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A Case Report of an Advanced Stage Gastrointestinal Stromal Tumor Successfully Treated by Surgery and Imatinib

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: The most prevalent gastrointestinal sarcoma is a gastrointestinal stromal tumor.It is frequently misdiagnosed due to its indolent symptoms, which only manifest at an advanced and potentially incurable stage.
Case Report: This case report is that ofa recent case of a GIST of gastric origin. Itdiscusses the case of a 56-year-old, non-smoking male with no comorbiditieswho presented to the emergency department with severe colicky intermittent adnominal pain that had occurred over the past three days, approximately three years ago. On September3, 2019, the patient underwent laparotomy in which a mass and related small bowel segment (the part of the omentum) was removed. Later, the pathology profile revealed a neoplasm of the small bowel-Ileum, Gastrointestinal stromal tumor (GIST) with a high-risk tumor of stage 4 with no recorded nodular involvement and no recorded metastasis pT4 pNxpMx but with clear margins. Moreover, the tumor markers KIT (CD117), CD34, and DOG1 (ANO1) were found to be positive. Ki67 was noted up to 35%. However, S-100 and SMA were found to be negative. On gross examination, the lesion's greatest dimension was 11 cm, and other dimensions were 9x6 cm. The tumor had a spindle-shaped morphology. On the basis of these laboratory findings and pathology profile, the patient's diagnosis was a Gastrointestinal Stromal

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tumor thatwas managed viasurgery. At that time, the patient was also prescribed Imatinib 400 mg. It has been three years since then, our patient is still alive, and no cancer recurrence has been reported yet.

Conclusion: This case report revealed that interventional radiology's early engagement with the surgical procedure was the cornerstone of our patient's effective treatment and should be investigated at different stages of the gastrointestinal tumor.

Keywords: Gastrointestinal stromal tumor; GIST; c-Kit; small intestine; imatinib.

1. INTRODUCTION

In the United States, gastrointestinal stromal tumor (GIST) has an estimated prevalence of 3,000–4,000 cases per year, making it the most prevalent primary mesenchymal gastrointestinal tumor in the country [1,2]. GISTs are believed to originate from interstitial cells of Cajal (ICC) or their stem cell predecessors, which are generally found in the intestine's autonomic nervous system [3]. ICC functions as a pacemaker in regulating motility [4]. Additionally, GIST has been shown to affect males (55%) more frequently than women with median age of (55–60 years) [5].

Furthermore, GIST is a rare tumor that requires a high index of suspicion for its diagnosis [6,7]. With the current radiologic choices available, there is no one procedure with 100% diagnostic certainty [8]. In contrast, computed tomography (CT) angiography provides the ability to pinpoint the bleeding.Hence, an early diagnosis can be made, resulting in a better prognosis [9].

Additionally, according to previousstudies, approximately 40–70% of GISTs originate in the stomach, 20–40% in the small intestine, and less than 10% in the rectum, colon, and esophagus [10]. Those are known as extra-gastrointestinal stromal tumors (eGIST) and typically behave aggressively [11]. On the other hand, the retroomentum, uterus, and mesentery are examples of extraintestinal sites where GISTs can grow [9]. The prognosis of GIST tumors depends on the location, mitotic rate, tumor size, tumor rupture, lymph node involvement, and molecular mutations [12]. For example, a large study investigated 5,138 adults with GISTs. According to this research, nodal involvement was observed in around 5% of patients and was linked with lower cancer-specific and overall survival [13]. On the other hand, another research showed that young patients presentingGIST with lymph node involvement due to mutations in succinate dehydrogenase had a less aggressive disease and a more favorable prognosis than adults with nodal involvement [12].

