Tomographic findings of gastric gastrointestinal stromal tumor: a 14-case study*

Aspectos tomográficos do tumor estromal gastrintestinal de origem gástrica: estudo de 14 casos

Gustavo Lemos Pelandré1, Maria Célia Djahjah2, Luiz Felipe Nobre3, Emerson Leandro Gasparetto4, Edson Marchiori5, Bruno Vilhena Pereira6, Marcus Valadão7, Eduardo Linhares8

Abstract OBJECTIVE: The purpose of this study was to describe the tomographic findings of gastric gastrointestinal stromal tumor. MATERIALS AND METHODS: Fourteen patients with histopathologically and immunohistochemically confirmed gastric gastrointestinal stromal tumors, who had already been submitted to computed tomography scans before the treatment, were evaluated in the period between January 1999 and December 2006. The following tomographic variables were analyzed: lesion topography, size/dimensions, homogeneity, contour, margins, morphology, pattern and intravenous contrast-enhancement intensity, growth pattern, invasion of adjacent organs, presence of ulceration, fistula, calcifications, mesenteric fat infiltration, lymphadenomegaly and presence of distant metastasis. RESULTS: Tumors were found in the body (57.1%) or in the gastric fundus (42.9%), with sizes ranging between 6.0 cm and 23.0 cm (mean, 11.5 cm). Predominantly extraluminal growth was observed in 57.1% of cases and intra/extraluminal in 35.7%. Subtle contrast-enhancement was observed in 50%, moderate in 50%, and heterogeneous in 64.3% of cases. Additionally, central hypodensity was observed in 64.3%, invasion of adjacent organs in 42.9%, and hepatic metastasis in 7.2% of cases. CONCLUSION: In the present study, the majority of tumors were found in the gastric body, with an average size of 11.5 cm, presenting with central hypodensity, heterogeneous contrast-enhancement and predominantly extraluminal growth.

Keywords: Gastrointestinal stromal tumors; Stomach neoplasms; Spiral computed tomography.

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is an uncommon abdominal disease representing about 80% of mesenchymal tumors.
Computed tomography is the most sensitive imaging method for detecting and characterizing GIST, allowing the definition of the tumor size, anatomic location, growth pattern, necrosis evidence, invasion of adjacent organs and metastases, besides the monitoring of the treatment and evaluation of the disease progression\(^2\)\(^9\).

The authors seek to describe the tomographic findings in a group of 14 patients with gastric GIST, emphasizing the relevance of this imaging method for the characterization of the lesion in its most frequent topography as well as for the definition of differential diagnoses.

**MATERIALS AND METHODS**

The present study has followed an observational-descriptive model for a series of cases including 41 patients admitted to the Hospital do Câncer I – Instituto Nacional de Câncer, Rio de Janeiro, RJ, Brazil, in the period between January 1999 and December 2006, with histopathological diagnosis of GIST. Out of these patients, 9 were excluded for lack of immunohistochemical staining data, and 18 either because they had not undergone abdominal computed tomography before being submitted to oncologic therapy, or their studies were incomplete or had not been found.

The study population included nine female patients (64.3%) and five male patients (35.7%). Mean age was 59.4 ± 18 years (mean ± standard deviation).

Clinical manifestations observed were: abdominal pain or discomfort (\(n = 10\)), weight loss (\(n = 4\)), increased abdominal volume (\(n = 3\)), hematemesis (\(n = 1\)), melena (\(n = 1\)), emesis (\(n = 1\)) and fever (\(n = 1\)). One patient was asymptomatic and the tumor was incidentally found during an abdominal ultrasonography.

Nine patients underwent computed tomography in other institutions, with different techniques, all of them utilizing oral contrast agents, and three intravenous contrast.

As regards topography, the lesions were classified according to their site of origin. Lesion contours were classified as regular, lobular or irregular, and limits as well-defined, ill-defined or invasive. The lesion morphology was defined as round, ovoid or irregular. Intravenous contrast-enhancement pattern was described as homogeneous or homogeneous, and the enhancement intensity was compared with the intensity of the liver and abdominal muscles: subtle enhancement if the density was equal or lower than the muscle density; mild enhancement, if the density was higher than the muscle and equal or lower than the liver density; marked enhancement if the density was higher than the liver.

