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(Case Report)

Extra-Gastrointestinal Stromal Tumor with Complications and Disease Progression: Case Report and a Brief Review of the Literature

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Abstract

Gastrointestinal Stromal Tumors (GISTs), derivatives of the Interstitial cells of Cajal, are the most common mesenchymal tumors of the gastrointestinal tract. Extra-gastrointestinal stromal tumors (EGISTs) are a subtype of GIST that represent less than 5% of all GISTs. EGIST arises either in the mesentery, omentum, or in the retroperitoneum, regardless of the gastrointestinal wall. Similar to GISTs, EGISTs are typically associated with mutations that result in gain of function in the KIT or PDGFRA receptor tyrosine kinase genes. Most EGISTs are found in the omentum and mesentery, and since they grow large in the abdominal cavity, most of them are large and palpable tumors. They are histologically defined as spindle or epithelioid cells, which are usually positive for CD117 (KIT) and DOG1.

EGISTs are rare mesenchymal neoplasms that pose a significant clinical challenge due to their potential for aggression and a tendency to recur. We report a case of a high-risk, large mesenteric EGIST that had exhibited a complicated clinical course. The case went through an intraoperative tumor rupture, adjuvant treatment with imatinib, recurrence, and progression with increasing dose and second-line sunitinib treatment. EGISTs are more likely to have an aggressive clinical course and recurrence than GISTs of the same size and mitotic rate; therefore, aggressive treatment and long-term follow-up are needed.

This case illustrates the impact of unfavorable prognostic factors, particularly tumor rupture and R1 resection, on the long-term prognosis of high-risk EGIST. It highlights the need for aggressive, multidisciplinary management, extended adjuvant therapy, and the challenges associated with managing sequential resistance in advanced EGIST treatment.

Keywords: Extra-Gastrointestinal Stromal Tumors; Mesenteric Mass; Recurrence; Prognosis

1. Introduction

The term GIST was first introduced in 1983 by Mazur and Clark. The first description of an EGIST was reported by Miettinen et al. in 1999, and the term "EGIST" was first used by Reith JD et al. in 2000. [1] [2] [3]

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The term EGIST is not a formal diagnosing entity in the latest (5th Edition, 2020) World Health Organization (WHO) classification of soft tissue tumors. Rather, EGISTs fall within the same category as GISTs, which fall under the section of gastrointestinal tumors in the applicable volume of the WHO classification on digestive tract. [4]

EGISTs are characterized by their location, they develop in the abdominal cavity but beyond the boundaries of the hollow viscera of the gastrointestinal (GI) tract. The more frequent GISTs develop from the Interstitial cells of Cajal in the stomach or intestine; however, EGISTs can develop from the omentum, the mesentery, or the retroperitoneum. EGIST has been also rarely reported in the lung, liver, uterus, vagina, heart, urinary bladder, prostate, testes, and pancreas. [5] They develop out of residual or primitive Interstitial cells of the Cajal-like cells in these extra-visceral sites. [6]

EGISTs can be asymptomatic in the early stages of the condition, thus resulting in variable presentations. They can be delayed until the tumor becomes large enough to produce mass-effect symptoms, such as abdominal pain, a palpable mass, or nonspecific symptoms, including fatigue and weight loss. [7]

A combination of imaging (CT or MRI) and histopathological confirmation is the determining factor of the definitive diagnosis. EGISTs share a common, important immunohistochemical (IHC) signature with GISTs: they are usually positive for the receptor tyrosine kinase CD117 (KIT gene product) and often for DOG1. The histological result is typically a combination of spindle cells, epithelioid cells, or both. [5]

Complete surgical resection with clear margins forms the cornerstone of the treatment strategy for localized EGIST, as they exhibit a high degree of resistance to conventional therapies, including chemotherapy and radiotherapy. The selective tyrosine kinase inhibitor imatinib mesylate has transformed the outcome in cases of unresectable or metastatic disease, as well as in adjuvant/neoadjuvant therapy. [8]

Although EGISTs are described as potentially malignant, the final prognosis and outcome of the disease severely depend on the tumor size, mitosis rate, and the presence of certain genetic mutations. Their recurrence and metastatic potential are high, requiring strict and prolonged follow-up. [9] A case of aggressive complicated EGIST is presented with the description of the diagnosis, treatment, and outcome of this rare tumor.

