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CASE REPORT

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Hybrid surgical approach excision of gastrointestinal stromal tumor (GIST): A case report of GIST at an unusual location and review of the literature

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Key Clinical Message

Gastrointestinal stromal tumors are the most common malignant subepithelial lesions involving the gastrointestinal tract. Surgical techniques have been the mainstay of treatment, however, in recent times hybrid surgeries are being introduced yielding better clinical outcomes.

KEYWORDS

endoscopic surgery, gastrointestinal stromal tumor, GI surgery, hybrid surgery

1 | INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are a type of cancer that initially form in the digestive system.[1] GISTs are the most common malignant subepithelial lesions involving the gastrointestinal (GI) tract. They occur most frequently in the stomach and small intestine and are rarely found at the esophagus and the gastroesophageal junction. These rare tumors take their origin from the interstitial cells of Cajal from the myenteric plexus.[2,3] As a GIST continues to grow, it can become symptomatic leading to the manifestation of clinical symptoms. Upon confirmation of the diagnosis, complete resection of GISTs is the only curative approach for the patient. Therefore, surgical resection must be the first choice of treatment for a permanent cure.[1] The innovation of endoscopic surgery represents a critical element and a valuable aspect in surgery. When these GISTs are found to be located around the esophagogastric junction, surgical risk of deformities or stenosis increases, which can lead to several complications and reduction in the quality of life. In the management of these cases, a more sophisticated approach should be considered. Hybrid surgery techniques which combine laparoscopic and

endoscopic procedures can result in better outcomes and results for these patients.[3,4] The better oncologic outcomes and safety in laparoscopic GIST resection are also well established as negative margins are the preferable choice of surgery in order to improve the patients' survival rate.[1,4] Based on inconvenient locations of the tumors, hybrid techniques, which are a new type of treatment options combining endoscopy and laparoscopy, are needed to correctly remove these lesions and to achieve a successful complete resection of the tumor.[1] The aim of our paper is to present a case of a patient who was successfully managed by this hybrid approach, share existing data on the adaptation of these type of surgical technique in the treatment of GISTs and shed some light on all previously published papers reporting hybrid surgery for GISTs. We have conducted a thorough literature review which entailed the search of "PubMed" as a primary database source to collect the available case reports that utilized hybrid surgical techniques for the treatment of GISTs. Demographic data, as well as the location of tumor, histopathological findings, treatment strategy, and technique, were all recorded (Table 1).

1.1 | Case history

This is a case of a 56-year-old male patient, a known case of diabetes mellitus and hypertension, who was referred to the surgical department for having a gastric mass with a history of anemia, syncopal attacks, and hematemesis. He presented to the general surgery clinic complaining of hematemesis, dizziness and fatigue, with a provisional diagnosis of a gastric lesion. Physical examination was unremarkable, and the patient was vitally stable. Multiple laboratory tests were ordered, starting with a complete blood count, which revealed a low hemoglobin level of 6.21 g/dL, white blood cells (WBC) were slightly elevated (10.70×10^9/L), red blood cells (RBCs) were low (2.32×10^{12}/L), and hematocrit was also low (20.70%). Likewise, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration were low (26.70 pg and 30.10 g/dL, respectively). Nevertheless, mean corpuscular volume (MCV) was normal (88.90 fL). Red cell distribution width (RDW) was high (18.10%). Also, platelet count was high (577×10^9/L), while mean plasma volume (MPV) was low (6.80 fL). Segmented neutrophil was high (62.90%). Monocytes (10.40%) and absolute monocytes (1.11×10^9) were elevated. Erythrocyte sedimentation rate (ESR) (58 mm/h) was found to be markedly elevated. The patient's blood group is A+ and was negative for antibodies. The Basic metabolic panel was all within normal limits except for serum creatinine (CRE2) which was marginally low (0.64 mg/dL). Coagulation profile was also normal. Lastly, serology tests were found to be nonreactive. Table 2 provides an overview of the abnormal results.

