A pictorial review of gastrointestinal stromal tumors (GISTs): radiologic findings with pathologic correlation

Poster No.: C-2170  
Congress: ECR 2017  
Type: Educational Exhibit  
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Keywords: Pathology, Neoplasia, Surgery, Staging, Biopsy, Ultrasound, MR, CT, Gastrointestinal tract, Abdomen  
DOI: 10.1594/ecr2017/C-2170

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Learning objectives

The authors' aim is to present a pictorial review of gastrointestinal stromal tumors (GISTs).
For that purpose, they illustrate the radiological features of GISTs along with the pathological correlation.
Background

Gastrointestinal stromal tumors (GISTs) are the most frequent mesenchymal tumors in the GI tract, even though they are rare tumors, representing only 1-3% of all gastrointestinal tumors.¹

In the past, GISTs were misdiagnosed as smooth muscle tumors because of their microscopic similarities.

GISTs have phenotypic resemblances with the interstitial Cajal cells, so a histogenetic origin from these cells has been suggested.²

The expression of kit receptor (CD117) Fig. 1 on page 6, also known as tyrosine kinase growth factor receptor, is important to recognize GISTs and to distinguish them from other mesenchymal tumors. Kit receptor is responsible for uncontrolled growth and resistance to apoptosis.¹

GISTs are histologically split by three categories Fig. 2 on page 6: spindle cell type (70%); epithelioid type (20%) and mixed type (10%).³

Three factors are used to assess the risk of progressive disease: mitotic rate Fig. 3 on page 7, tumor's size and the affected organ.⁴

The most satisfactory index of malignancy is the degree of mitotic activity. Size also shown to be an important predictive characteristic of malignancy.

Tumor until 5 cm are frequently benign.

Gastric GISTs usually have a more favorable prognosis than intestinal GISTs.

Nevertheless, histopathologic criteria, including the tumor size, are not always trustworthy for benign and malignant differentiation. It is known that large tumours (> 10 cm), with no detected mitotic activity are responsible for late recurrences and metastases.

Anyway, it is important to integrate the three risk factors for disease progression to conclude about tumor's behaviour.⁴

The great majority of GISTs occur in the stomach (60%), followed by jejunum and ileum (30%) duodenum (5%) colon and rectum (<5%), and esophagus and appendix (<1%).⁵

Primary gastrointestinal stromal tumors can also be found in the omentum, mesentery and retroperitoneum, possibly disconnected from their origin along the gastrointestinal tube. However, the great majority of extra-GIST is part of metastatic disease.⁶
Clinical presentation depends on the size and the origin organ of the tumor. Sometimes, asymptomatic GISTs are discovered during procedures performed for other reasons Fig. 4 on page 8.

Spontaneous rupture endo- or extra-luminally and hemorrhage into the GI tract or the peritoneal cavity are possible major complications.\(^7\)

The diagnosis of GIST can be suggested on CT (or MRI).

CT is the first choice to detect, stage, plan surgery and follow-up GISTs.

GISTs may have different sizes and appearances.

At presentation, GISTs are typically large, bulky, heterogeneously enhancing masses Fig. 5 on page 9.\(^8\)

Enhancement areas represent viable tumor, which are usually peripheral.

Smaller lesions tend to have round shape with smooth margins and enhance homogeneously, with a moderate attenuation Fig. 4 on page 8.

With large and exophytic pattern, it can be difficult to determine the origin site.

Thus, magnetic resonance (MR) imaging is used as an add-on to computed tomography, specially with exophytic and anorectal masses Fig. 6 on page 10, in order to determine the origin of large GISTs and their relationship with adjacent structures.

MR imaging features Fig. 6 on page 10 depend on the degree of tumor necrosis and the age of internal haemorrhage.

The solid component appears with low signal intensity on T1-weighted images, with high signal intensity on T2-weighted images, and enhance after administration of gadolinium.

Depending on the age of the bleeding, the signal can vary from high to low on both T1 and T2-weighted images.