Nine patients underwent computed tomography in the author’s institution in a helical CT SCT 7000 TS Shimadzu equipment (Shimadzu Corp.; Kyoto, Japan), through axial images acquisition with 5 mm collimation and 7 mm reconstruction interval, pitch 1.5, 120 kV and 130 mA. Ionic iodinated contrast agent (1,000 ml) in a 2% solution was orally administered one hour before each examination (diatrizoate meglumine). Two acquisitions were performed before and after intravenous injection of 100 ml non-ionic iodinated contrast agent (ioexol 300 mgI/ml, 2 ml/s, 55 seconds after the infusion was initiated). Five patients had undergone computed tomography in other institutions, with different techniques, all of them utilizing oral contrast agents, and three intravenous contrast.

The tomographic images were independently analyzed by three radiologists. In cases of interobserver disagreement, the final decision was reached by consensus. The following characteristic were considered: lesion topography, dimensions, homogeneity, contour, limits, morphology, intravenous contrast-enhancement intensity and pattern, lesion growth pattern, adjacent organs invasion, presence of ulceration, fistulas, calcifications, mesenteric fat infiltration, lymphadenomegaly and distant metastases.

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All of the patients were submitted to surgical treatment, as follows: wedge resection in eight cases (57.1%), total gastrectomy in four (28.6%) and subtotal gastrectomy in two (14.3%). Three patients (21.4%) underwent supplementary therapy with imatinib mesylate.

The present study was approved by the Committee for Ethics in Research with Humans of the institution.

RESULTS

The main tomographic findings in the 14 gastric GIST patients are shown on Table 1. The tumors were localized in the gastric body (n = 8; 57.1%) or gastric fundus (n = 6; 42.9%). Lesions dimensions ranged between 6.0 cm and 23.0 cm, with a mean size of 11.5 ± 4.4 cm (mean ± standard deviation). The lesion growth pattern was predominantly extraluminal in eight patients (57.1%) (Figure 1), intraluminal in one (7.2%) patient (Figure 2), and intra/extraluminal in five (35.7%) patients (Figure 3).

Lesion with extraluminal growth presented dimensions ranging between 5.0 cm and 10.0 cm in five cases, and > 10.0 cm in three, with mean size of 11.4 ± 5.1 cm (Table 2). Lesions with intra/extraluminal growth pattern presented dimensions between 5.0 cm and 10.0 cm in two cases, and > 10.0 cm in three, with mean size of 11.5 ± 4.1 cm. The only intraluminal lesion measured 11.5 cm (Figure 2). No lesion < 5 cm was found in the present study.

As regards the intravenous contrast-enhancement pattern, nine patients (64.3%) presented heterogeneous contrast-enhancement, and three (21.4%), homogeneous contrast-enhancement. Intravenous contrast agent was not utilized in two patients (14.3%). Among the patients who received

Table 1 Main tomographic findings in 14 GIST patients.