2. Case presentation

2.1. Clinical Presentation

A 54-year-old male presented to the office because of 4 months of progressive abdominal pain and early satiety. He initially considered his symptoms were due to an irregular dietary practice and self-prescription of anti-acids available over the counter, with no improvement. During the 6 weeks before presentation, he had complained of progressive abdominal distension and a left upper quadrant palpable mass. He denied gastrointestinal bleeding but had noted 11lb of unintended weight loss 1 month prior to the presentation.

He presented to the medical practitioner because he was experiencing a worsening abdominal pressure, difficulty with swallowing, and concerned about the palpable abdominal mass. He denied fever, having night sweats, or changes in bowel movements. He had not yet encountered reduced exercise tolerance and said that he could perform his every-day tasks.

2.2. History and Physical Examination

The patient was an otherwise-healthy man with no acute distress on physical examination. Vital signs were stable. Abdominal palpation revealed a left upper quadrant/epigastrium distension of a solid, painless, and mobile, 15x12 cm mass extending to the left flank. There was no evidence of hepatosplenomegaly, ascites, and lymphadenopathy. Bowel sounds and rectal examination were normal.

The patient report well controlled hypertension for several years. He has no history of abdominal surgery. There was no family history of gastrointestinal malignancy or hereditary syndromes. He did not smoke or drink alcohol.

2.3. Investigations and Differential Diagnosis

Lab tests showed normal complete blood count, metabolic panel, and liver functioning. Tumor markers CEA, CA 19-9, and AFP were within the normal range. Abdominal/pelvic contrast CT revealed a well-defined and heterogeneous mass

of soft tissue with a central necrosis and peripheral enhancement, originating in the mesentery/omentum. The mass was fixed to loops of small bowel and the mesentery of the transverse colon: no liver metastases, peritoneal implants, or lymphadenopathy. MRI showed intermediate T1 and heterogeneous T2 intensity, with a mesenteric origin rather than the bowel wall. PET-CT depicted an FDG-active mass (SUVmax 8.5) without any traces of metastatic disease.

Radiological differential diagnoses included: primary EGIST (most probable), mesenteric/omental sarcoma (liposarcoma, leiomyosarcoma), desmoid tumor, solitary fibrous tumor, lymphoma, metastatic disease of an occult primary, or a mesenteric cyst with secondary changes. EGIST was the favored diagnosis because of its position, size, and highly suggestive imaging findings.

2.4. Multidisciplinary Tumor board and First management plan

The Tumor board comprised of surgical oncology, medical oncology, radiology, and pathology. The discussion revolved around the diagnostic method and treatment plan of this suspected EGIST. There was a debate on the use of pre-operative biopsy or primary resection. Arguments against biopsy were (1) resectable disease with probable curative purpose, (2) avoiding a chance of tumor rupture/seeding, (3) a small biopsy might not be representative of the entire mass, and (4) a sufficient specimen to make a diagnosis would be obtained at surgery. The reasons why pre-operative biopsy was argued to be beneficial were: confirmation of a major surgery, particularly when some form of neoadjuvant therapy was thought to reduce the risk. It was agreed upon to turn to surgery, as the disease was resectable and had classic imaging appearances.

2.5. Management

2.5.1. Surgery and intraoperative findings

During surgery, a mesenteric mass was detected, measuring 16 cm, with massive adhesions to the nearby loops of the small bowel, the transverse colon mesentery, and the greater omentum. The extra-gastrointestinal origin of the mass was confirmed by the attachment to the mesentery, not the bowel wall. The tumor had a friable surface, which caused concern about imminent rupture. The adhesions between the tumor and a 15 cm segment of the jejunum were highly vascular during the mobilization of the mass. The adhesions could not be easily separated, and the surgical team conducted a frozen section examination of a peripheral margin of the mass, which revealed a spindle cell neoplasm typical of gastrointestinal stromal tumor. The results were pending permanent CD117 (c-KIT) immunohistochemistry (IHC) and other studies.