Moreover, surgical excision has been the cornerstone of the treatment ofGIST for many years. But unfortunately, up to 50% of patients have experienced tumor recurrence overthe first five years, which indicates that the results of surgery alone have been insufficient [14]. Additionally, radiation therapy and traditional postoperative chemotherapy have failed to work effectively in the case of GIST [15,16]. On the other hand, the treatment of GIST has been revolutionized by the introduction of small-molecule kinase inhibitors that specifically target the underlying pathogenic mutant kinase. However, recently published cases demonstrate the formation of tumor clones that are resistant to these medications, which limits their potential for long-term success [17]. Therefore, we must find new advanced treatment options to improve the survival of GIST patients. This case report discusses the case of a56-year-old malewho suffered from stage IIIB high-grade small bowel GIST, T4N0, status post-surgery in 2019and who has been successfully treated throughsurgery and Imatinib 400mg as no recurrence was reported in the lastthree years.

2. CASE PRESENTRATION

This is a recent case of a GIST of gastric origin. A56-year-old, non-smoking male with no comorbiditiespresented to the emergency department with severe colicky intermittent adnominal pain that lasted for the pastthree days,approximatelythree years ago. The patient had a significant medical history. He previously underwent an open appendectomy in 1980, a lap cholecystectomy in 2013, and a parathyroid adenoma (left inferior) excision in 2018. However, there were no associated complaints of any hematological or chronic disorder. On September 3, 2019, the CT abdomen showed a heterogeneous lobulated mass with central necrosis related to small bowel with a size of 16.3x11.8x7.5 cm .The patient underwent a laparotomy duringwhich the mass and related

small bowel segment(the part of the omentum) was removed. During the operation, the small bowel segment wasfound to be severely encased by the tumor, but not obstructed. Additionally, a resection anastomosis of the small intestine was performed. At this time, the patient had gained full recovery and was discharged from the hospital on September 7, 2019. Histopathological testing was performedand indicated negative margins of resection and GIST tumor of high risk with spindle-shaped cells (stage IIIB). The pathology profile revealed a neoplasm of the small bowel-Ileum, resection, Gastrointestinal stromal tumor (GIST), Spindle cell type, and high-risk tumor of staging pT4 pNxpMx, but with clear margins. Additionally, on B-Omentum,no significant pathology was seen. Moreover, the tumor markers KIT (CD117),CD34, and DOG1 (ANO1) were found to bepositive.Ki67 was noted up to 35%. However, S-100 and SMA were found to be negative.

Furthermore,.Later, a resection of asmall intestine segment and an omentectomy were performed. On gross examination, the lesion's greatest dimension was 11 cm, and other dimensions were9x6 cm. The tumor type was a gastrointestinal stromal tumor and had a spindle-shaped morphology. There was focally seen necrosis. Additionally, the Mitotic rate was 15 per 50 high power fields, and the resection margins were negative for GIST.

Table 1. Microscopic description

Tumor Site	Small intestine
Tumor Size	Greatest dimension:11 cm Other dimensions: 9x6 cm
Tumor Focality	Unifocal
Tumor type	Gastrointestinal stromal tumor
GIST Subtype	Spindle cell
Necrosis	Focally seen
Mitotic Rate	15/50HPF
Histologic Grade	G2 High grade; mitotic rate >5/50 HPF
Risk Assessment	High risk
Margins	Negative for GIST (3 cm from one surgical end and 2cm from another surgical end

2.1 Pathologic Staging

Primary Tumor (pT):pT4: Tumor more than 10 cm in greatest dimensions

Regional Lymph Nodes (pN): Not applicable

Distant Metastasis (pM): Not applicable

Table 2. Immunohistologicalresults

KIT (CD117)	Positive
DOG1 (ANO1)	Positive
CD34	Positive
S-100	Negative
SMA	Negative
Ki67	35%

These findings confirmed the diagnosis of a gastrointestinal stromal tumor.Based onhisdiagnosis, the patient was asked to visit the Oncology department. Therefore, he first wentto the oncology department on September 18, 2019. At this time, the patient had been prescribed Imatinib 400 mg for three years and was asked to visit Mafraq Hospital'sOncology department for a follow-up. He has been on continuous follow-upsfor three years. Now, on September 9, 2022, in SSMC,he underwent a positron emission tomography scan which showed no recurrence.

