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Beyond the Obvious: A Case Study and Literature review on Large Jejunal Gastrointestinal Stromal Tumor causing Vague Abdominal Discomfort

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Abtract

Background: Gastrointestinal stromal tumors (GISTs) represent only 1-2% of all primary gastrointestinal malignancies. The incidence of jejunal GIST is extremely rare. GISTs are usually asymptomatic. We report a case of symptomatic large jejunal GIST.

Case presentation: A 47-year-old male presented with vague abdominal discomfort and abdominal distention for few weeks' duration. His physical examination showed a large palpable mobile hard mass in the center of the abdomen. Abdominal ultrasonography and contrast-enhanced computed tomography showed large intraperitoneal mass with cystic changes, adjacent to the jejunal loops. The features were suspicious for GIST. Exploratory laparotomy and removal of the intraperitoneal mass was performed. The mass was arising from the proximal jejunal loops. The histopathological examination confirmed the diagnosis. The jejunal GIST in this case was symptomatic. The initial diagnosis was done based on the contrast-enhanced computed tomography. Preoperative biopsy was not indicated due to the complex cystic component of the mass. Surgical excision was done as the therapeutic golden standard with satisfactory outcome.

Conclusion: Jejunal GISTs are extremely rare tumors of the digestive tract, and they may reach large sizes without causing significant symptoms. Surgical resection is associated with an excellent recovery and low recurrence rates. Postoperative Imatinib is used in cases with higher recurrence rates.

Keywords: Gastrointestinal stromal tumors; Interstitial cells of Cajal; Platelet-derived growth factor receptor alpha; Imatinib

Abbreviations: GIST: Gastrointestinal stromal tumors; ICCs: Interstitial cells of Cajal; PDGFRA: Platelet-derived growth factor receptor alpha; CECT: Contrast-enhanced computed tomography; MRI: Magnetic resonance imaging

Introduction

Gastrointestinal stromal tumors (GISTs) are the most prevalent mesenchymal tumor of the gastrointestinal tract [1]. However, they only make up a small percentage, ranging from 1-2%, of all primary gastrointestinal malignancies [2,3,4]. The majority of GISTs, about two-thirds, occur in the stomach, while approximately one-fourth develop in the small intestine, typically in the duodenum [5,6]. The incidence of GIST is extremely low, estimated to be around 2 in 100,000 cases, with jejunal GIST being exceptionally rare, accounting for only 0.1-3% of all gastrointestinal tumors [7].

GISTs arise from the interstitial cells of Cajal within the autonomic nervous system of the intestine [8]. They are more common in males with a median age range of 50 to 70 years [9]. While GISTs typically do not cause symptoms, they may manifest as gastrointestinal bleeding, pain, a palpable mass, or may be found incidentally during radiological imaging [10-12]. We report an interesting case of large jejunal GIST with symptoms of abdominal discomfort and distention. This case report has been reported in line with the SCARE Criteria [13].

Case Report

A 47-year-old male patient presented to Al Ahli Hospital' surgery clinic with mild vague central abdominal discomfort for few months' duration associated with mild abdominal distention. He had no associated nausea, vomiting, anorexia, chest pain, cough, fever, or urinary symptoms. There were no changes in bowel habits, and no loss of weight. The patient is married, non-smoker and non-alcoholic. He has a medical history of hypertension, dyslipidemia, and gout, which are controlled by oral medications.

The physical examination showed no signs of anemia or jaundice. The abdomen was soft and lax, with palpable mobile hard mass in the center of the abdomen, slightly towards the left side, measuring approximately 15x10cm. Other systems examination was unremarkable. His laboratory tests (complete blood count, liver function test, pancreatic enzymes, and renal function test) were all within normal range.

Abdominal ultrasonography showed 13 x 5.5. cm intraperitoneal mass in the left flank with cystic changes. There was mild ascites, predominantly in the right iliac fossa, fatty liver, and mild enlarged prostate. Contrast-enhanced computed tomography of abdomen (CECT) showed 16.5x7.5x9cm large intraperitoneal mass with cystic changes adjacent to the jejunal loops. The mass was suspicious for GIST. There was an incidental finding of a small nodule in the left adrenal gland in line with adenoma, focal steatosis of the right lobe of the liver, and non-obstructing tiny left renal stones. The ileocecal valve was found to be fatty with mesenteric adenitis in the right iliac fossa. (Figure 1)