Since it was impossible to excise the tumor with the bowel attachment without violating the principle of oncologic resection, an en bloc resection of both the tumor and the attached jejunal segment was done, and a primary jejuno-jejunal anastomosis was performed. However, when the mass had to be moved, a small region of capsular rupture was observed, resulting in minimal spillage of the tumor, which was immediately sprayed with a large amount of warm saline. A full macroscopic resection was achieved; however, the fact that the capsule was breached necessitated reclassification of the resection as an R1, with possible microscopic positive margins at the point of rupture.

The resected specimen was 16.5 cm x 13 cm x 11 cm and weighed 1240 grams. Gross pathological observation showed a fleshy-tan gray mass with a large area of central necrosis and hemorrhage. The patient had a complicated postoperative course due to the presence of prolonged ileus, which took seven days of nasogastric decomposition. He, however, slowly improved and was released on the postoperative twelfth day, awaiting final surgical pathology, IHC, and molecular analysis.

2.5.2. Final Pathology and Risk Stratification

Final pathological analysis revealed an EGIST with several high-risk characteristics. The intraoperative gross findings were a 16.5 cm mesenteric mass with a focal mesenteric margin and focal capsular disruption. Microscopically, the tumor was characterized by a mixed morphology of spindle and epithelioid cells with moderate cellularity and an 11 mitoses/50 high-power fields, which is typical of high-grade disease. Perinuclear vacuolation was noted in many tumor areas. It had a large central necrosis representing twenty-five percent of the tumor volume and focal hemorrhage. (Figure 1 A, B) The surgical margins at the site of the capsular rupture and mesenteric attachment were microscopically positive, which confirmed R1 resection.

IHC studies revealed diffuse, strong cytoplasmic staining of CD117 (c-KIT) (Figure 1 C) and DOG1, with positive CD34 expression in 70% of tumor cells. The results of desmin and S100 showed negative, and smooth muscle actin was focally positive. The Ki-67 proliferation index was 25%, indicating high proliferation. Molecular analysis revealed a deletion at

codon 557- 558 within the KIT exon 11, and PDGFRA was normal with no deletion in KIT exons 9, 13, or 17. Table-1 summarizes the main characteristic features of the differential diagnosis of EGIST.

The tumor was graded as a high-risk tumor under the modified NIH criteria and AFIP Miettinen classification system with various adverse characteristics, including a size of more than ten centimeters, a high mitotic rate of more than five per fifty high-power fields, an extra-gastrointestinal site, an R1 resection with tumor rupture, and a high Ki-67 proliferation index. The mutation of the KIT exon 11 was expected and advantageous because it indicated a positive prognosis for response to imatinib treatment.

