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Characterization of gastrointestinal stromal tumors (GIST): experience at an oncology center

Abstract

Introduction: Gastrointestinal stromal tumor (GIST) was first described by Santiago Ramón y Cajal. It originates from the nerve cells that bear his name, "Cajal" cells, which function as pacemakers within the intestine. GIST represents 3% of all gastrointestinal tract tumors but accounts for 80% of gastrointestinal sarcomas.

Materials and methods: A retrospective descriptive study was conducted on patients diagnosed with gastrointestinal stromal tumor (GIST) from January 2016 to December 2021 at the Instituto de Cancerology and Dr. Bernardo del Valle S Hospital (INCAN), Guatemala City – Guatemala. Tumor staging was performed using the American Joint Committee on Cancer (AJCC) 8th edition classification from 2017. The objective was to characterize the primary site of involvement of GIST tumors.

Results: The mean age was 60.83 years, with a predominance of female patients (69.2%). The most common tumor location was the stomach (61.5%). All patients underwent laparotomy, and the most frequently reported symptom was abdominal pain (69.2%). The mean tumor size was 12.38 cm, with the majority being larger than 5 cm (92.3%) and high-grade (69.2%). During surgery, 15.4% of the tumors were advanced. Partial/atypical gastrectomy was performed in 30.8% of cases. Postoperative complications occurred in 23.1% of patients, with positive margins in 15.4%. Additionally, 15.4% experienced recurrence and progression to the lungs and liver. Imatinib was administered in 38.5% of cases.

Keywords: gastrointestinal stromal tumor, GIST

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Introduction

Gastrointestinal stromal tumor (GIST) was first described by Santiago Ramón y Cajal. It originates from the nerve cells that bear his name—"Cajal" cells—which act as pacemakers in the intestine by generating electrical waves. These cells are located between the circular and longitudinal muscle layers of the intestine.[1]

GIST accounts for 3% of all gastrointestinal tract tumors but represents 80% of gastrointestinal sarcomas. In Spain, approximately 600 new cases are identified each year. In the United States, around 4,000 new cases are reported annually. GIST has been associated with mutations in certain proto-oncogenes such as KIT (CD117) and PDGFRA, which suggests a hereditary component to this type of tumor. Based on this analysis, GISTs are classified according to the loss of specific features; for example, so-called "wild-type" (WT) GISTs are characterized by the absence of KIT or PDGFRA mutations. Some tumors even exhibit quadruple-negative profiles (BRAF, RAS, NF1, WT).[2,3]

Histopathologically, GISTs are recognized by their cell morphology and may be spindle cell type (the most common), epithelioid, or mixed.[2,3]

Several syndromes are associated with the development of GIST, including Carney's triad, Carney-Stratakis syndrome, neurofibromatosis type 1, and familial GISTs. GISTs has been reported to arise in patients over 50 years old at any point in the gastrointestinal submucosa, between the esophagus and the anus, with ages ranging from 60 to 69 years old, and no significant statistical difference between men and women. The anatomical locations occurrence frequency for the stomach is reported to be between 40–70%, for the small intestine is 20%, colon and rectum with 5%, and less than 5% in the esophagus, omentum, mesentery, or retroperitoneum.[1,3]

Symptoms may be insidious and vary depending on the tumor's location and size. Reported clinical presentations include mild abdominal pain, early satiety, progressing over time to nausea, vomiting, intestinal obstruction, and changes in bowel habits. Rarely, these tumors may be associated with ulceration, presented as melena, iron deficiency anemia, or occult blood in the stool. However, these signs are uncommon, as GISTs rarely affect the mucosa and usually develop in the submucosa.[3]

Diagnosis is based on a thorough clinical history combined with imaging studies. Computed tomography (CT) provides information about the presence of the tumor, its location, and its relationship to adjacent structures. These lesions typically appear as well-defined, solid masses with regular borders. Magnetic resonance imaging (MRI) offers similar data and supports diagnosis. Positron emission tomography (PET) using fluorodeoxyglucose is used primarily for patient follow-up and to detect recurrence.[3,4]

Tumor size correlates directly with its aggressiveness. Important factors to consider include the mitotic rate, tumor location, and other features that allow classification of GISTs into different risk categories.[4,5]

≤ 2 cm

> 2 cm a ≤ 5 cm

> 5 cm a ≤ 10 cm

> 10 cm

Endoscopy is the cornerstone in the investigation of gastrointestinal lesions; however, in many cases, it only provides information on solid mass that may cause extrinsic compression, presenting as a smooth protuberance covered by mucosa that appears to originate from

the submucosa. In this context, combining diagnostic tools such as endoscopic ultrasound (EUS) allows for the differentiation of the lesion's origin, as it can determine the specific layer from which it arises. In the case of GIST, an expert operator can identify whether the tumor originates from the muscularis mucosae or muscularis propria.[3]