<table>
<thead>
<tr>
<th>Features</th>
<th>Patients</th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td>Location</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Gastric body</td>
<td></td>
<td>8</td>
<td>57.1</td>
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<tr>
<td>Gastric fundus</td>
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<td>6</td>
<td>42.9</td>
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<tr>
<td>Size</td>
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<tr>
<td>&lt; 5 cm</td>
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<td>5–10 cm</td>
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<td>7</td>
<td>50.0</td>
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<tr>
<td>&gt; 10 cm</td>
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<td>7</td>
<td>50.0</td>
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<tr>
<td>Growth</td>
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<tr>
<td>Extraluminal</td>
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<td>8</td>
<td>57.1</td>
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<tr>
<td>Intra/extraluminal</td>
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<td>Intraluminal</td>
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<td>Morphology</td>
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<tr>
<td>Ovoid</td>
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<td>7</td>
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<td>Irregular</td>
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<td>28.6</td>
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<tr>
<td>Round</td>
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<td>3</td>
<td>21.4</td>
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<td>Limits</td>
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<tr>
<td>Well-defined</td>
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<td>71.4</td>
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<tr>
<td>Ill-defined</td>
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<td>2</td>
<td>14.3</td>
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<tr>
<td>Invasive</td>
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<td>2</td>
<td>14.3</td>
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<tr>
<td>Intravenous contrast-enhancement</td>
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<tr>
<td>Heterogeneous</td>
<td></td>
<td>9</td>
<td>64.3</td>
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<tr>
<td>Homogeneous</td>
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<td>3</td>
<td>21.4</td>
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<tr>
<td>Non-evaluated</td>
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<td>14.3</td>
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<tr>
<td>Contrast-enhancement intensity</td>
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<tr>
<td>Subtle</td>
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<td>6</td>
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<td>Mild</td>
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<tr>
<td>Present</td>
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<td>9</td>
<td>64.3</td>
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<td>Absent</td>
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<td>5</td>
<td>35.7</td>
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n, number of patients. * Only for patients who received intravenous contrast agent.
contrast agent, six (50%) presented mild contrast-enhancement. Marked contrast-enhancement was not observed in any case of the present study.

Among the tumors measuring 5–10 cm, 50% presented heterogeneous contrast-enhancement and 50% homogeneous contrast-enhancement. All the tumors with >10 cm presented heterogeneous contrast-enhancement (Table 2). Heterogeneous tu-

mors presented mean size of 12.9 ± 4.6 cm, while homogeneous tumors presented mean size of 8.4 ± 1.1 cm.

In the majority of cases, the lesions were ovoid (50%), with regular contour (71.4%) and well-defined limits (71.4%). A central area of hypodensity was observed in nine cases (64.3%), ulceration in six (42.9%), fistula in four (28.6%), mesenteric fat infiltration in four (28.6%) and intratumoral calcification in two (14.3%). Adjacent lymphadenomegaly was observed in only one patient (7.2%).

Adenocarcinoma invasion was observed in six cases (42.9%), with diaphragm (n = 3; 21.4%), spleen (n = 2; 14.3%) and pancreas (n = 2; 14.3%) being most frequently affected (Figures 4 and 5).

Hepatic metastases were identified in only one case (7.2%) (Figure 6).

**DISCUSSION**

Although rare, GISTs are the most common mesenchymal neoplasms of the gastrointestinal tract, representing 1% to 3% of all gastrointestinal tumors and 2.5% of

<table>
<thead>
<tr>
<th>Tumor size (cm)</th>
<th>Extraluminal</th>
<th>Intra/extraluminal</th>
<th>Intraluminal</th>
<th>Contrasted-enhancement pattern</th>
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<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
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<tr>
<td>&lt; 5</td>
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<td>5–10</td>
<td>5</td>
<td>71.4</td>
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<td>&gt; 10</td>
<td>3</td>
<td>42.9</td>
<td>3</td>
<td>42.9</td>
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* Only for patients who received intravenous contrast agent. n, number of patients.

**Table 2** GIST growth pattern and contrast-enhancement*, according to the lesion dimensions.

Figure 3. Computed tomography image with both oral and intravenous contrast-enhancement showing an expansile, heterogeneous lesion with a central hypodense area and intra/extraluminal growth, located on the anterior wall and great gastric curvature.

Figure 4. Computed tomography image with both oral and intravenous contrast-enhancement showing a large expansile, heterogeneous lesion with extraluminal growth, located in the gastric fundus and extending towards the spleen (A) and left diaphragmatic pillar (B).

Figure 5. Computed tomography image with both oral and intravenous contrast-enhancement showing an expansile, hypodense formation, with irregular margins, located in the great gastric curvature and extending towards the pancreatic body and tail.