3. DISCUSSION

A gastrointestinal stromal tumor can arise anywhere in the gastrointestinal tract [18]. It is typically a submucosal lesion with endophytic growth [19]. In addition, itmanifestsexophytically [20]. According to previousstudies, this kind of tumor has been reported to range from 1 to 40 cm in diameter [21]. Additionally, between fifty and seventy-five percent of these originate in the stomach, twenty percent in the small intestine, and less frequently, in the rectum and colon [22]. In our case, the primary tumorsite was the small intestine, and the tumor's maximum dimension was 11 cm.

Additionally, studies indicate that although abdominal ultrasonography is typically the first imaging test performed on a patient with abdominal pain or a mass, the tumor identified is frequently so enormous that the organ of origin cannot be determined [23]. The ultrasonography generally reveals the existence of a massive mass, frequently occupying the abdomen, with heterogeneous reflectivity and frequent necrosis [24]. On the other hand, CT and pathological profiles set the foundation for the diagnosis and staging in the majority of patients [24]. The CT examination will typically providea rapid and reproducible evaluation of the primary tumor's size and connection to other structures

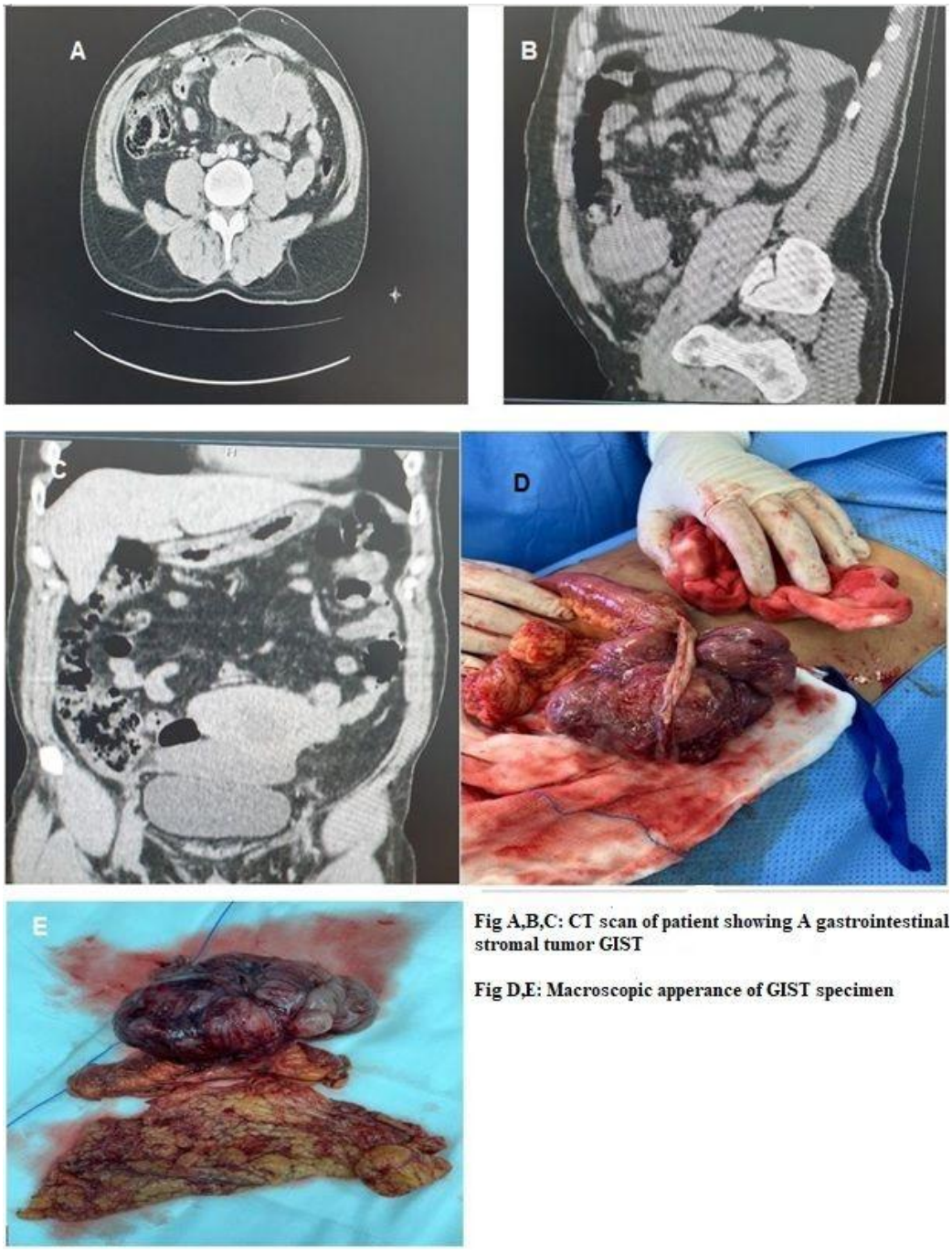

Fig A,B,C: CT scan of patient showing A gastrointestinal stromal tumor GIST

Fig D,E: Macroscopic apperance of GIST specimen

[24].Variable levels of necrosis are typically observed in the mass. In our case, the CT abdomen showed a heterogeneous lobulated mass with central necrosis related to the small bowel and measuring 16.3x11.8x7.5 cm.

Furthermore, surgery can be the best option for patients with gastrointestinal cancer. The treatment has a curative goal of operational excision with a clean margin, R0. Additionally, the prognosis of the patient depends on the risk factors associated withthe tumor's size and mitotic activity [25]. Tumors greater than 5 to 10 cm in size, with a mitotic count greater than 10/50 HPF, carry a significant risk of malignant potential and recurrence. In these high-risk