Gadolinium-enhanced imagens help the definition of regions of tumor necrosis.\(^9\)

Transabdominal ultrasound (Fig. 7 on page 11, A) has a limited contribution, helping in internal GIST characterization. GISTs are well-circumscribed hypoechoic abdominal masses. Larger tumors tend to be irregular, with variable central areas of necrosis and internal hemorrhage. Ultrasound can play a role in percutaneous needle biopsy.\(^10\)

Barium studies can show characteristic findings of submucosal masses: rounded tumors with an intact overlying mucosa; and "bull's-eye" appearance, if there is mucosal
ulceration. However, barium studies are not specific and almost always require another complementary imaging method.

Abdominal radiography can suggest the presence of a large mass when intestinal dilatation and/or displacement of abdominal viscera is visualized. Calcifications and air-fluid levels can also be identified.

Surgical resection is the gold standard treatment for potentially resectable tumors. Lymphadenectomy is usually not necessary because these tumors do not spread via lymph nodes.\textsuperscript{11}

GISTs have a high recurrence rate, despite of apparently complete resection surgery, with clear margins.\textsuperscript{12}

Thus, biopsies of GIST masses are controversy, not only because of the risk of hemorrhage, but also because of the high probability of peritoneal implants.\textsuperscript{7}

There is also adjuvant KIT-inhibitor therapy.\textsuperscript{12}
Fig. 1: Strong and diffuse expression of CD117 (c-kit)

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Fig. 2: GISTs cellular subtypes. A - Cellular proliferation in the submucosa and muscularis propria of cells in whorls or short intersecting fascicles (H&E, 40x magnification) B - Bland spindle cells with eosinophilic cytoplasm, minimal pleomorphism and oval nuclei (H&E, 200x magnification) C - The tumour is composed of a sheet of polygonal cells with well defined cell borders, moderate-to-abundant eosinophilic cytoplasm and oval nuclei with visible nucleoli. Mitotic figure in the bottom field. (H&E, 400x magnification) D - This tumour shows a mixed pattern of both epithelioid (on the left) and spindle cells (on the right). (H&E, 200x magnification)

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Fig. 3: A, B - Very low risk GIST. Fusocellular proliferation of cells in intersecting fascicles with bland morphology: moderate eosinophilic cytoplasm, minimal pleomorphism and oval nuclei. Mitotic figures were very rare (H&E, 40x and 200x magnification); C - High risk GIST. Neoplasm with high cellularity, cells in intersecting fascicles with high nuclear-cytoplasmatic ratio and pleomorphic nuclei with vesicular chromatin. Mitosis were frequently seen (center field)

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Fig. 4: A - oral and intravenous CE-CT image demonstrates an endogastric homogeneously enhancing solid mass with smooth margins (*) in the proximal portion of the stomach wall. B - Upper endoscopy shows a submucosal intraluminal mass at the gastric cardia

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**Fig. 5:** Gastric GIST. CE-CT, axial plane; Large, bulky, heterogeneously enhancing mass (with peripheral enhancement). Hypoattenuating central area due to extensive necrosis.

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**Fig. 6:** Rectal GIST. A - Axial T1-weighted MRI reveals the lesion to be isointense. With a few areas of hyperintensity representing hemorrhage. B - Axial T2-weighted MRI reveals an heterogeneously isointense to hypointense mass, with central fluid signal, arising from the anterior wall of the rectum and projecting into the rectoprostatic space. C - Coronal contrast-enhanced MRI demonstrates intense enhancement of the solid component with central areas of non-enhancement representing necrosis.

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**Fig. 7:** Pelvic Extra-GIST. A - Transabdominal ultrasound reveals a round-shape, well-circumscribed hypoechoic pelvic mass; B, C - oral positive contrast and intravenous CE-CT; axial (B) and coronal (C) planes; huge pelvic mass, with a large necrotic center.

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Findings and procedure details

The authors gathered samples of different GISTs, with diagnosis, treatment and follow-up Hospital pedro Hispano, Matosinhos, Portugal. The tumors underwent fully histopathologic examination.

**Esophageal GIST**

In contrast to gastric GIST, this kind of tumors is very rare in the esophagus. Furthermore, larger lesions at presentation are even rarer.

