochemistry (CD117+, DOG1+) and mitotic index. In this patient, the tumor exhibited high-risk features, justifying the need for long-term surveillance and consideration of adjuvant therapy.

This case underscores the importance of integrating clinical suspicion, imaging, and histopathological data in the management of GISTs. Complete surgical resection remains the cornerstone of treatment for localized disease, and multidisciplinary coordination is vital for optimizing outcomes, especially in high-risk cases. Continued adherence to international clinical guidelines ensures appropriate stratification and individualized management, contributing to improved survival and quality of life in affected patients.

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