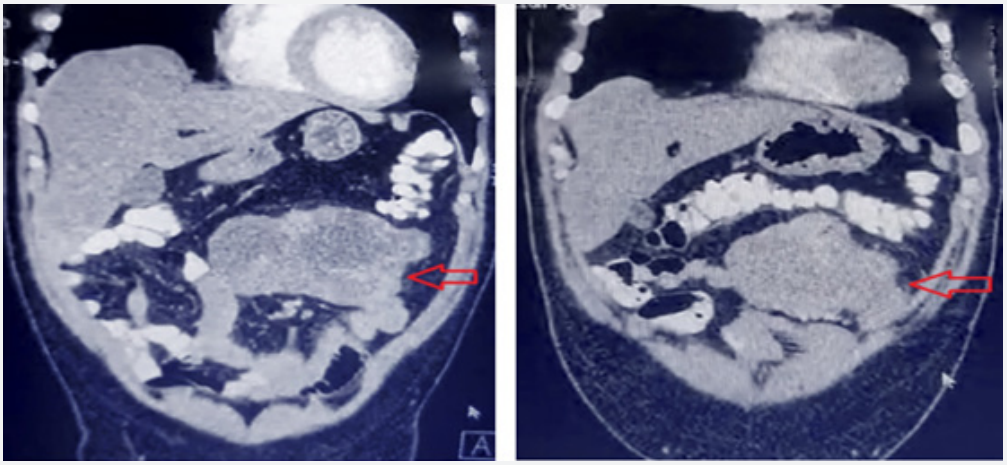

Figure 1: Contrast-enhanced CT scan of the abdomen showing an intraperitoneal mass showing large cystic changes, adjacent to the jejunal loops.

The case was discussed by the surgical team and the decision for exploratory laparotomy and surgical removal of the intraperitoneal mass was taken.

Intraoperatively, an intraabdominal complex cystic-solid mass was found arising from the proximal part of the jejunal loops (40cm from the ligament of Treitz) and measuring 20cm x 15cm. The whole peritoneal cavity was explored and there was no other abnormality. Resection of the proximal part of the jejunum including the mass lesion was performed (10 cm proximal to the mass till 10 cm distal to the mass) using linear staplers. Side-to-side jejuno-jejunal anastomosis was done using linear stapler. The mesenteric defect was closed properly, and drain was inserted in the peritoneal cavity. (Figure 2)

The patient had an uneventful postoperative recovery course and was discharged from the hospital within the expected timeframe on the fifth postoperative day

Pathological examination revealed loop of small intestine measuring 21cm in length with an attached mesentery measuring 12 x 6cm. was excises. There was an adherent mass measuring 13 x 8 x 7cm adherent to the outer surface of the small intestine. The tumor was lobulated partly solid and partly cystic, with congested outer surface and the cut section showed extensive hemorrhage with foci of necrosis and cystic changes. The tumor arising from the small intestine which is 7.5cm from one resection margin and 11.5cm from the other resection margin. Microscopical examination of the mass showed, spindle cell tumor with foci of atypia. The tumor cells were solid in appearance with foci of cystic changes, necrosis, and hemorrhage. The tumor extended from the submucosa to the serosa which was intact with no breeching (pT4). Mitotic figures were 2 per 25 HPF (less than 5 per 5m2) i.e., histological grade 1. Both proximal and distal resection margins of the specimen were free of the tumor. Immunohistochemical stains showed tumor cells staining positive for C-kit (CD 117) and DOG1, while staining negative for SMA and S 100p. Appearances were consistent with Gastrointestinal Stromal Tumor (GIST). (Figure 3,4,5)

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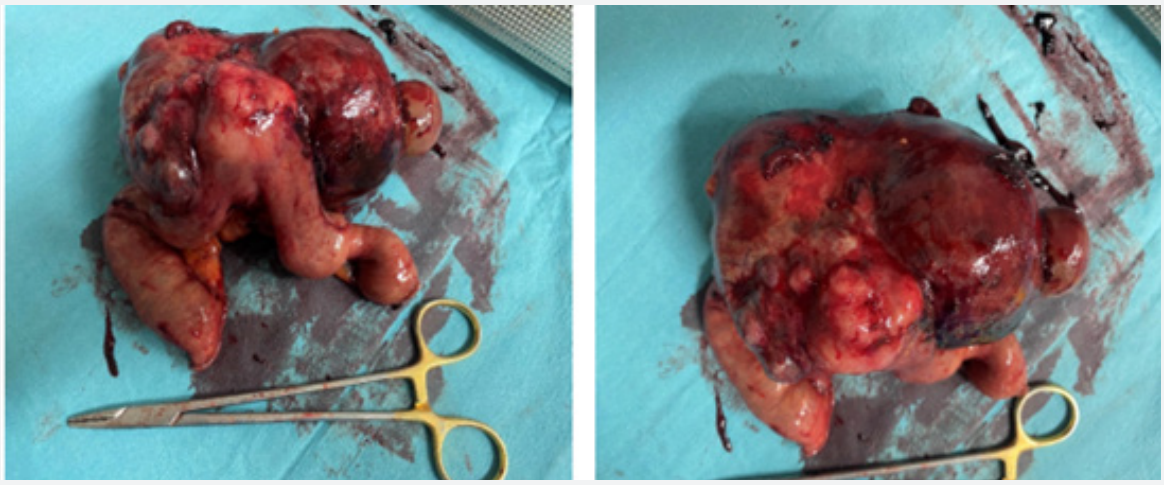

