v. 2, n. 23, 2022

International Journal of Health Science

GASTRIC GASTROINTESTINAL STROMAL TUMORS (GIST): CASE REPORT OF HIGH MALIGNANT POTENTIAL GASTRIC GIST AND COMPARISON OF THE CLINICAL CASE WITH THE SCIENTIFIC LITERATURE BASES

Leonardo Salviano da Fonseca Rezende
General Surgeon Physician. Preceptor in Residency and Medical Specialization in General Surgery at Santa Casa de Misericórdia Hospital in Belo Horizonte

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).

Abstract: Gastrointestinal Stromal Tumors (GISTs), despite representing less than 1% of neoplastic lesions of the Gastrointestinal Tract (GIT), are the most common mesenchymal tumors among sarcomas, with an incidence between 1 to 2/100,000 people per year. It can be present throughout the GI tract, although it is more common in the stomach. Immunohistochemical analysis is necessary for diagnosis and its behavior is uncertain, with a high rate of recurrence. Its treatment ranges from monitoring potentially benign lesions to surgery, in cases with some malignant potential.
Keywords: Gastrointestinal Stromal Tumor, GIST, Gastric GIST.

INTRODUCTION

Gastric Gastrointestinal Stromal Tumors (GIST) have been classified for several years as neoplasms of origin in the smooth muscle of the stomach. In the 60's, the advent of electron microscopy (EM) questioned this origin, as an ultrastructural analysis showed that they had few characteristics of smooth muscle fibers. Immunohistochemical analysis (IHC) from the 1980s onwards showed that GISTs rarely had smooth muscle markers. From 1983 onwards, IHCs and ultrastructural studies have been developed and research has been able to conclude the real origin, in the myenteric plexus of the Gastrointestinal Tract. (TGI).12 This article aims to review the literature on gastric GIST, report the case evaluated and conducted by the General Surgery team of Santa Casa de Misericórdia de Belo Horizonte (SCMBH) and correlate the literature, its guidelines and protocols with the evolution of the evaluation. and patient treatment.

DISCUSSION

Gastrointestinal Stromal Tumors are tumors of the Gastrointestinal Tract, derived from the interstitial cells of Cajal, which make up the myenteric plexus, known as intestinal pacemaker cells. Despite representing less than 1% of GI tumors, GIST is the most common mesenchymal tumor among sarcomas, with incidences around 1 to 2/100,000 per year.[1,9,10] They affect the entire GI tract, although more common in the stomach (40 - 60%) and small intestine (30%), they can also be diagnosed in the colon and rectum (5 - 15%), and esophagus. (< 1%).[1,2] The diagnosis of stromal tumors beyond the GIT is not common, being rare in the retroperitoneum, omentum and mesentery.

Gastric GISTs affect patients of any age group, with a higher incidence in patients over 50 years of age. They have a slightly higher incidence in males, tending to balance the sexes.[2] Typical symptomatology begins with abdominal pain, bleeding, or GI discomfort. Bleeding usually occurs in the form of melena, due to bleeding from the lesions. Hematemesis is rarely present, as is weight loss. Incomplete obstruction of the stomach lumen, causing a feeling of bloating and dysphagia, may be present, as well as compression of neurovascular structures, causing neurological symptoms. Some patients remain asymptomatic for long periods, with incidental diagnoses during other surgeries or imaging tests.[2]

Computed tomography (CT) of the abdomen is the main imaging method for the evaluation of these tumors, since the muscular layer of the stomach can be neglected in the evaluation by Upper Digestive Endoscopy (EDA).