2 | METHODS

A computed tomography (CT) scan of the abdomen identified a polypoidal-looking neoplastic mass at the gastric fundus measuring 4×3 cm. The patient underwent esophagogastroduodenography (EGD) to further investigate the tumor. A sisal fundic paracardial submucosal lesion with a single small active ulcer was found. A biopsy was sent for histopathological analysis, showing a submucosal spindle cell lesion suggesting a GIST. The patient was urgently admitted to the intensive care unit for blood transfusions and resuscitation to treat his acute anemia. He had a transfusion of 2 units of packed RBCs initially, which corrected his hemoglobin to 8.7 g/dL. The patient was later evaluated and was prepared to be taken to the OR for the excision of the gastric mass.

Surgical excision of the tumor via a hybrid approach was decided considering the location of the tumor. The patient was scheduled for laparoscopic assisted excision of the gastric polyp with endoscopy assistance. Under general anesthesia, in anti-Trendelenburg position, intraoperative endoscopy was done to localize the mass. Then, dissection of the greater omentum over the greater curvature of the stomach through four ports was done. Three openings in the stomach were created for the trans-gastric surgical resection of the gastric GIST (measured 4×4 cm) through laparoscopy to achieve complete resection (Figure 1). The tumor was then extracted through an endoscope as shown in Figure 2. Subsequently, the openings were closed by a 2–0 sterile synthetic absorbable monofilament (Polydioxanone [PDS]; Johnson and Johnson, New Brunswick, NJ) in a two-layer continuous inverting suture pattern. Finally, methylene blue leak test was performed. The specimen was sent for histopathological analysis, in which it was paraffin block labeled (Figure 3). The rest of the procedure was well executed without any complications.

Histopathology reported a 4×3×2.5 cm soft tissue mass with a grayish–white cut section, embedded in two cassettes on gross examination. Microscopically, a spindle cell type GIST; G1 low grade (mitotic rate less than 5 per 5 mm^2) was found with no identified necrosis and no evidence of tumor infiltrating the margins (Figure 4A,B). Moreover, for immunohistochemistry, KIT (CD117) and DOG1 (ANO1) were seen to be positive (Figure 4C,D), while negative for S100, and smooth muscle actin (Figure 4E). Thus, confirming the diagnosis of GIST.

TABLE 1 Published studies reporting cases of hybrid surgeries performed for GISTs.

Author	YOP	Age & gender	Chief complaint	Location of lesion	Procedures for diagnosis confirmation	Findings	Treatment & surgeries
William G. Aguayo, et al[1]	2021	42, male	Nausea, vomiting, abdominal distension	2 cm away from the esophagogastric junction in the lesser curvature	Upper endoscopy Endoscopic ultrasound (EUS) Color doppler Immunostaining Contrast-enhanced abdominal computed tomography	Two small (1 × 1 × 0.5 cm & 0.5 × 0.5 × 0.3 cm) gastric lesions covered with normal mucosa Two small hypoechoic lesions with clear margins in the submucosal layer Pulsating vascular signal extending into the center of the low-echo lesion from the periphery Positivity for CD34 and CD 117, and were negative for S100 and anti-α-Sm-1 Did not reveal any masses or lymph nodes	Hybrid trans-gastric resection of the gastric GIST achieving complete resection Hybrid procedure with endoscopy and laparoscopy
Naoto Fujiwara, et al[5]	2020	68, female	Mild dysphagia	Lower esophagus	CT Esophagogastroduodenoscopy Endoscopic ultrasound-guided fine needle aspiration Immunohistochemical analysis F-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography	Solid tumor, approximately 7 cm in size, in the lower esophagus Esophageal submucosal tumor with an ulcer at the top Spindle-shaped tumor cells with a high mitotic rate of 8/50 high power fields (HPFs) Positivity for CD34 and c-kit, and negativity for α-smooth muscle actin and S-100 High FDG accumulation, with a maximum standardized uptake value of 11.8, in the tumor	Hybrid procedure of video-assisted thoracoscopic surgery (VATS) and hand-assisted laparoscopic surgery (HALS) techniques achieving tumor resection
Hishaam Ismae, et al[4]	2016	64, male	Umbilical hernia	Gastric fundus and lesser curvature 2 cm from the GE junction	CT EGD/EUS Fine needle aspiration	4.7 cm mass involving the gastric fundus and lesser curvature 2 cm from the GE junction and a fat containing umbilical hernia 5 cm submucosal hypoechoic nodule located within 2 cm of the gastroesophageal junction along the anterior wall of the stomach Spindle cells, DOG-1 and CD117 (C-kit) positive	Lesion-lifting endoscopically assisted laparoscopic wedge resection Hybrid approach via laparoscopy and endoscopy