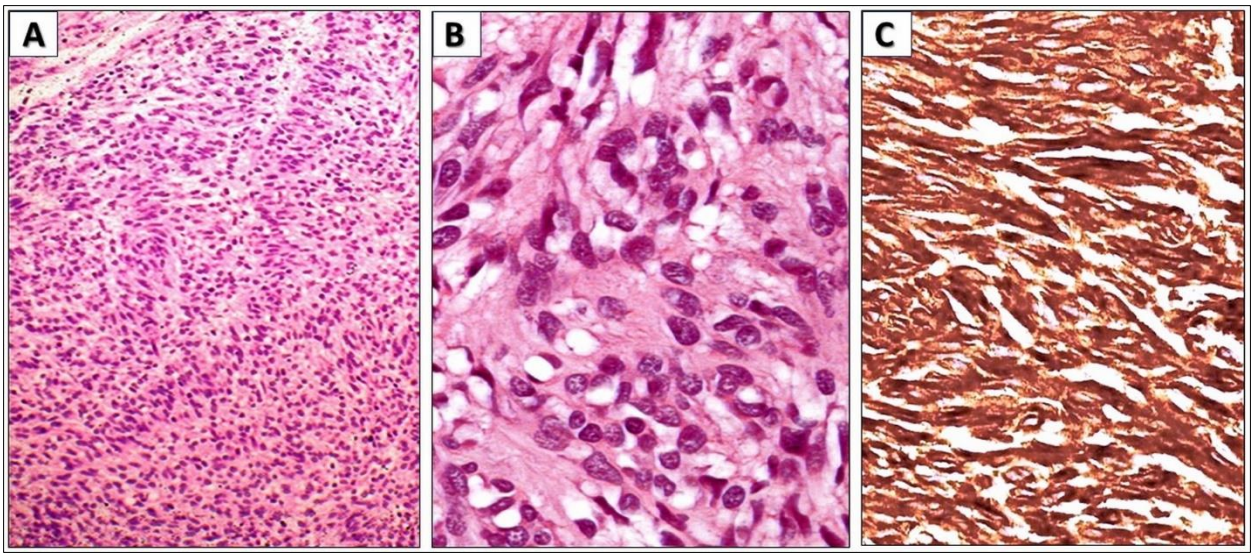

Figure 1 Microscopic examination of the Extra-Gastrointestinal Stromal Tumor (EGIST)

- **1A:** Low power view showing sheets of sclerosing spindle and epithelioid cells rich in collagenous matrix. (H and E stain X20)
- **1B:** High power view showing mixed spindle and epithelioid cells with atypia and pleomorphism. Prominent vacuolation is noted. (H and E stain X60)
- **1C**: Tumor cells strongly positive for CD117 (c-KIT)

2.5.3. Initial Adjuvant Therapy and Response

Due to the high-risk characteristics and R1 resection, the patient was placed on adjuvant imatinib mesylate 400 milligrams per day. Three weeks after surgery, treatment started when good wound healing was established. The tumor board, comprising a multidisciplinary team, suggested that the patient should receive extended adjuvant therapy of at least three to five years, and indefinite consideration was possible due to the R1 resection status and the intraoperative tumor rupture.

The patient initially responded well to imatinib, with minimal side effects, including grade 1 periorbital edema, which was treated with leg elevation and diuretics as needed. Mild nausea was treated with ondansetron; grade 1 diarrhea was managed with dietary adjustments, and mild fatigue was also noted. Laboratory monitoring revealed mild anemia and a decrease in hemoglobin levels, ranging from 14.5 to 11.2 g/dL. There was also an occasional mild elevation of transaminase levels, with ALT at 68 units per liter, which returned to normal with further treatment. Otherwise, his complete blood count was also normal.

Surveillance imaging was performed according to protocol. At six weeks after surgery, a postoperative CT of the abdomen and pelvis was made as a baseline, which revealed anticipated post-surgical changes without any residual mass and without metastatic disease. The first two years were scheduled to undergo CT scans every three months, and a PET-CT scan was performed after six months to evaluate the metabolic response. During the first eighteen months of treatment, all surveillance imaging revealed no evidence of disease recurrence. Three months after CT, no recurrence was observed, and further post-surgical changes were showing improvement. At six months, CT and PET-CT scans showed no recurrence and no metabolic activity at the surgical site, with an SUVmax of 2.1. The twelve- and eighteen-month CT scans still indicated no sign of disease recurrence.

During the first period of treatment, the patient was able to resume work and performed excellently, with an Eastern Cooperative Oncology Group (ECOG) score of zero. He was also adherent to daily imatinib therapy, and his consistent mild side effects did not greatly affect his quality of life. The plasma imatinib trough levels at 6 months were therapeutic, with a concentration of 1,100 nanograms per milliliter, exceeding the target level of more than 1,100 nanograms per milliliter.

2.5.4. Recurrence and progressive management of the disease

A twenty-two-month adjuvant-based surveillance CT scan portrayed some new, alarming findings. Several peritoneal nodules had been identified, and three peritoneal implants were located to be 2.1, 1.8, and 1.5 centimeters, located in the left mid-abdomen and the pelvis. The observation of the new finding was small-volume ascites. Fortunately, he did not have liver metastases or lymphadenopathy. PET-CT showed these peritoneal lesions were FDG-avid with a SUV max of 6.8, which were consistent with recurrent and progressive gastrointestinal stromal tumor. The patient reported that his abdominal pain did not get better but slightly increased, otherwise, he had no symptoms.