groups, recurrence rates can exceed 80% [26]. Moreover, according to Fletcher's Risk Factors, 62.5% of high-riskgroup cases had recurrence or metastasis [27]. Our patient was also at high risk, and cancer had a mitotic activity of 10/50 HPF. However, in his case, after surgeryand imatinib therapy, no recurrence has been reported up untilnow.

Moreover, since the introduction of Imatinib mesylate in 2000, targeted molecular therapy has made significant strides in the care of patients with operated GIST without clean margins, unresectable tumors, or recurrences. In the past few years, this medication and the recently introduced Sunitinib have been utilized with encouraging results as adjuvant and neoadjuvant therapy [28]. The FDA approved the medicine for the treatment of metastatic GIST in 2001,and in 2008 for the prevention of recurrences in operated GIST in intermediate and high-risk patients [29].

Imatinib mesylate is a multitargeted inhibitor of "c-KIT,""PDGF–R," and "c-ABL" that inhibits T-cell proliferation. Experts suggested that Imatinib inhibits signal transmission by binding preferentially to ATP-binding sites on "c-KIT proto-oncogene product," Abelson Kinase (c-ABL), and "platelet-derived growth factor receptor" (PDGF-R) [30]. The use of adjuvant Imatinib mesylate has effectively boosted both overall survival (OS) and progression-free survival in cancer patients [29]. Our patient was also given Imatinib, and favorable outcomes were noted as he is alive and no recurrence has been reported so far.

4. CONCLUSION

GIST is a life-threatening condition. Despite surgery and neoadjuvant therapy, it continues to severelyaffect patients' mortality and healthcare. Immunohistochemical staining and CT scan are valuable diagnostic tools for GISTs.This case report suggeststhat interventional radiology's early involvement with the surgical procedure was the cornerstone of our patient's successful therapy.An evaluation of how early diagnoses can be made or when early surgery should be performed requires additional research.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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