TABLE 2 Abnormal lab results.

Test	Normal values	Result
Complete blood count (CBC); with differentials		
Hemoglobin (HGB)	13–17	6.21 g/dL
White blood cells (WBC)	4–10	10.70×10^9/L
Red blood cells (RBCs)	4.5–5.5	2.32×10^{12}/L
Hematocrit (HCT)	40–50	20.70%
Mean corpuscular hemoglobin (MCH)	27–32	26.70 pg
Mean corpuscular hemoglobin concentration (MCHC)	31.5–34.5	30.10 g/dL
Red cell distribution width (RDW)	11.5–14.5	18.10%
Platelet count	140–440	577×10^9/L
Mean plasma volume (MPV)	83–99	6.80 fL
Segmented neutrophil		62.90%
Monocytes		10.40%
Absolute monocytes	0.1–0.8	1.11×10^9
Erythrocyte sedimentation rate (ESR)	4–10	58 mm/h
Basic metabolic panel		
Serum creatinine (CRE2)	0.72–1.25	0.64 mg/dL

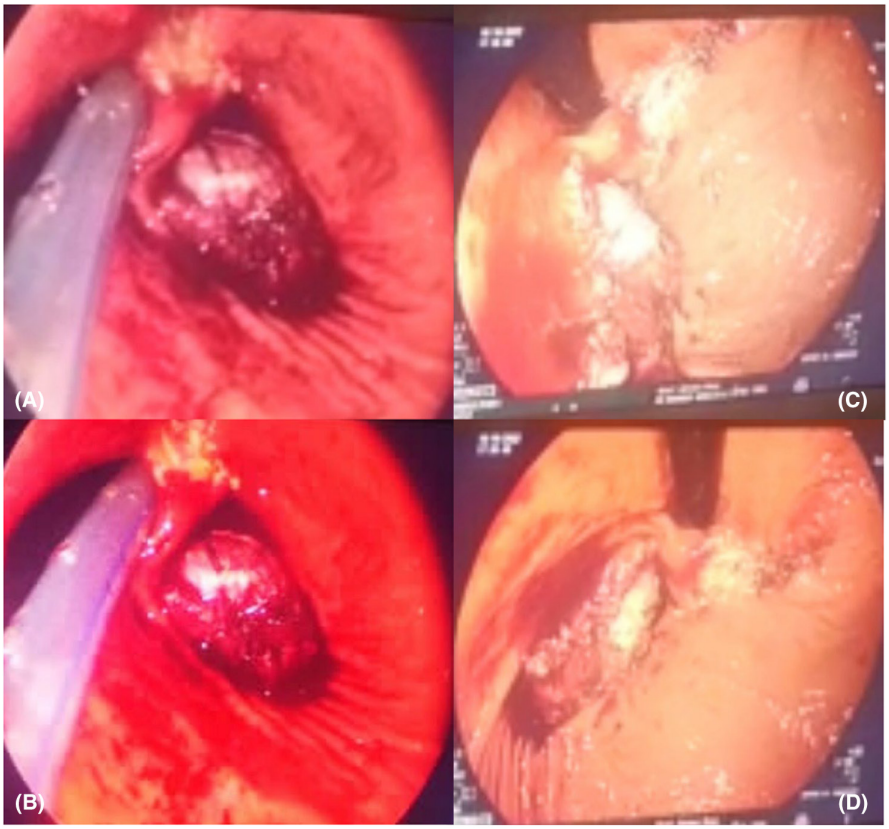