CT guidance was used to perform a biopsy of the largest nodule of the peritoneal nodule, which was diagnosed as recurrent GIST with a histology similar to that of the initial tumor. Recurrent molecular analysis revealed that the KIT exon 11 mutation remained present, and no other resistance mutations were identified during this time. The tumor board convened and discussed management plans, with the available options including an increase in the dose of imatinib to 800 milligrams per day, surgical debulking, and later continuation of tyrosine kinase inhibitor therapy or second-line sunitinib. The minimal disease burden, absence of secondary mutations, and the risk of imatinib resistance at the standard dosage led to the decision to increase the dose of imatinib to 800 milligrams per day, administered in two 400-milligram doses. The plasma trough levels were monitored to ensure an adequate exposure to drugs.

The patient responded in the subsequent months on dose-escalated imatinib with a modest response at initiation. Three months after dose escalation (or approximately twenty-five months in general), imaging revealed stable disease with minimal change in the size of the peritoneal nodules; the size of the largest nodule had decreased by 10 percent to 1.9 centimeters. However, a higher dose of imatinib introduced more side effects, including grade 2 periorbital and lower extremity edema, which required daily furosemide; grade 2 fatigue, which began to affect job performance; grade 2 diarrhea, which necessitated loperamide; and deteriorating anemia with a hemoglobin level of 9.8 grams per deciliter. Despite these toxicities, the plasma imatinib trough levels of the 800 mg dose were therapeutic at 2,400 ng/mL.

By the month thirty, CT imaging revealed progressive disease. The peritoneal nodules were now enlarged (the largest one 3.2 centimeters), a half-growth in diameter as compared with the diameter of the month twenty-five. New peritoneal nodules were formed, and the lesions had already increased to seven; ascites was becoming more severe. The most alarming was that a new 1.2-centimeter lesion in the liver segment six was detected by MRI, suggesting a likely metastasis. A repeat biopsy was also considered but later deferred due to the clear radiographic evidence of progression. The patient had experienced increased abdominal pain and early satiety, and lost 7 lb of his weight over the last two months. His performance status had deteriorated to ECOG 1.

2.5.5. Second-Line Therapy and Further Progression

Since there was evident high-dose imatinib progression, the patient was switched to sunitinib at thirty-one months. His initial dose was 37.5 milligrams per day, administered on a continuous dosing schedule, which was preferred over a four-week-on, two-week-off regimen in GIST due to ~~its~~ better tolerability with the same effect. The change to sunitinib was accompanied by a new set of side effects such as grade 2 hand-foot syndrome that was treated with topical emollients, grade 2 fatigue, development of new-onset hypertension that necessitates the addition of amlodipine to his treatment plan, hypothyroidism with TSH elevation requiring levothyroxine therapy, mild myelosuppression with thrombocytopenia peaking at 95,000 per microliter, and typical yellow skin discoloration that was graded as grade 1.

The thirty-fourth-month response assessment, which was three months on sunitinib, revealed a promising partial response, characterized by a thirty percent reduction in the peritoneal disease load, a stable liver lesion, and a reduction in ascites. The partial response persisted at month thirty-seven; the patient's symptoms improved greatly, and his ECOG performance status returned to 0-1. At month forty, the disease had become stable, and the patient was now enjoying a better quality of life, even as treatment-related toxicities continued. Nevertheless, in month forty-four, CT investigation showed the second progression. The peritoneal nodules were re-enlarging with an increment of thirty-five percent in size. The liver metastasis had increased significantly from 1.2 to 2.8 centimeters, and three other liver lesions of 0.8 to 1.5 centimeters had developed. The ascites had already become so severe that therapeutic paracentesis was needed to alleviate the symptoms. The patient's performance status had dropped to ECOG 2. He felt extremely exhausted, had lost

his appetite, and had lost eight kilograms of his initial weight. He needed therapeutic paracentesis twice to relieve the ascites symptoms.

During the forty-fifth month, the tumor board was reconvened to discuss third-line treatment options, including regorafenib, the standard third-line treatment as a tyrosine kinase inhibitor. His performance status had also become stable, with an ECOG score of 2, and he continued to experience a markedly reduced quality of life. Toxicities that were associated with treatment were managed using various drugs. He had repeated cases of ascites that needed paracentesis every four to six weeks to relieve the symptoms. Chronic pain was a major problem that needed to be treated using opioid analgesics. He could not work anymore and had moved to the status of disability. The mental stress of his condition had also taken a psychological form of depression, for which he was prescribed sertraline and has been using supportive counseling services.