They are usually discovered during upper endoscopy.

Esophageal GIST typically appear in the distal portion of this organ\(^{13}\). They can be intraluminal, intramural or exophytic lesions.

Esophageal GIST may even suffer perforation.

Barium studies can show an ulcerative mass, protruding into esophageal lumen, or a smooth intramural lesion.

On CT scans, esophageal GIST are alike GISTs located in other organs. They are rounded well-circumscribed, predominantly hypoattenuating / isoattenuating masses compared to smooth muscle, with mild enhancement on CE-CT\(^{14}\). Larger Lesions may show necrosis, cystic or hemorrhagic regions, as other GIST types.\(^{15}\)

They may spread locally (to the pleura) or hematogenously (to the liver).\(^{14}\)

The radiologic differential diagnosis for these tumors is based on tumor size and growth pattern.\(^{15}\)

In contrast to other gastrointestinal tract organs, leiomyomas are the most common mesenchymal neoplasm of the esophagus instead of GIST.\(^{13}\)

**Gastric GIST**

Stomach is the most common site to find GISTs.

These tumors tend to be restricted to gastric wall for long periods of time, before spread to other structures. Thus, the prognosis is almost always better than gastric carcinoma.

Tumor calcifications are uncommon findings.
The presence of a mass or the displacement of the gastric air shadow can be a radiographic signal. Calcifications, although rare, can be also shown on the abdominal radiography.\textsuperscript{15}

In barium studies, there are classic findings of submucosal masses: the lesions margin forms obtuse angles with the gastric wall (en profile) and masses have smooth well-defined margins (en face). When covered with barium, if there are no ulcerations, gastric GISTs have smooth mucosal surfaces.\textsuperscript{16}

CT is particularly helpful at showing mass characteristics, invasion of adjacent structures and distant metastatic disease.\textsuperscript{17}

CT commonly show an enhancing solitary mass in the wall of the stomach.

Peripheral enhancement Fig. 5 on page 22 is the most common contrast-enhanced CT pattern. A minority, usually small lesions, can have homogeneous enhancement. The correlation of CT images with gross pathologic findings Fig. 8 on page 19 show than the enhanced areas are related to viable tumor areas.\textsuperscript{15}

Large gastric GISTs tend to have exophytic growth pattern, heterogeneous enhancement and big central areas of necrosis, hemorrhage or cystic changes.

Ulcerative forms Fig. 9 on page 19 and cavitations can be identified on CT images.

Rarely, endogastric lesions can have a polypoid configuration, indistinguishable from primary gastric adenocarcinoma.

Small gastric GISTs can show intense enhancement Fig. 10 on page 20 in CECT images. This finding is less seen in small bowel GISTs, due to its larger and more malignant behavior at presentation\textsuperscript{18}.

Malignant GISTs may have endogastric pattern but they usually have exogastric growth. Exogastric GISTs usually cause extrinsic compression of gastric wall and adjacent structures.

Water-density lesions due to extensive necrosis can rarely be seen.

Pedunculated GISTs Fig. 11 on page 21 are usually classified with high risk of malignancy leading to typical large dimension and high mitotic number, even if they only have expansive growth without infiltrating surrounded structures.\textsuperscript{19}

Attending to the extension of necrosis, hemorrhage, cyst formation or the degree of contrast enhancement, there is no correlation between radiologic appearance and malignant potential of gastric GISTs.\textsuperscript{15}
Magnetic resonance is a useful complement tool of CT studies, particularly with large tumors.

RM can show variable features of gastric GISTs. Signal intensity is affected by necrosis and hemorrhage.\(^9\)

The differential diagnosis of gastric GIST includes other mesenchymal tumors, such as leiomyomas, leiomyosarcomas, schwannomas, neurofibromas, and solitary gastric carcinoids\(^20\).

Schwannomas Fig. 12 on page 23 are rarer than gastric GISTs but they have similar radiologic findings. Carcinoids are commonly seen in the antrum and usually have central ulceration.