FIGURE 1 Operative photograph showing (A and B) Laparoscopic and (C and D) Endoscopic view during the surgical resection of the gastric gastrointestinal stromal tumor.

3 | CONCLUSION AND RESULTS

On the day of the surgery, the patient received 2 units of packed RBCs to reach a hemoglobin goal of 10 g/dL. He was transferred to the ward for observation. Postoperatively, the patient initially had poor bowel function with nausea and abdominal distension. Ambulation was gradually encouraged with close observation. He started feeding gradually, this wasn't tolerated at the initial trial, but eventually improved and was tolerated. The patient was vitally stable

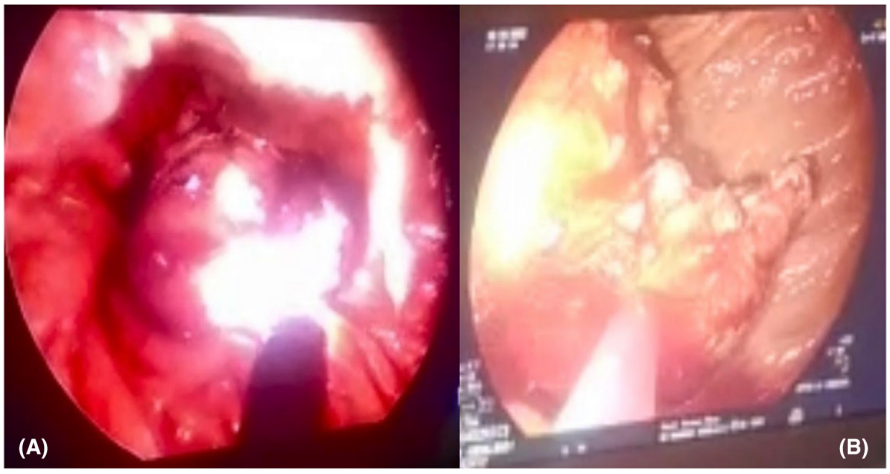

FIGURE 2 Hybrid view of the procedure (A) laparoscopic and (B) endoscopic view at the time of tumor extraction by the endoscope.