2.5.6. Outcome

As the patient had been identified to have a chronic and advanced disease, palliative care consultation had been engaged to manage his symptoms and initiate the discussion of advanced care planning. The medical team was open with the patient and his family in the prognostic discourse by admitting that his disease is now chronic and incurable. The patient decided to return to his country and was subsequently lost to further follow-up.

Table 1 Differential Diagnoses of a Large Extra-Gastrointestinal Stromal Tumor (EGIST)

Diagnosis	**Typical Location / Origin**	**Key Imaging Features**	**Histopathologic / Immunohistochemical Features**	**Distinguishing Clues from EGIST**
Gastrointestinal Stromal Tumor (GIST)	Arises from GI tract (most commonly stomach, small bowel) but may extend extraluminally	Well-defined mass, heterogeneous enhancement, necrosis; may be exophytic	c-KIT (CD117) +, DOG1+, CD34+	EGIST is essentially extra-GI form; true GIST shows clear GI tract origin
Leiomyosarcoma	Smooth muscle origin—mesentery, retroperitoneum, bowel wall	Large, heterogeneous soft-tissue mass; infiltrative	SMA+, desmin+; usually c-KIT-negative, DOG1-negative	Lack of CD117/DOG1 positivity
Liposarcoma (Dedifferentiated)	Retroperitoneum, mesentery	Fat-containing components; soft-tissue nodules; possible calcifications	MDM2+, CDK4+	Presence of macroscopic fat or MDM2 amplification
Fibrosarcoma / Undifferentiated Pleomorphic Sarcoma (UPS)	Mesentery, retroperitoneum	Solid, infiltrative mass, often very heterogeneous	Non-specific; vimentin+; negative for GIST markers	Highly pleomorphic histology; lack of KIT/DOG1
Schwannoma	GI tract (rare extraluminal), mesentery	Well-circumscribed, homogeneous, or mildly heterogeneous	S-100 strong positivity	Uniform S-100 staining; absence of KIT/DOG1
Desmoid Tumor (Aggressive Fibromatosis)	Mesentery (common)	Infiltrative, ill-defined, homogeneous soft-tissue mass	Nuclear β-catenin+, SMA variable; KIT-negative	Younger patients, less necrosis; β-catenin nuclear staining
Lymphoma (e.g., non-Hodgkin)	Mesenteric nodes, small bowel	Homogeneous soft-tissue mass, minimal necrosis; may encase vessels	CD45+, subtype markers (CD20, CD3, etc.)	Uniform lymphoid pattern; systemic symptoms; vessel-encasing pattern

Metastasis (e.g., Melanoma, Sarcoma)	Mesentery, serosal surfaces	Variable appearance depending on primary	Markers depending on primary (e.g., HMB-45, S-100 for melanoma)	History of primary malignancy; multifocal disease

Compiled from [2] [5] [10] [11]

3. Discussion

3.1. Comparative analysis of our case with the existing literature

The given case is consistent with, but also extrapolates several crucial results in the EGIST literature.

3.1.1. EGIST rarity and presentation

The large EGIST in our patient, measuring 16.5 cm in the mesentery, is in line with the literature, which often describes EGISTs as large masses in the omentum or mesentery, typically exceeding 10 cm, a universally accepted high-risk factor. [**5**] [6] [12]

3.1.2. Prognostic Factors

The high mitotic rate (11/50 HPF) of the tumor, its large size, and extra-gastrointestinal location are prognostic factors that make the tumor high-risk according to the modified NIH criteria. [13] More importantly, the intraoperative tumor rupture and R1 resection are some of the most important adverse prognostic factors that significantly raise the risk of peritoneal recurrence. [14]

3.1.3. Treatment and Resistance

The first outstanding response to imatinib, which is caused by the deletion of the exon 11 of the KIT gene, is the anticipated response when the tumor has this deletion. [9] [16]