In contrast to GIST, adenocarcinoma and lymphoma tend to spread along the gastric wall. These lesions are associated with lymphadenopathies. Bulky exophytic masses are uncommon presentations.\(^15\)

Malignant GISTs can spread to contiguous structures; sometimes are responsible to intraperitoneal seeding and may metastasize to the liver or lung, hematogenously.

Lymphatic spread is rare. Thus, lymphadenopathy is unusual.

Metastasis tend to be large heterogeneous lesions. Fluid-fluid levels may be present, as in primary lesions.\(^17\)

After treatment, necrosis and cavitations are frequently seen.

**Duodenal and jejunoileal GISTs**

Jejunum Fig. 13 on page 25 Fig. 14 on page 26 is the most common section of the small intestinal where GISTs appear, followed by ileum Fig. 15 on page 26 and duodenum Fig. 16 on page 27.

As happened with gastric subtype, small bowel GISTs can be responsible for mass effect of an intestinal segment, leading to small bowel dilatation as a sign of obstruction at the abdominal radiography. An opaque round mass may also be seen. Cavitary masses can be responsible for irregular gas collection on radiographies.

An intraluminal or submucosal mass, smoothly- or irregularly-margninated, can be seen on barium studies, depending on the absence or presence of ulceration, respectively.\(^15\)

At CT scans, small bowel GISTs can be intraluminal polyps or intramural masses with extension into the mesentery.\(^21\)
Small intestinal GISTs tend to be significantly larger and highly vascularized than other primary sites. They commonly have peripheral enhancement, with central areas of low attenuation Fig. 17 on page 28.

Biopsy is controversy due to the high bleeding risk of these neoplasms.

MR images are very similar to that of gastric GISTs Fig. 14 on page 26.

GIST can span to other non-contiguous parts of small bowel Fig. 17 on page 28, as well as to colon, abdominal wall, ureter and bladder. Malignant GIST of the small bowel can metastasize to the liver, to the peritoneum and the omentum Fig. 18 on page 29 Fig. 19 on page 30.

The differential diagnosis includes primary and secondary small intestinal neoplasms.

Adenocarcinoma remains the most common malignant tumor of the small bowel, usually with a different appearance than GIST.

Nevertheless, in contrast to gastric lymphoma, small intestinal lymphoma is responsible for large heterogeneous masses, similar to GISTs. However, the absence of lymphadenopathy would favor the diagnosis of GIST.

The differential diagnosis also includes mesentery neoplasms, such as mesenteric fibromatosis (desmoid tumor), inflammatory pseudotumor, lymphoma, sclerosing mesenteritis, and metastatic disease.

GISTs occur sporadically as solitary masses. Multiplicity is very rare but when it happen, the possibility of KIT or PDGFRA germline mutations, as well as the diagnosis of neurofibromatosis type 1 (von Recklinghausen's disease) must be thought Fig. 20 on page 31. These patients usually develop small bowel tumors, including GIST.

Colon

Although colon is an uncommon site of primary GIST, the external aspect of the colon is frequently involved in metastatic GIST.

They are described as transmural masses, with smooth or multinodular contours, and with possible central areas of necrosis, hemorrhage, cystic change or calcification Fig. 21 on page 32.

Imaging appearance is similar to those of leiomyosarcomas.

Barium studies show small colonic GISTs as mural or submucosal masses, with or without ulceration.
Adenocarcinoma, lymphoma, metastatic melanoma, and leiomyosarcoma and retroperitoneal sarcomas are the main differential diagnosis.\textsuperscript{15}

**Anorectum**

The most common appearance is a well-circumscribed mural mass.

Intraluminal polypoid mass is the most unfrequent presentation.\textsuperscript{25}

Ulceration can occur and low attenuation areas of internal hemorrhage is often visible at CT scans.

Anorectal GIST can spread into ischiorectal fossa, prostate, or vagina.\textsuperscript{26}

MR images usually show uniform, intermediate signal intensity on T1-weighted images, and heterogeneous high signal intensity on both T2-weighted and after administration of gadolinium Fig. 6 on page 34.\textsuperscript{27}

The differential diagnosis of anorectal GISTs is extensive, including both epithelial and nonepithelial neoplasms of the anorectal region.