Figure 2: Images of the intraabdominal complex cystic-solid mass, arising from the proximal part of the jejunal loops.

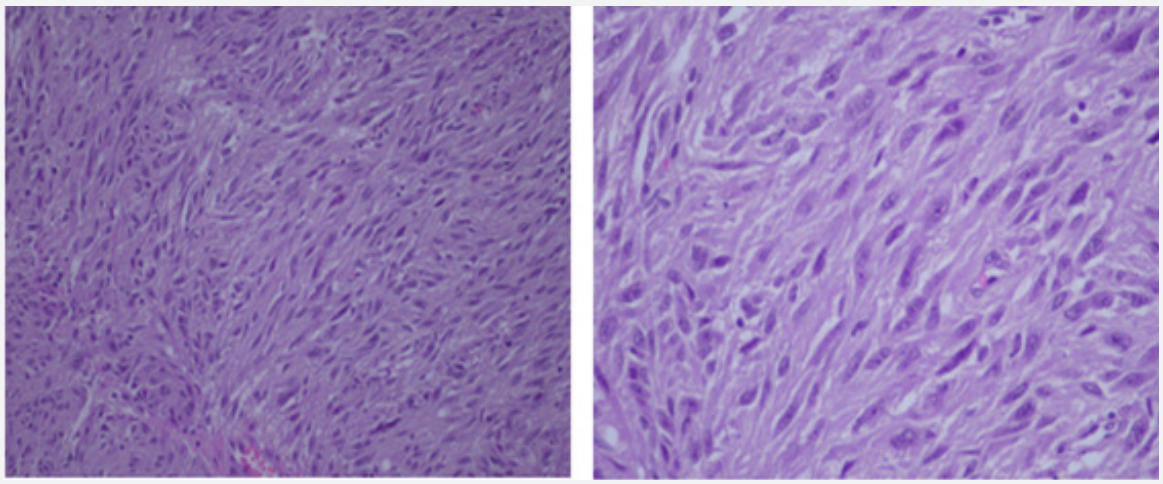

Figure 3: Microscopic appearance of the GIST (Hematoxylin and Eosin ×20, ×40).

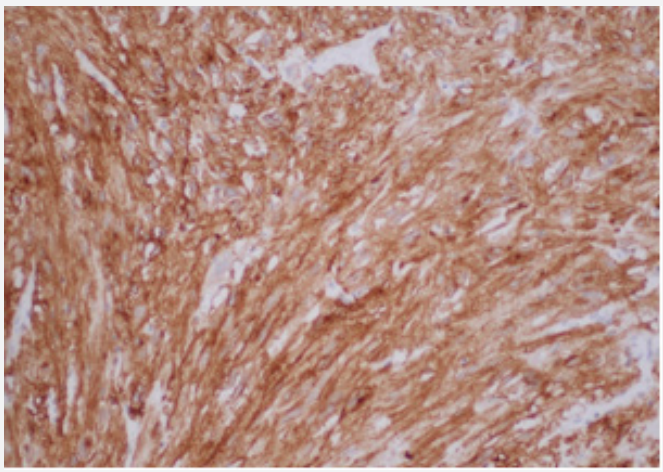

Figure 4: Immuno-histochemical stain CD117 (C Kit), positive

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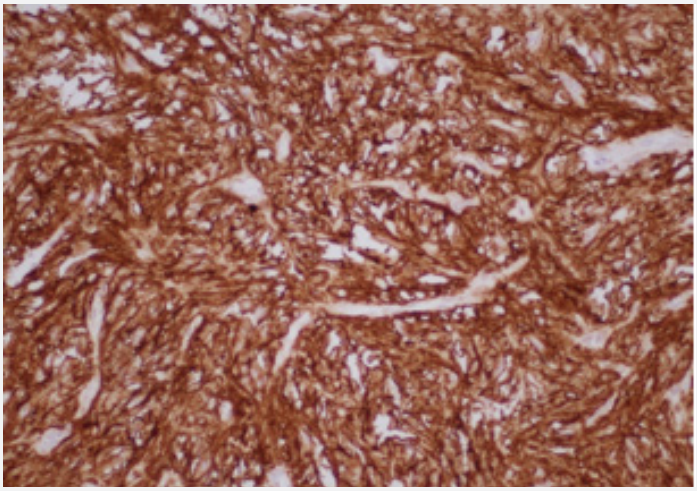