The recurrence during standard-dose adjuvant therapy, followed by a transient response to dose escalation and a second partial response to second-line sunitinib, however, is indicative of the common sequential drug resistance and disease progression pattern of advanced high-risk GIST/EGIST. [15] The ultimate progression of the patient despite the second-line treatment, which results in palliative care, supports the aggressive character of EGIST, especially when it is complicated by tumor rupture, and indicates the necessity of developing new treatment approaches in this difficult group of patients. [15]

Several prognostic variables had adverse effects on the result in our case. The primary tumor was characterized by a large size of 16.5 centimeters, a high mitotic rate of eleven per fifty high-power fields, an extra-gastrointestinal site, R1 resection with tumor rupture, and a high Ki-67 proliferation index of twenty-five percent. Recurrence was also experienced early within a period of twenty-four months, despite surgical resection and the use of adjuvant therapy. [17]

Regarding the general survival prognosis, the patient returned to his home country, and we lost the follow-up; however, recent series suggest that the median overall survival with sequential tyrosine kinase inhibitor treatment in the metastatic environment is between 5 and 7 years following the initial diagnosis. [5]

The quality-of-life factor has also gained greater significance as patients transition from incurable intent treatment to chronic disease management. [17] Our patient had suffered a lot of treatment burden, numerous toxicities with various therapeutic agents, and a progressive deterioration of functional status. Incorporation of palliative care services has become critical in the comprehensive management of symptoms and in enabling continuous goals-of-care conversations that respect the values and preferences of the patient as they progress through this advanced disease. We hope that the patient and his family followed this guidance to provide him with as much comfort as possible.

3.1.4. What Have We Learned from this Case

The case provides useful insights into the management of high-risk EGIST. First, it supports the strong adverse prognostic effect of tumor rupture and R1 resection. Although there was a positive KIT exon 11 mutation and immediate adjuvant treatment, the intraoperative complication resulted in early recurrence, therefore, it is important to pay more attention to the surgical technique and lower the threshold of neoadjuvant therapy in large and friable tumors.

Second, the case illustrates the efficiency and limitations of dose escalation in determining recurrence on standard-dose imatinib. This strategy is supported by the temporary stabilization observed with 800 mg/day, which does not involve secondary resistance mutations, and is a viable, albeit temporary, measure prior to transitioning to second-line agents.

Lastly, the chronological progress of treatment with imatinib and sunitinib highlights the chronic and relapsing characteristics of high-risk EGIST. Aggressive surveillance over an extended period is essential, along with early integration of palliative care to manage symptoms and maintain quality of life as the disease inevitably progresses through various treatment lines.

Abbreviations

- (GISTs): Gastrointestinal Stromal Tumors;
- (EGISTs): Extra-gastrointestinal stromal tumors;
- (IHC): Immunohistochemistry;

4. Conclusion

In the case of EGIST, we describe a high-risk case that illustrates the complex and challenging clinical course following an unfavorable surgical outcome. This report serves as a crucial reminder of the catastrophic consequences of intraoperative tumor rupture and R1 resection in GIST/EGIST, even in the presence of a mutation that suggests a favorable response to imatinib. Moreover, it presents an elaborate and practical case study of the multidisciplinary approach to the sequential treatment of therapeutic resistance, beginning with adjuvant therapy and progressing to dose escalation and the switch to second-line therapy. This case contributes to the limited literature on EGIST outcomes by providing a practical reminder to oncologists and surgeons on risk stratification, surgical planning, and long-term management of this rare and aggressive tumor. The patient's response, toxicity, and disease progression serve as evidence of the effectiveness of these strategies.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors make the following declarations:

- Payment/services information: All authors have declared that they received no financial support from any organization for the submitted work.
- Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might be interested in the submitted work.

Statement of ethical approval

Ethical review and approval were not required for this study involving human participants. The paper has been sufficiently anonymized to maintain the patient's confidentiality.

Statement of informed consent

The patient was lost to follow-up, and all attempts to reach the patient were unsuccessful. Therefore, the paper has been sufficiently anonymized to maintain patient confidentiality.

Data access statement

All relevant data are included in the paper.

Author contributions

All authors contributed equally to producing this manuscript.

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