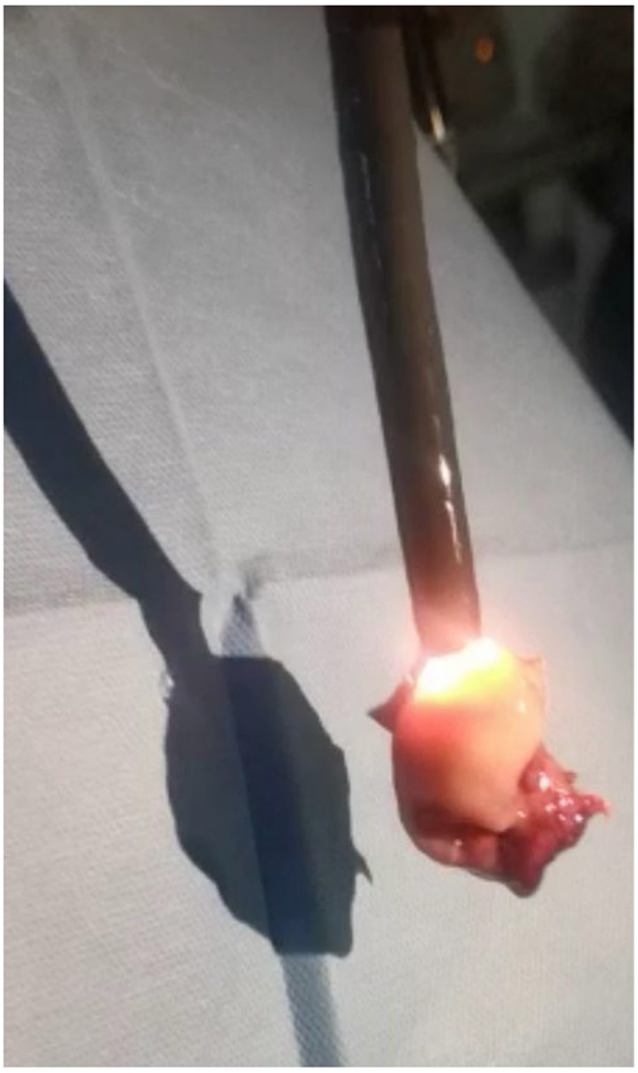

FIGURE 3 An image showing the resected tumor that is 4×3×2.5 cm in size.

and discharged on his third postoperative day in good general condition with no complications and was encouraged to follow up in OPD.

4 | DISCUSSION

Gastrointestinal stromal tumors are rare neoplasms that are thought to arise from the interstitial cells of Cajal in the myenteric plexus. The global prevalence is estimated to be 130 cases per million, and the annual incidence ranges from 10 to 22 per million. Men and women are equally affected, and the median age of onset is 63 years. Most cases of GIST are sporadic, where there are mutations in receptor tyrosine kinase genes KIT and platelet-derived growth factor alpha (PDGFRA) genes. Where KIT accounts for 75%–80% of cases and PDGFRA accounts for one-third of the remaining cases. In less than 5% of cases, GIST can occur in tumor syndromes like neurofibromatosis type 1 (NF1), familial GIST syndrome, Carney–Stratakis syndrome, and Carney triad. The most common location for GIST is the stomach (50%–60%) followed by the small intestine (30%–35%), and it can less commonly affect other areas of the GI tract and rarely affect other intra-abdominal soft tissues as well. The chief concern of patients with GIST largely depends on tumor location as well as its size. Symptoms in the outpatient setting can be abdominal pain, melena, fatigue or alterations in bowel habits, and dyspepsia. While in an emergency setting, GIST can present with clinical features of bowel perforation, bowel obstruction, or even acute upper GI bleeding. On physical examination, abdominal tumors can be palpable.[6,7]

In the year 1995, Huizinga et al. reported findings that resulted in the development of the hypothesis that KIT was needed for the development and growth of the interstitial Cajal cells.[8] In 1998, Hirota et al. discovered KIT mutations in GIST.[9] In addition, it was also observed that 95% of GISTS are immunohistochemically positive for the receptor tyrosine kinase KIT, which is also known as CD117.[9,10] Now, we know that mutations in KIT, which result in the activation of the kinase, are observed in 70%–80% of GISTs. Subsequently, CD117