In cases where complete tumor resection is possible, it is preferable to perform surgery with adequate margins to allow for histopathological examination of the specimen, thus avoiding disease spread. If resection is not feasible, a fine needle aspiration biopsy should be performed—preferably under endoscopic ultrasound guidance—to minimize tissue damage and avoid complications such as perforation.[3,6]

Definitive diagnosis is made by pathological examination of the surgical specimen and confirmed through immunohistochemistry, using markers such as CD117 (95%), CD34 (70%), smooth muscle actin (40%), S100 protein (5%), and desmin (2%). Epithelioid GISTs rarely express CD34 in the absence of CD117. These markers determine the subtype of GIST and poor prognosis in relation to recurrence and disease-free period. Thanks to advances in microscopy and immunohistochemical techniques, many tumors previously thought to be leiomyosarcomas of smooth muscle origin have now been identified as deriving from Cajal cells.[6]

According to the "Society of American Gastrointestinal and Endoscopic Surgeons" (SAGES), a favorable prognostic factors include gastric tumors no bigger than 5 cm in diameter, a mitotic index of ≤ 5 mitoses per 10 high-power fields (HPF), no trace of necrosis, Ki-67 <10%, tumor confinement, and absence of metastasis.

Poor prognostic factors include tumor location in the esophagus, colon, or rectum, tumor size >10 cm, a mitotic index ≥ 10 mitoses per 10 HPF, presence of necrosis, adjacent organ invasion, and presence of metastasis.[7]

Imatinib, as neoadjuvant therapy pharmaceutical in selected cases, is considered optimal in developed countries. The goal of neoadjuvant therapy is to reduce tumor load to guarantee borderline resection in surgery and better overall survival and, in cases of irresectable tumor, provides a local control to improve quality life. However, in regions with socioeconomic limitations, surgery remains the cornerstone for treating resectable tumors. Depending on the tumor's size, location, and the expertise of the surgical center, different surgical approaches can be employed. Open surgeries are becoming less common, while laparoscopic approaches are a good option due to their advantages, including shorter hospital stays, less pain, reduced bleeding, and faster recovery.[6,8]

The liver is the most frequently invaded organ, while the peritoneum is the most frequent site of dissemination. Lymph node involvement is very rare, occurring in less than 10% of cases.[2,6]

For resectable tumors, surgical treatment is based on achieving macroscopically negative margins of 1 to 2 cm of healthy tissue. En bloc resection should be carried out, when possible, to all the locally invaded organs. Lymphadenectomy is not routinely performed due to the low rate of lymphatic spread. However, if there is clear lymph node involvement, regional lymphadenectomy may be considered in exceptional cases.[6,7,9]

Each case must be evaluated individually based on its poor prognostic factors. In cases of unresectable tumors or distant metastatic disease, the treatment of choice is imatinib, as these tumors generally respond poorly to traditional chemotherapy.[10]

Materials and Methods

A retrospective descriptive study was conducted on patients diagnosed with gastrointestinal stromal tumor (GIST) from January 2016 to December 2021 at the "Instituto de Cancerology y Hospital Dr. Bernardo del Valle S." (INCAN), in Guatemala City, Guatemala. For staging, the American Joint Committee on Cancer (AJCC) 8th edition, 2017 classification was used.

General objective

To characterize the primary site of involvement of GIST tumors.

Specific objectives

To describe the sociodemographic characteristics and symptoms of patients diagnosed with GIST.

To identify the surgical treatments and immunotherapy employed in patients diagnosed with GIST.

Study population

All patients with a histological diagnosis of gastrointestinal stromal tumor, confirmed by immunohistochemistry, who underwent surgery at the INCAN in Guatemala City, from January 2016 to December 2021, were included.

Results

A total of 13 patients older than 18 years old, diagnosed and surgically treated at the institution, were analyzed (Table 1).

Table 1 General characteristics of patients and tumors

Age	60.83 (36 - 79)
Sex	
Female	9 (69.2%)
Male	4 (30.2%)
Location	
Stomach	8 (61.5%)
Small intestine	5 (38.5%)
Surgical Approach	
Laparotomy	13 (100%)
Symptoms	
Dyspepsia	1 (7.7%)
Constipation	1 (7.7%)
Nausea	1 (7.7%)
Vomiting	1 (7.7%)
Melena	2 (15.4%)
Abdominal distension	3 (23.1%)
Abdominal pain	9 (69.2%)

The mean age was 60.83 years, with a predominance in female patients (69.2%). The most common tumor location was the stomach (61.5%). All patients underwent surgical intervention via laparotomy, and the most frequently reported symptom was abdominal pain (69.2%).

