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

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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 Misericória 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,
albeit 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
<table>
<thead>
<tr>
<th>Size of the tumor</th>
<th>Presence of metastases</th>
<th>Metastate by distance</th>
<th>histological grade (mitotic index)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 ≤ 2 cm</td>
<td>N0 without metastasis</td>
<td>M0 without metastasis</td>
<td>G1 low grade ≤ 5 mitoses/50 hpf</td>
</tr>
<tr>
<td>T2 &gt; 2 and ≤ 5 cm</td>
<td>N1 with metastasis</td>
<td>M1 with metastasis</td>
<td>G2 high grade &gt; 5 mitoses/50 hpf</td>
</tr>
<tr>
<td>T3 &gt; 5 and ≤ 10 cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4 &gt; 10 cm</td>
<td></td>
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</tbody>
</table>

Table 1: TNM Classification.


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

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

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 10x8 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 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