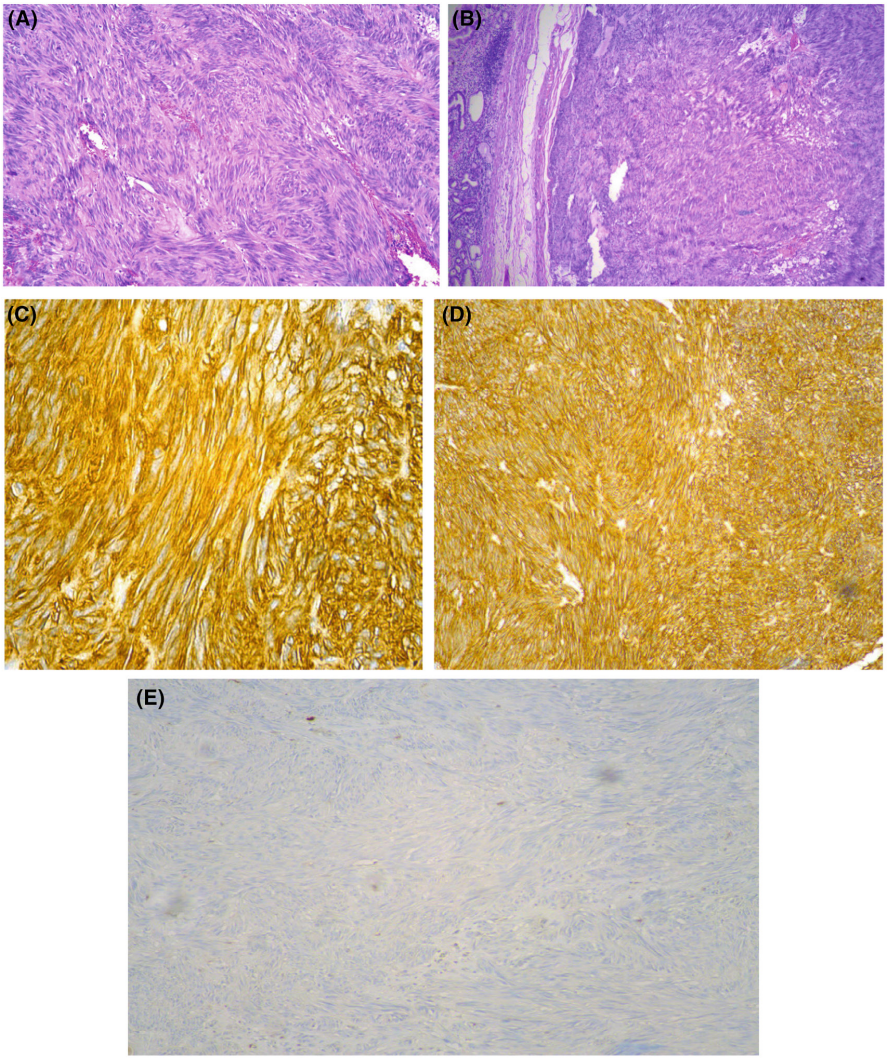

FIGURE 4 Microscopic view (A) high power view (×40) and (B) low power view (×10) denoting spindle cell type gastrointestinal stromal tumor; Grade 1 (low grade) with no identified necrosis and margins negative for tumor. (C) Immunohistochemistry study showing strong positivity for C-KIT (CD117) and (D) DOG1(ANO1). (E) Negative immunostaining for smooth muscle actin.

became a very important diagnostic marker for GIST. Furthermore, it is also an important target therapeutically. Mutations in KIT are not the only mutations responsible for GIST. Mutations in PDGFRA were found in 5%–10% of patients, whereas 9%–15% patients neither had mutations in KIT nor PDGFRA; these patients were classified as having "wild type" mutations.[11] In a nonpathological state, KIT binds with stem cell factor and this results in receptor dimerization and kinase activation. Thus, the presence of receptor activating mutations in KIT receptors will lead to oncogenic activation of kinase.[12] Each mutation results in different pathologic features, including tumor location, morphology, and clinical features.[13–15]

GISTs are the most common tumor of the GI tract, despite this fact, other probable diagnoses should be excluded as management differs from one tumor to the other. As reported by Kirsch et al[16] some important differential diagnoses would include leiomyomas, schwannoma, desmoid fibromatosis, and inflammatory myofibroblastic tumor. A definitive diagnosis can be made by performing a comprehensive histopathological examination of the specimen. 95% of GISTs are known to have positive CD117 and DOG1,[11] this was also seen in our patient.