**Extra-GISTs**

Extra-gastrointestinal stromal tumors (EGIST) originate primarily from mesentery, omentum or peritoneum Fig. 7 on page 35.

Hemorrhage, cystic change and necrosis are often present. It results in a complex mass, indistinguishable from different sarcomas.

With a homogeneous EGIST, mesenteric fibromatosis (desmoid tumor) and inflammatory pseudotumor should be included in the differential diagnosis.\textsuperscript{15}

Furthermore, primary GISTs can metastasize to the omentum and mesentery. In this case, scans show multiple masses through the peritoneal cavity, with different sizes and appearances Fig. 18 on page 29. The differential diagnosis of metastasis should consider peritoneal carcinomatosis, lymphomatosis, and leiomyomatosis peritonealis disseminata.\textsuperscript{15,28}

**Liver metastases**

Before chemotherapy, small liver metastases are usually hypervascular on CT and MRI. Necrosis is common in larger masses Fig. 19 on page 30.
It is very important to perform a dual phase CT or MR, to avoid missing metastases. Liver metastasis show bright homogeneous enhancement in the late arterial (portal venous inflow) phase and (almost) complete washout on the hepatic venous phase. In the same liver, there may be different vascular pattern masses due to different times of hematogeneous spread.¹

On MR, liver metastases usually show low or intermediate signal on T1-weighted sequences and marginally bright on T2-weighted sequences.

Hemorrhage is rare; it appears with increased signal on T1-weighted sequence.

Before therapy, purely cystic metastases are rare. After specific treatment, are a common finding on CT Fig. 22 on page 33.
**Fig. 8:** Gastric GIST. Large intramural gastric mass (A), 15 cm in greatest dimension, with an heterogeneous cut surface, with extensive necrosis and haemorrhage (B).

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**Fig. 9:** Oral and intravenous CE-CT; axial plane. Endogastric GIST with a central ulceration.

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Fig. 10: Small GIST. A, B - Oral contrast, before (A) and after (B) intravenous CE-CT; small well-circumscribed lesion at the gastric wall (arrow), with homogeneous enhancement; C - Intramural, well-circumscribed mass in the gastric wall, with a compact and solid cut surface, with tan appearance.

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Fig. 11: Pedunculated GIST. Oral and intravenous CE-CT, axial plane. Pedunculated (arrow) and exophytic gastric mass, with heterogeneous enhancement located at the anterior wall of the antrum

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Fig. 5: Gastric GIST. CE-CT, axial plane; Large, bulky, heterogeneously enhancing mass (with peripheral enhancement). Hypoattenuating central area due to extensive necrosis.

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Fig. 12: Endogastric Schwannoma. A - Oral and intravenous CE-CT, axial plane; CT shows a well-defined endoluminal soft tissue mass with homogeneous density, with a central ulcer. B - Partial gastrectomy with a nodular submucosal mass in the lesser curvature and anterior wall, with 4.7 cm in greatest dimension, with central ulceration. C - The neoplasm was located on the submucosa and muscularis propria, with a multinodular, solid and whitish cut surface. D - Well circumscribed cellular proliferation on the submucosa, with interlacing bundles of spindle cells (H&E, 40x magnification); E - Nuclear palisading and Verocay bodies were often seen. No nuclear atypia and mitotic figures were noticed. (H&E, 100x magnification); F - No expression of CD117 (c-kit) was seen; G - Diffuse and strong expression of S100
Fig. 13: Small bowel GIST (jejunum). A, B - oral contrast CT, axial (A) and coronal (B) planes; exophytic lesion located at the right side, apparently well-circumscribed with an air-fluid level inside. C, D - Small bowel resection specimen with a 6 x 5 x 4 cm lobulated mass on the antimesenteric side of the bowel. The cut surface reveals a mass extending to the subserosal connective tissue and ulcerating the mucosa, with solid whitish areas and haemorrhagic areas.