Figure 6. A: Abdominal ultrasonography demonstrating expansile, nodular, heterogeneous lesions in the right hepatic lobe. B: Noncontrast-enhanced computed tomography image demonstrating solid lesions with a hypodense center, corresponding to the sonographic findings (liver metastasis).
Tomographic findings of gastric gastrointestinal stromal tumor

gastric tumors\(^{(10)}\). The stomach is the most frequent site of this disease, accounting for 45–65% of cases, followed by the small bowel in 15–25% of cases\(^{(2)}\). Most rarely these tumors are found in the rectum, colon, esophagus, appendix, mesenterium, omentum, retroperitoneum and other sites not related to the gastrointestinal tract\(^{(11)}\). The incidence of this disease is higher in individuals with > 50 years, with mean age ranging between 55 and 67 years\(^{(9,12)}\), and is rarely found in individuals with < 40 years\(^{(1)}\). Association between the disease incidence and geographic location, race and occupation has not been established.

Additionally, some authors have indicated a slight prevalence of the disease in men\(^{(13)}\) and increased incidence in patients with type-1 neurofibromatosis\(^{(14)}\). The present casuistic included nine female (64.3%) and five male patients (35.7%). Mean age was 59.4 years.

Clinical manifestations in GIST patients are non-specific and depend on the lesion location. Digestive hemorrhage is the most frequent symptom presenting as hematemesis, melena, hematopoietic or signs of anemia due to occult bleeding\(^{(9-11,15,16)}\). Other common manifestations are non-specific abdominal pain, dysphagia, weight loss, nausea, emesis, abdominal mass or obstructive symptoms. Approximately 20% of cases may present with asymptomatic lesions incidentally found and diagnosed during imaging evaluation or surgical procedures\(^{(2,11)}\). In the present casuistic, abdominal pain was the most frequent symptom.

Classification of mesenchymal tumors can be based on findings at optic microscopy and immunohistochemistry. The histopathological classification is based on the predominant cellular type: spindle cells, epithelioid cells or pleomorphic cells\(^{(17)}\). Gastric GISTs are characterized by the presence of spindle cells in 70–80% of cases. The diagnosis is achieved by means of immunohistochimical staining based on the expression of KIT protein (CD117), a product of c-Kit proto-oncogene (a growth factor receptor with tyrosine kinase activity). GISTs are CD117-positive (95%) and CD34-positive (30–40%) tumors\(^{(17)}\). Many studies have demonstrated that about 4% of cases present clinical and pathological characteristics compatible with GIST although KIT-protein expression is absent. Heinrich et al.\(^{(18)}\) have demonstrated that this group of tumors presents activating mutation in other tyrosine kinase receptor similar to KIT (platelet-derived growth factor receptor, alpha polypeptide – PDGFRα), representing an alternative hypothesis in the pathogenesis of this neoplasm. Differential diagnoses also include other mesenchymal neoplasms with a different histochemical profile such as leiomyomas, leiomyosarcomas, schwannomas, neurofibromas and neuroendocrine tumors\(^{(11,16)}\). In the present study, the majority of patients presented spindle cell tumor (85.7%), while epitheloid cell tumors (7.2%) or pleomorphic cell tumors (7.2%) were less frequently found.

In the literature, many factors are identified as variables capable of predicting GIST progression: size, mitotic index, presence of tumor necrosis, cell proliferation markers, tumor site\(^{(19)}\). Findings, however, are controversial and a consensus is still to be reached; so the biological behavior of the tumor can hardly be predicted. So, the terms “benign” or “malignant” have been avoided, and GIST is classified according to their potential for malignancy based on the most relevant prognostic factors described in the literature (tumor site, size and mitotic index)\(^{(20)}\). So, gastric tumors may be classified as follows: high risk, intermediate risk, low risk or very low risk. High-risk tumors are those with > 10 cm in size, more than 10 mitoses per 50 high magnification fields (50 HMF), or even those with > 5 cm in size with more than 5 mitoses per 50 HMF; intermediate risk if less than 5 cm with 6 to 10 mitoses per 50 HMF or measuring 5–10 cm with less than 5 mitoses per 50 HMF; low-risk tumors are those with 2–5 cm in size, and less than 5 mitoses per 50 HMF; and very low-risk tumors are those with < 2 cm in size and less than 5 mitoses per 50 HMF\(^{(21)}\).