The diagnosis is based on ultrastructural analysis of the tumor, by microscopy, through material collected by EDA with biopsy. This histopathological analysis evidences the presence of neuromyenteric characteristics, referring to its origin in the interstitial cells of Cajal. Immunohistochemical analysis

identifies the tumor by studying the c-proto-oncogene kit CD117, present in more than 90% of GISTs and CD34, found in 80%.[3,4] The Asian guideline recommends that only the analysis of KIT CD117 by IHC would be necessary for diagnosis. If the result was negative, the investigation would continue with the other analyses, such as CD34 or PDGFRA, another transmembrane protein such as KIT.[11]

The patient's preoperative workup establishes the TNM staging for the GIST. This staging is established by evaluating the size of the tumor (T), lymph node metastases (N), distant metastases (M) and histological grade (G). This staging occurs through CT of the abdomen, pelvis and chest. In locally advanced or unresectable diseases, Proton Emission Computed Tomography (PET-CT) is indicated if available at the hospital service.[7]

The TNM cluster generates tumor classifications into groups, as follows:

. IA: T1-2N0M0 and G1;

. IB: T3N0M0 and G1;

. II: T1-2N0M0 and G2 or T4N0M0 and G1;

. IIIA: T3N0M0 and G2;

. IIIB: T4N0M0 and G2;

. IV: any TN1M0 and any G or any T any NM1 and any G.

The treatment of these tumors varies according to the size of the lesions, and can be performed through wide local excision and organ preservation if tumors between 2 and 5 cm, partial or total gastrectomy in larger tumors and/or resection of adjacent organs. Tumors smaller than 2 cm, located in the stomach, without symptoms and with characteristics of benign potential, can be followed up with imaging examination - ideally with endoscopic ultrasound (US) - every 6 to 12 months.[8] The recurrence rate of these tumors is approximately 40%, most commonly through liver metastasis and can occur up to 20 years after surgical treatment. About 30% of patients evolve only with isolated local recurrence.[5] Survival after complete tumor excision is about 50% in the long term. The worsening of the prognosis follows the criteria suggestive of malignant disease, which take into account the combination of size greater than 10 cm and more than five mitoses/50 hpf. Benign diseases, with a size of up to 2 cm and a maximum of 5 mitoses/50 hpf, are not related to mortality from the disease..[3]

The high rate of tumor recurrence and the malignancy potential of larger lesions with a higher mitotic rate were the basis for studies to indicate adjuvant therapy. Chemotherapy (CT) with the tyrosine kinase inhibitor imatinib proved to be effective in metastatic or relapsed diseases. In unresectable or metastatic tumors, imatinib therapy has increased survival to up to 70% at two years. In patients with completely resected tumors, adjuvant therapy with imatinib for one year decreased the relapse rate to 8%, compared with a rate of 20% in patients not undergoing this therapy. This drug also showed good results as a neoadjuvant therapy in patients with unresectable and non-metastatic tumors, maintaining resectability as an option, although further studies are needed.[6]

MATERIALS AND METHODS

This is a case report of a patient evaluated by the General Surgery Service of the Santa Casa de Misericórdia Hospital in Belo Horizonte and conducted from the initial evaluation to the surgical treatment, correlating his clinical case with the bibliographic references that address the topic "Gastrointestinal Stromal Tumors". of the stomach".

CASE REPORT

Patient B.R.S.L., female, 68 years old, previous history of anxiety in regular use of

Size of the tumor	Presence of metastates	Metastate by distance	histological grade (mitotic index)
T1 ≤ 2 cm	N0 without metastasis	M0 without metastasis	G1 low grade ≤ 5 mitoses/50 hpf
T2 > 2 and ≤ 5 cm	N1 with metastasis	M1 with metastasis	G2 high grade > 5 mitoses/50 hpf
T3 > 5 and ≤ 10 cm			
T4 > 10 cm			

Table 1: TNM Classification.

De Rubin BP, Blanke CD, Demetri GD, DeMatteo RP, et al: protocol for the examination of specimens from patients with gastrointestinal stromaltumors, *Arch Patol Lab Med* 134:165, 2010.