Figure 5: Immuno-histochemical stain DOG1, positive

The case was discussed in the specialized multidisciplinary team meeting in Hamad Medical Corporation, the primary oncology hospital in the country, and adjuvant therapy by Imatinib for 3 years was recommended.

Discussion

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal neoplasms of the gastrointestinal tract. The incidence of GIST is quite rare, with a rate of 2 in 100,000 [7], whereas jejunal GISTs are exceptionally uncommon, representing only 0.1–3% of all gastrointestinal tumors [2]. Some studies have indicated a slightly higher occurrence of GISTs in males [14-16], while others have found no gender bias in the literature [17,18].

GISTs originate from the bowel wall and manifest as subepithelial neoplasms primarily in the stomach and small intestine. Nevertheless, they can also emerge in various regions of the gastrointestinal tract, including the omentum, mesentery, and peritoneum. The majority, approximately two-thirds, of GISTs are found in the stomach [5], while around one-fourth develop in the small intestine, commonly in the duodenum [6]. According to the available literature, jejunal GISTs are the least common subtype among all types of GIST [7].

GISTs arise from the interstitial cells of Cajal (ICCs), which are also known as the GI pacemaker cells. These ICCs are situated in the intramuscular layer beneath the epithelium of the bowel wall, where they play a crucial role in regulating peristalsis by forming the interface between the autonomic innervation of the bowel wall and the smooth muscle. KIT (CD117) and CD34 immunopositivity were observed in immunocytochemical studies, which are characteristics that are restricted in the interstitial cells of Cajal in the gut [19]. These interstitial cells of Cajal are derived from mesoderm and become associated with the autonomic myenteric plexus during development. They are believed to play a role in regulating peristalsis [19].

The majority of GISTs possess distinct mutations in either KIT or platelet-derived growth factor receptor alpha (PDGFRA), with less frequent mutations occurring in succinate dehydrogenase (SDH) or other genes. Approximately 95% of GIST cells exhibit mutations in either KIT (CD117) or PDGFRα [20,21]. CD117 (KIT) serves as the most accurate diagnostic indicator for GIST.

Hirota et al. found that approximately 72-78% of GIST lesions tested positive for CD 34 [22]. Previous research studies have shown higher positivity rates for the same marker, with West et al. reporting 97.8% positivity [23], and Sözütek et al. reporting 87% positivity [24]. Additional studies have indicated that 30-40% of GIST cases exhibit positivity for SMA, while only 5% show positivity for S-100 protein [22,25,26].

Patients with GISTs may exhibit a wide range of symptoms, although these symptoms are often nonspecific. In most cases, patients with subepithelial masses do not experience any symptoms, and the presence of their tumors is usually discovered incidentally. The primary clinical manifestations of symptomatic GISTs are typically occult gastrointestinal bleeding caused by mucosal ulceration, and abdominal pain [27]. A different study indicated that the initial symptom would vary depending on the location of the lesion. The authors found that luminal bleeding was the most frequent presentation for duodenal lesions (25%), while epigastric symptoms were more commonly associated with lesions in the jejunum and ileum (43.9% and 38.3% respectively) [28]. The prolonged duration of symptoms can be attributed to various factors, as GISTs tend to grow slowly and typically present with nonspecific symptoms. In addition, the symptoms are not specific and resemble those of several other abdominal conditions [29].

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It is essential to conduct a thorough abdominal examination during the physical examination. GISTs can manifest as detectable masses in the abdomen, either originating from the primary tumor or intra-abdominal metastases (such as the liver, omentum, or peritoneum). The use of computed tomography (CT) is recommended for the initial assessment of the primary tumor. In cases where CT contrast is contraindicated or if the primary tumor is located in the rectum, magnetic resonance imaging (MRI) can be a suitable alternative. Research has shown that CT angiography is effective in diagnosing these lesions, with a sensitivity of 90.9% for small bowel GIST.