Also the pattern of contrast-enhancement is variable according to the lesions dimensions\(^{(15,24-26,27)}\). In the study developed by Kim et al.\(^{(15)}\), 49% of heterogeneous tumors were > 10 cm in size, and 77% of the homogeneous tumors were < 5 cm. On the other hand, Lee et al.\(^{(26)}\) have found a mean size of 11.6 cm among heterogeneously contrast-enhanced tumors and 3.8 cm among homogeneously contrast-enhanced tumors. Similar results have also been reported by Horton et al.\(^{(24)}\) and Nishida et al.\(^{(27)}\). In the present study, the authors observed 66.7% of heterogeneous tumors with > 10 cm in size and 100% of homogeneous tumors measuring between 5 cm and 10 cm.

Besides heterogeneous contrast-enhancement, large tumors may present mu-
cossal ulceration, cavitation and central hypodense areas likely corresponding to cystic degeneration, hemorrhage or necrosis. The necrotic cavities can also communicate with the gastrointestinal lumen forming fistulas with gas, air-fluid level or oral contrast agent(28). In the present study, central areas of hypodensity were found in 64.3% of patients, while other authors report this finding in 20–49% of cases(12,15). The presence of gas or contrast agent within the lesion also may suggest the presence of mucosal ulceration with fistula formation. Other studies report ulceration in 3–88% of cases, most of them with high histological degree(9,12,13,15,16). In the present casuistic, signs of mucosal ulceration were found in 42.9% of patients, and fistula in 28.6%.

Liver and peritoneum are the most frequent sites of GIST metastases which may occur in up to 38% of cases(12). Other less common sites of metastasis are: lungs, mesenterium, omentum, ovaries and bladder(12). Liver metastases may be visualized at computed tomography as hypodense lesions, isodense lesions in the portal phase, with intense contrast-enhancement in the arterial phase, or cystic lesions with peripheral soft tissues density(15). Implants may become hypovascular or cystic after chemotherapy, and this pattern should not be confused with a sign of disease progression of new lesions(10,12). In the present study, only one patient (7.2%) presented liver metastasis at presentation, and six patients (42.9%) presented adjacent organs invasion with predominant involvement of the diaphragm, spleen and pancreas.

Computed tomography still remains as the imaging method of choice in the GIST characterization, as well as in the evaluation of adjacent organs involvement, abdominal metastases and treatment response(11). The addition of new technologies to this imaging method, particularly with the utilization of multidectors and multiplanar reconstruction, has allowed a better evaluation of great exophytic tumors and of the relationship between gastric lesions and adjacent structures, besides allowing tumors characterization in specific circumstances, such as masses of unknown origin or originating from endoscopically hardly accessible regions(23,25). Parameters such as progressive mass hypoattenuation, decrease in the nodular enhancement and vascularization indicate a good treatment response(26).

Complete surgical resection is the standard treatment for GIST, considered as the sole modality capable of providing curative therapy, although about 20% to 50% of patients submitted to complete surgical resection present recurrence of the disease(29). The post-procedural five-year survival rate in cases of GIST ranges between 30% and 65%(29). In cases of unresectable or metastatic tumors, the treatment of choice is performed with imatinib mesylate (STI 571), a selective tyrosine kinase enzyme inhibitor that has been utilized as an adjuvant or neoadjuvant therapy for large tumors initially unresectable or in cases where complete resection is unfeasible(28). Many authors suggest that a disease involution may occur, allowing the resection of previously unresectable tumors(30). Recent studies have demonstrated that imatinib presents a significant activity in patients with advanced stages of GIST, achieving a partial response rate in 53.7% of cases and disease stabilization in 27.9%(8). In the present casuistic, all the patients underwent surgical treatment, most of them with wedge resection (57.1%), and three patients (21.4%) were also submitted to imatinib mesylate therapy.

CONCLUSION

In the present study the majority of GISTs were located in the gastric body, with a mean size of 11.5 cm, a central hypodense area, heterogeneous contrast-enhancement and predominantly extraluminal growth. The knowledge of typical findings and tomographic variations of this neoplasm in its most frequent topography allows the radiologist to establish the differential diagnosis for gastric tumors, as well as guiding the subsequent phases of the diagnostic investigation, aiding in the therapeutic planning for GIST patients.

REFERENCES

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