Malign Potential	Conditions	Mortality
Benign	Maximum 2 cm and 5 mitoses/50 hpf	-
Probably benign	> 2cm and ≤ 5cm, and up to 5 mitoses/50 hpf	< 3%
Uncertain or low malignant potential	≤ 2 cm and > 5 mitoses/50 hpf	NR
Low to Moderate Malignant Potential	> 10 cm and up to 5 mitoses/50 hpf or > 2cm and ≤ 5 cm, and > 5 mitoses/50 hpf	12 -15%
High Malignancy Potential	> 5 cm and ≤ 10 cm, and > 5 mitoses/50 hpf or > 10 cm and > 5 mitoses/50 hpf	49 - 86%

Table 2: Guidelines for Assessing the Malignant Potential of GISTs.

De Miettinen M, Sobin LH, Lasota J: Gastrointestinal stromal tumors of the stomach: A clinicopathologic, immunohistochemical, and molecular genetic study of 1765 cases with long-term follow-up, *Am J Surg Pathol* 29:52-68, 2005.

Rivotril 2.5mg/ml 3 drops once a day. She started with abdominal pain in the epigastrium two months ago, initially looking for a Basic Health Unit (BHU) in Brumadinho, where she was treated for Gastroesophageal Reflux Disease (GERD), with Omeprazole 20mg once a day and without success. She progressed with myasthenia, nausea, vomiting, dysphagia for solid foods, and mild weight loss. He started an investigative workup at the unit of origin through Upper Digestive Endoscopy with biopsy and Computed Tomography of the abdomen, which showed a sub-epithelial mass with a neoplastic appearance, measuring approximately 5.5 x 3.5 cm, in the pre-pyloric region of the lesser curvature. of the stomach and histology of ulcerated spindle cell injury, in addition to chronic antral gastritis. There was no free fluid in the cavity, no signs of locally advanced injury or metastases to other organs of the abdomen. Forwarded for evaluation by the General Surgery team of the Hospital Santa Casa de Misericórdia de Belo Horizonte and complementary workup of the case. In the first evaluation with the General Surgery team, Immunohistochemistry was requested on a slide of material collected in biopsy by EDA, CT of the chest for staging, laboratory review and guidance was given to the patient and their families. In this same consultation, guides were issued for Authorization of Hospitalization (AIH) by the Unified Health System (SUS) and request for Pre-Anesthetic Assessment (APA).

Patient attends the follow-up appointment to present the exams, evaluation and AIH authorized by the Municipal Commission of Oncology (CMO) of Belo Horizonte. IHQ diagnosed with Gastrointestinal Stromal Tumor and APA informing ASA I patient. Surgery Notice guide issued and Partial Gastrectomy in Oncology scheduled for patient.

Three months after the start of the investigative workup, the patient underwent Partial Gastrectomy in Oncology, with Roux-en-Y intestinal bypass and DII lymphadenectomy - surgery date 09/14/2016 - without complications. The option for lymphadenectomy was due to the fact that, during the perioperative period, the tumor presented macroscopic characteristics that were not consistent with GIST. The cavity inventory showed a neoplastic lesion in the lesser curvature of the stomach, pre-pyloric, approximately 10 x 8 cm, adjacent fat adherence to the anterior gastric wall with an infiltration aspect of the lesion, without pancreatic invasion, liver free of macroscopic lesions on its surface, without metastatic implants in intestinal loops or peritoneum and absence of free fluid in the cavity. The removed piece had margins of two centimeters, both proximally and distally, and there was no tumor rupture within the cavity. The patient had a good evolution in the immediate postoperative period at the Intensive Care Unit (ICU), with an episode of Atrial Fibrillation (AF) without repercussion or progression, evaluated by Cardiology, which adopted a conservative approach. Referred to the infirmary, she maintained a good recovery. She is discharged for outpatient follow-up with Clinical Oncology and General Surgery.