(Table 2) A mean tumor medium size of 12.38 cm was observed, with 92.3% of tumors measuring greater than 5 cm and 69.2% classified as high grade. During surgery, 15.4% of tumors were found to be advanced. Partial/atypical gastrectomy was performed in 30.8% of cases. Postoperative complications occurred in 23.1% of patients, and positive surgical margins were reported in 15.4%. Tumor recurrence occurred in 15.4%, and disease progression to the lungs and liver was also observed in 15.4% of cases. Imatinib was administered as adjuvant therapy in 38.5% of patients.

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Table 2 Tumor characteristics and treatments performed

Mean tumor size	**12.38**
< 5cm	1 (7.7%)
> 5cm	12 (92.3%)
Risk classification	
High Grade	9 (69.2%)
Low Grade	4 (30.8%)
Intraoperative findings	
Localized Tumor	11 (84.6%)
Advanced Tumor	2 (15.4%)
Surgical technique	
Partial/Atypical Gastrectomy	4 (30.8%)
Total Gastrectomy	2 (15.4%)
Intestinal Resection	5 (38.5%)
Biopsy	2 (15.4%)
Surgical Complications	3 (23.1%)
Positive Margins	2 (15.4%)
Tumor Recurrence	2 (15.4%)
Disease progression	
Lung	1 (7.7%)
Liver	1 (7.7%)
Adjuvant treatment	
Inmunotherapy (Imatinib)	5 (38.5%)

Discussion

GISTs are tumors that originate from the interstitial cells of Cajal, predominantly affecting patients over the age of 50. In the patient series analyzed, the predominant age group was 55 to 64 years (38.5%), with a mean age of 60.83 years. Global reports indicate that the mean age for a GIST diagnosis is 65 years. It was more common in females in 69.2% of cases. Worldwide, there is no significant difference between sexes, but in our institution, this phenomenon is explained by the fact that up to 70% of consultations are from female patients, as reported by the INCAN Hospital Registry.[11,12]

The highest percentage of GIST tumors are diagnosed in the stomach, a trend similarly observed in our analysis, where 61.5% of the tumors were in the stomach. In some cases, these lesions are discovered incidentally, allowing diagnosis of tumors ranging in size from 1 to 40 cm. After analyzing the cases included in this study, the average tumor size was determined to be 12.38 cm; the majority were larger than 5 cm (92.3%) and classified as high grade in 69.2% of cases.[12]

Most cases are initially asymptomatic, and many symptoms are associated with tumor size and anatomical location. Larger tumors tend to be extensive and pedunculated, often adhering to neighboring organs. Several of these tumors may have cystic components.[12]

Due to tumor volume, an open approach is typically employed, involving exploratory laparotomy and resections. In the study by Martí et al., open surgeries were reported in 67% of patients, laparoscopic approaches in 30%, and endoscopic procedures in 2.5%. Partial/atypical gastrectomy was performed in 41%, and total gastrectomy in 15%. In our experience, conventional partial/atypical gastrectomy was performed in 30.8% of cases, and total gastrectomy was performed in 15%, consistent with previously reported data. Postoperative complications occurred in 23.1% of cases.[9]

Oncologic surgery consists of resection with a minimum margin of 1 cm. However, in practice, even though resections aimed for this margin, in our cases up to 2 cm of macroscopic tumor-free margins were observed. Upon reviewing pathology reports, positive margins were found in 15.4% of cases. Similar series to ours reported positive margins of 7%, which is 50% lower than our findings. This difference can be understood when considering the disease stage, with 15.4% of tumors in our series being in advanced stages.[13,14]

In the study by Sorour et al. which included 92 GIST patients, 4.4% experienced tumor recurrence. In our analysis, tumor recurrence occurred in 15.4%, with progression to the lungs and liver in 7.7% of cases, respectively. A total of 38.5% of patients received Imatinib.[13,15]

Conclusion

The primary treatment for gastrointestinal stromal tumors in centers with limited access to immunotherapy continues to be surgery based on wide resection with 1 cm surgical margins. Only 38.5% of patients were able to benefit from this treatment due to socioeconomic reasons. Diagnosis of this type of tumor is often made at advanced stages, with a high tumor burden that carries a risk of tumor recurrence. Therefore, the administration of adjuvant treatments such as Imatinib is necessary, and even neoadjuvant therapy in these cases.

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Conflicts of interest

The authors have no financial conflicts of interest, real or perceived, in the publication of this manuscript.

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