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Fig. 14: A - Axial T2-weighted MRI reveals an isointense to hypointense mass, with central fluid signal, arising from small bowel wall B - CT image (see Fig. 13) C - Contrast-enhanced MRI demonstrates intense enhancement with a central area of non-enhancement representing necrosis.

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Fig. 15: Small bowel GIST. A, B, C - CE-CT, axial (A), sagittal (B) and coronal (C) planes; well-circumscribed mass with soft-tissue (low) attenuation in the pelvic / hypogastric region; heterogeneous and peripheral enhancement, containing air and debris (air-fluid level inside) due to extensive necrosis. D - Small bowel resection specimen with a 21cm mass, adherent to the bowel wall. The cut surface was heterogeneous, with multinodular areas and extensive necrosis and haemorrhage, with residual whitish tumor tissue on the periphery.

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Fig. 16: Duodenal GIST. Different axial CT planes before (A) and after (B) intravenous CE-CT; CT scan shows an exophytic soft tissue mass (A,B - dashed red lines) with a punctate calcification (arrow) and heterogeneous enhancement with an hypoattenuating area at the center of the mass (B).

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Fig. 17: CE-CT, axial plane; two GIST lesions at non-contiguous parts of the small bowel, with similar CT characteristics.

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Fig. 18: GIST - Peritoneal Metastasis. CE-CT, axial plane; multiple round lesions with different sizes (arrows), homogeneously enhanced in the peritoneal cavity, representing multiple GIST metastasis

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Fig. 19: Liver(A) and peritoneal metastases(B). CE-CT, axial planes; images show round, two heterogeneously enhanced liver metastases with necrotic areas (A) and a huge high vascularized peritoneal mass (B), peripherally enhanced with central hypoattenuating areas due to extensive necrosis.

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Fig. 20: von Recklinghausen’s disease (Neurofibromatosis type I). Gastric GIST previously resected. Multiple small bowel GISTs. A, B - CE-CT, axial (A) and coronal (B) planes; Huge mass at the left side of the abdomen, with heterogeneous enhancement and multiple hypoattenuated areas, related to necrosis. The mass causes intestinal obstruction and dilatation. C, D - Small bowel resection specimen (C) with 8 nodular masses in the bowel wall and subserosa, the largest one measuring 9.5 x 7 x 4.5 cm. The masses were well-defined, with greyish cut surface with spongy and cystic areas (D).

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Fig. 21: Cecal GIST. CE-CT, axial plane; CT scan reveals a transmural mass, heterogeneously enhanced with an air-fluid level (necrosis).

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**Fig. 22:** Liver metastases from a GIST. CE-CT, axial plane; large and poorly-defined mass at the liver, with extensive hypoattenuating areas (necrosis).

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**Fig. 6:** Rectal GIST. A - Axial T1-weighted MRI reveals the lesion to be isointense. With a few areas of hyperintensity representing hemorrhage. B - Axial T2-weighted MRI reveals an heterogeneously isointense to hypointense mass, with central fluid signal, arising from the anterior wall of the rectum and projecting into the rectoprostatic space. C - Coronal contrast-enhanced MRI demonstrates intense enhancement of the solid component with central areas of non-enhancement representing necrosis.
Fig. 7: Pelvic Extra-GIST. A - Transabdominal ultrasound reveals a round-shape, well-circumscribed hypoechoic pelvic mass; B, C - oral positive contrast and intravenous CE-CT; axial (B) and coronal (C) planes; huge pelvic mass, with a large necrotic center.

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Conclusion

It is of the utmost importance to know the imaging features of GIST. A large, bulky and exophytic mass with heterogeneous enhancement is very predictive of GIST.

Hypervascular liver metastases and smooth low-density mesenteric masses suggest metastatic disease.

Expressive adenopathies, concentric bowel involvement, spiculated mesenteric lesions and massive ascites should suggest another diagnosis.

Different imagiological modalities help the documentation of abdominal masses, although CT, with or without the MR adjunction, had the crucial role through the process of diagnosis, staging and subsequent follow-up.

Nevertheless, only histological analysis can provide definitive diagnosis.
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