In the first post-operative outpatient consultation, at the Centro de Especialidades Médicas Dr. Dário de Faria Tavares (CEM), patient presented a result of the anatomopathological study of the piece, confirming the diagnosis of GIST, a positive lymph node for neoplasia in a total of 10 (1/10), infiltrating adjacent fat and 10% of mitosis. According to the TNM grouping, the patient would fit into group IV. Suggested IHQ of material, requested and referral of patient to Clinical Oncology. He reported good tolerance to the free oral diet, with no complaints of nausea or vomiting, in addition

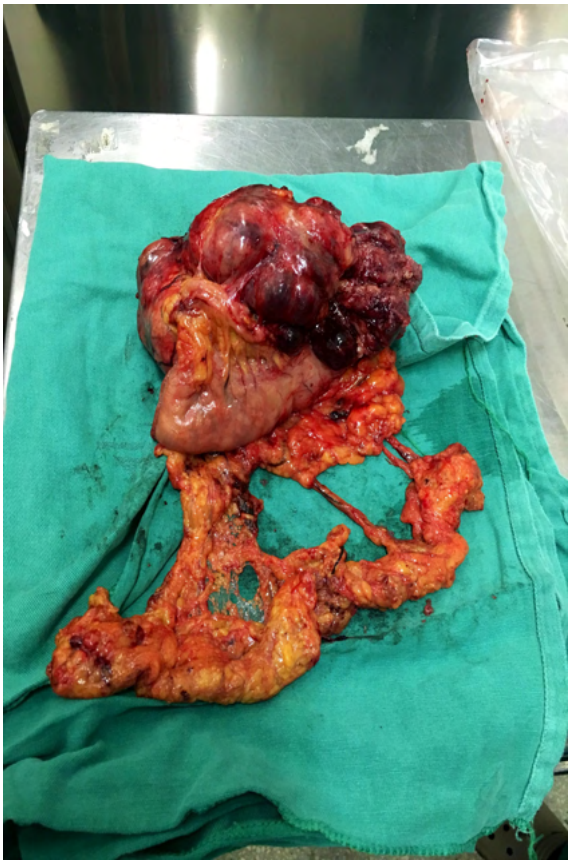
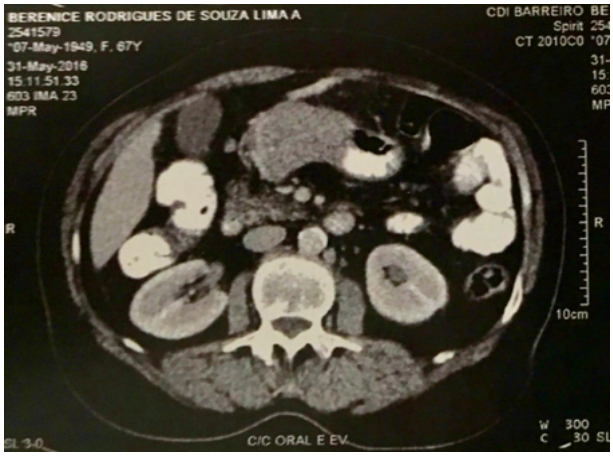


Image 1: photo of gastric antrum and greater omentum affected by the tumor. Piece removed through partial gastrectomy in oncology. (Personal collection) (14/09/2016).



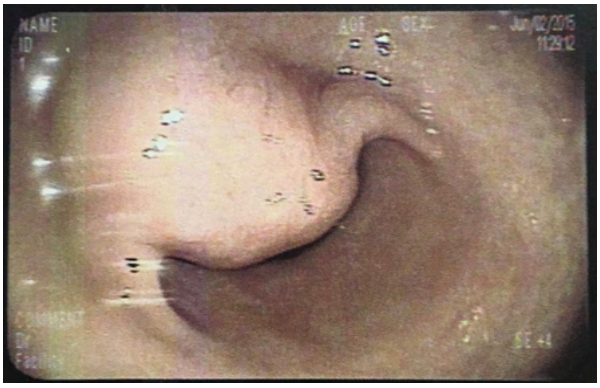


Image 2 (top): CT section of the abdomen showing an expansive image in the stomach, suggestive of neoplasia.

Image 3 (bottom): photo of UDE indicating a voluminous mass, with intrinsic growth and without mucosal involvement. (Personal Collection).

to preserved physiological habits. Upon return, IHQ confirms a diagnosis of GIST due to positivity for CD117 and a proposal for adjuvant chemotherapy with imatinib. Postoperative outpatient follow-up was maintained.