The prognosis is primarily determined by mitotic rate, tumor size, tumor location, and surgical margins.[17] Smaller GISTs (<2cm) are considered to be essentially benign.[18] Tumors located in the stomach, have a better prognosis when compared to those in the small intestine and rectum.[19]

The sole potentially curative management of GIST is complete surgical resection of the tumor.[20,21] GISTs uncommonly involve lymph nodes; hence, regional lymph node dissection is not done routinely.[18,22] Achieving an R0 resection of all gross and microscopic disease is associated with decreased recurrence and improved overall survival rate.[2] The tumor was located at the gastroesophageal junction in our case. Owing to its position, a conventional approach would be to perform a partial or total gastrectomy.[23,24] However, in recent times, hybrid surgeries have been performed, which include the utilization of laparoscopy and endoscopy. These new techniques have been associated with improved

clinical outcomes and are less invasive as compared to the conventional treatment modalities.[23,25] With these novel techniques, postoperative complications of gastrectomy like stenosis or deformity of the gastric inlet can be evaded.[23,24] The endoscope can be used to localize the tumor, help in dissection, and in extraction of the tumor.[26,27] Advanced tumors are managed medically. The first line therapy for GIST is imatinib, which is an inhibitor of three tyrosine kinase receptors.[28] For GIST which are not responding to imatinib, sunitinib can be used.[29] Since our patient's case was not advanced, it was managed only by surgery.

The National Comprehensive Cancer Network (NCCN) Guidelines[30] recommends follow-up using an abdominal and pelvic CT scan every 3–6 months for 3–6 years. In smaller tumors, the observation can be less frequent. In cases of partial resection or presence of metastases, follow-up needs to be done with CT or MRI every 3–6 months for 3–5 years, and if the aforementioned tests are inconclusive then PET scans can be used instead. In unresectable, metastatic, or recurrent cases, an abdominal and pelvic CT or MRI needs to be performed every 8–12 weeks.[30]

Finally, there is a necessity for the population of standardized criteria to advise for the adaptation of a hybrid approach in managing GISTs, outlining the possible complications, benefits, and long-term outcomes. Currently, the NCCN Guidelines[30] as well as clinical evidence and data[25,31] shared by experts in this field advise for the consideration of this technique, especially for tumors located at challenging locations. In addition, this hybrid approach offers a less invasive surgical intervention, which is of importance to consider in friable GISTs where intraoperative rupture or damage to the capsule is a possibility.

Cancerous growths known as GISTs begin in the digestive tract. Due to the tumor's proximity to the stomach's fundus in our patient, it was surgically excised using a hybrid approach. For the diagnosis, CT scans and esophagogastroduodenoscopy in particular are crucial. The only effective method for enhancing patients' life quality is by early surgical resection and histologic diagnosis. These methods seem to be the sole viable option and are incredibly dependable. Surgery will eventually define the future and, in some cases, the life of the patient when treating minor GISTs or GISTs in unusual locations. In order to adapt to these unusual and difficult situations, surgeons must have the flexibility to change their plans from orthodox methods to novel techniques such as hybrid surgical methods.

AUTHOR CONTRIBUTIONS

Islam Khaled: Data curation; formal analysis; supervision. **Ahmed Hafez Mousa:** Conceptualization; data curation; formal analysis; writing – original draft. **Houriah Yasir Nukaly:** Methodology; writing – original draft. **Mohammed Talha Mohammed Zubair:** Data curation; writing – original draft. **Mohammad Hassan Alsharif:** Methodology; writing – original draft. **Jakleen Ziyad Abujamai:** Data curation; methodology; writing – original draft. **Ruqayyah Ali Ahmed:** Data curation; writing – original draft. **Temaa Alklani:** Writing – review and editing. **Farah Ennab:** Writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY STATEMENT

All relevant data including all images supporting the findings of this report are included within the article.

ETHICS STATEMENT

The study was conducted in accordance with the world medical association declaration of Helsinki. Single case reports are exempted from ethical approval at our hospital.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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