Tumor size and mitotic rate are two distinct prognostic factors that are utilized in prognostic models to anticipate the aggressive behaviour of tumors, in addition to the primary tumor site. According to the authors, there was a gradual increase in the mean size of GISTs from the duodenum to the ileum. In a study by Giuliano et al., it was found that the median size of tumors was 6.2cm, with an IQR of 3.8-10cm [30]. Another study, which focused on 27 small intestinal GIST lesions, reported a mean size of 8.5cm [31]. In their study, Baheti et al. found that small bowel GISTS with low, intermediate, and high malignant risk were identified in 20.59%, 16.67%, and 62.64% of patients, respectively [16]. The authors also observed a higher occurrence of high-risk lesions in the ileum when compared to the proximal sections of the small bowel [14].

It is advisable to perform a preoperative biopsy for patients with large, locally advanced lesions suspected to be GIST in order to confirm the diagnosis. This is particularly important for patients with metastatic disease or those who are eligible for neoadjuvant imatinib. Surgical resection of the primary tumor is recommended for cases where biopsy is not safe. The current gold standard treatment for small bowel GISTs is radical surgical resection [32]. In cases where the disease is unresectable or metastatic, surgical resection of a symptomatic primary tumor may be necessary if immediate surgical intervention is required.

Surgery has been the only effective treatment for GIST, with a 5-year survival rate of 45-55% overall. However, in 2001, the introduction of Imatinib, a small molecule that inhibits the kinase activity of c-kit, PDGFRα, and BCR-ABL, brought about a significant breakthrough in the treatment of metastasized and/or unresectable GIST [20]. Imatinib effectively targets the mutated genes responsible for GIST and disrupts cellular communication, thereby impeding tumor growth.

According to the guidelines set by the National Cancer Institute for GIST, patients with tumors exceeding 10 cm in size are classified under the high-risk category in histopathology and are likely to derive greater benefits from imatinib compared to those with smaller tumors. In December 2008, the Food and Drug Administration (FDA) granted approval for the utilization of imatinib as adjuvant therapy in adult patients following the complete removal of localized primary GIST. Histologically, these tumors typically exhibit one of three relatively consistent categories in terms of appearance: Spindle cell type (70%), Epithelioid type (20%), and Mixed type (10%).

Generally, primary tumors originating in the stomach tend to have better survival rates than those originating in the small intestine. Large tumors with a high mitotic rate, on the other hand, have a similarly poor prognosis regardless of where they originate, with over 86% progressing to metastatic disease.

Zhou et al. found no instances of recurrence within the intended 30-month follow-up period (ranging from 3 to 54 months) [17]. Conversely, other researchers observed a higher recurrence rate, with 44 out of 85 patients who underwent curative resection experiencing recurrence. The recurrence typically occurred between 3.7 and 125.1 months after the surgical procedure. Disease-free survival rates were 85.2%, 53.8%, and 43.7% at 1, 3, and 5 years, respectively [15].

Our patient developed vague mild central abdominal discomfort with abdominal distention due to the large size of the jejunal GIST. Initial diagnosis was made based on abdominal ultrasonography and CECT study. We performed the surgical removal of the large jejunal GIST in line with radical curative surgery. Histopathological examination confirmed the diagnosis of large jejunal GIST. Postoperatively, the case was discussed in the specialized multidisciplinary team meeting, and adjuvant therapy by Imatinib for 3 years was started.

Conclusion

Jejunal gastrointestinal stromal tumors (GISTs) are extremely rare tumors of the digestive tract, and they and they can grow to considerable sizes without causing significant symptoms. Palpable mobile intraperitoneal lesions presenting with vague abdominal discomfort without signs of obstruction should raise the concern for GIST. Utilizing preoperative imaging can aid in the diagnosis of small intestine GISTs. Radical surgical resection is the effective treatment with low recurrence rates. Studies recommend that imatinib mesylate should be considered as adjuvant therapy after radical surgery in high-risk cases, as it further reduces the risk of recurrence.

Author Contributions

Bakhos Alhaddad: study concept and design, data collection and analysis, writing the paper.

Rami Shamiah: study concept and design, data analysis, writing the paper.

Abdul Azim Hussain: study concept and design, supervision, final approval of the paper.

Haitham Al-Rawi: manuscript writing and histopathology photo acquisition.

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Rafif Mahmood Al Saady: manuscript writing and final editing.

Declarations

➢ Ethics approval and consent to participate

This case report was approved by the ethics committee, Al Ahli Hospital, Doha, Qatar. A copy of the approval letter is available for review upon request.

➢ Consent

Verbal and written informed consent were obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

➢ Competing interests

The authors declare that they have no competing interests.

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