CONCLUSION

Although GISTs represent a small percentage among the neoplastic lesions of the GIT, the gastric GIST is the largest representative of this category, presents a diagnostic difficulty and high recurrence rates, in addition to a high mortality rate in its condition of High Malignancy Potential. This way, it is important to deepen their studies and updates.

In the present case, the common epidemiology of the disease was present. More common in patients from the fifth decade of life and without a strong prevalence between the sexes, the female patient and 68 years old fits the presentation profile. The accidental diagnosis, through UDE due to GERD and warning signs, such as unexplained weight loss, progressive dysphagia, and epigastralgia refractory to treatment with a proton pump inhibitor, fits the description of a commonly painless disease and diagnosis by imaging examination by another. recommendation.

The extension of the investigative workup and staging of the patient did not include PET-CT, due to the unavailability of the exam at Santa Casa de Misericórdia in Belo Horizonte. Although IHC and anatomopathological analysis indicated histology compatible with gastric GIST, the macroscopic image did not match the pattern of the disease, as well as the extension of the lesion through the layers of the stomach. For these reasons, staging was extended to the gastric adenocarcinoma protocol and partial gastrectomy was performed with safety margins and complemented with DII lymphadenectomy. The IHC of the resected specimen did not indicate the ratio of mitoses/50 hpf, but the size of the tumor has already been defined as the malignant potential in the case in question, and adjuvant therapy with chemotherapy and prolonged outpatient postoperative follow-up is indicated, due to the high risk of relapse.

After an extensive review of the literature, the conduct adopted in the case report is in accordance with that recommended by the guidelines and major centers specialized in the treatment of GIST. The deviation in the management of the case, extending the propaedeutics and therapy, increased safety and reduced the risk of a need to re-approach the patient, leaving the team satisfied with the result.

REFERENCES

1. Nilsson B, Bumming P, Meis-Kindblom JM, et al: Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era, *Cancer* 103:821, 2005.

2. Townsend CM ET al. Sabiston, Tratado de Cirurgia. 19. ed. Rio de Janeiro: Elsevier, 2050. P. 1120.

3. Miettinen M, Sobin LH, Lasota J: Gastrointestinal stromal tumors of thestomach: A clinicopathologic, immunohistochemical, and molecular genetic study of 1765 cases with long-term follow-up, *Am J Surg Pathol* 29:52-68, 2005.

4. Hirota S, et al: Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors, *Am J Pathol* 163:691, 2003.

5. DeMatteo RP, Lewis JJ, Leung D, et al: Two hundred gastrointestinal stromaltumors: Recurrence patterns and prognostic factors for survival, *Ann Surg* 231:51-58, 2000.

6. Blanke CD, Rankin C, Demetri GD, et al: Phase III randomized, intergroup trial assessing imatinib mesylate at two dose levels in patients with unresectable or metastatic gastrointestinal stromal tumors expressing the kit receptor tyrosine kinase: S0033, *J Clin Onco* 26: 626-632, 2008.

7. Rubin BP, Blanke CD, Demetri GD, DeMatteo RP, et al: protocol for the examination of specimens from patients with gastrointestinal stromal tumors, *Arch Patol Lab Med* 134:165, 2010.

8. Sepe PS, et al: A guide for the diagnosis and management of gastrointestinalstomal cell tumors, *Nat Rev Gastroenterl Hepatol,* 363:71, 2009.

9. Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM. Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestenal stromal tumors show phenotypic charac- teristics of the intestinal cells of Cajal. *Am J Pathol* 152:1259-69, 1998.

10. Li A, Nordberg ML, Herrera GA. Gastrointestinal stromal tumors: current concepts and controversies. *Pathol Case Rev* 7:226-33, 2002.

11. Corless CL, Barnett CM, Heinrich MC. Gastrointestinal stromal tumours:origin and molecular oncology. *Nat Rev Cancer*. 11:865-78, 2011.

12. Nilsson B. et al., Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimantinib mesylate era – apopulation-based study in Western Sueden. *Cancer*: 103(4):p.621- 9, 2005.