CLINICAL IMAGING

Gastrointestinal Stromal Tumors: a Pictorial Review

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Abstract

We describe the pertinent organ-specific clinical manifestations of gastrointestinal stromal tumors (GISTs) as well as the radiological appearances that allow optimal depiction of pathology and diagnosis. Radiologic features of GISTs vary depending on tumor size and organ of origin. They most commonly have an exophytic growth pattern and manifest as dominant masses outside the organ of origin. Intramural and intraluminal masses are less common radiologic manifestations. GISTs may contain areas of hemorrhage, necrosis, or cyst formation that appear as focal areas of low attenuation on computed tomographic images. Most metastases of GISTs involve the liver and peritoneum by hematogenous spread and peritoneal seeding. CT and MRI are considered to be the imaging modality of choice for the detection, staging, surgical planning and follow-up of patients with GIST. A reduction in tumor size, extensive cystic changes, and calcification in primary and metastatic GISTs on CT and MRI indicate disease response to therapy. Radiologists and clinicians must recognize the imaging features of GISTs, detect, characterize the lesions and evaluate the tumor response during specific treatment.

Keywords

Gastrointestinal stromal tumors – CT – MRI

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract. The term GIST defines a unique group of mesenchymal neoplasms that are distinct from true smooth muscle and neural tumors [1].

GISTs display spindle cell or epithelioid morphologic characteristics and specific immunohistochemical properties. The most specific and important immunohistochemical marker is the c-kit (CD117) protein, a tyrosine kinase growth factor receptor. Many tumors previously diagnosed as leiomyomas, leiomyoblastomas, or leiomyosarcomas have been found to be positive for CD117 and are now considered GISTs. This includes tumors involving most sites in the gastrointestinal tract except the esophagus, where true leiomyomas are more common than GISTs. All GISTs should be considered as having malignant potential, although they display varying degrees of aggressiveness [2, 3].

Although some families with hereditary GISTs have been described, most cases are sporadic. GISTs occur in 10-20 per one million people. The true incidence might be higher, as new laboratory methods are much more sensitive in diagnosing GISTs [4].

GISTs can occur anywhere in the gastrointestinal (GI) tract from the esophagus to the rectum, as well as the omentum, mesentery, and retroperitoneum. Approximately 60–70% of GISTs occur in the stomach, and 25–35% arise in the small intestine. Colon, rectum, appendix (together 5%) and esophagus (2-3%) are rare sites. Less commonly, they may arise in the mesentery, or omentum [1].

GISTs are usually solitary tumors. Most individuals are over 50 years of age at the time of presentation, and GISTs are rarely seen in patients younger than 40 years, although there are several reports in the pediatric population [5].

Patients with neurofibromatosis type 1 (NF1) have an increased prevalence of GISTs. Classically, patients with NF1 have multiple small intestinal GISTs [6].

The clinical manifestations of GISTs depend on the location and size of the tumors and are often nonspecific [7, 8].

Imaging

The role of imaging includes the detection (subjects with occult gastrointestinal bleeding, incidental recognition etc), characterisation, analysis of relations between mass and gastrointestinal wall, staging, prognostic assessment...
(recognition of signs of malignancy and unfavourable prognosis) and follow-up during specific treatment.

CT is considered to be the imaging modality of choice for the detection, staging, surgical planning and follow-up of patients with GIST. Because GISTs usually involve the outer muscular layer, they have a propensity for exophytic growth. Therefore, the most common appearance is that of a mass arising from the wall of the gastrointestinal tract and projecting into the abdominal cavity. Mucosal ulceration is seen on the luminal surface of the tumor in up to 50% of cases [9]. The majority of GISTs appear to be well-defined, extraluminal or intramural masses with varying attenuation on CT based on size. Small lesions, which are usually benign, tend to be well-defined and relatively homogeneous (Fig. 1). Larger lesions normally show well-defined or ill-defined margins, inhomogeneous density both on unenhanced and on contrast-enhanced scans, with combined intraluminal/ extraluminal growth and a tendency to spread to surrounding structures. Large tumors (>6cm) frequently show central areas of necrosis or haemorrhage (Fig. 2). Central gas and mural calcification are uncommon findings. Varying degrees of necrosis may be frequently demonstrated within the mass. A peripheral enhancement pattern correlated with central hemorrhage, necrosis, or cyst formation and peripheral areas of viable tumor have been reported [10, 11]. The masses usually displace adjacent organs and vessels, but direct invasion of the adjacent structures is sometimes seen with advanced disease. Ascites is an uncommon feature [12]. The above description applies to GISTs in all locations.

![Fig 1. Gastric GISTs. a) CT of the abdomen in a 58 year old woman complaining of pelvic pain shows an incidental homogeneous exophytic ovoid mass in the gastric fundus (arrow). b) Gastric GIST in a 64-year-old man who presented for an annual check-up with mild epigastric discomfort. CT image shows an ovoid, homogeneous, mural-based mass along the fundus of the stomach with intraluminal and exophytic component (arrows).](image1)

However, there are features of GISTs that may be unique to location. Gastric GISTs commonly demonstrate extension into the gastrohepatic ligament (Fig. 3), gastroepiploic ligament, and lesser sac, and frequently, the bulk of the tumor is seen in an extragastric location. Furthermore, the cavities that develop from central necrosis or hemorrhage in the larger tumors may communicate with the gastric lumen (Fig. 4) [13].

GISTs may occur throughout the small intestine, usually presented with signs and symptoms of obstruction or rarely with hemorrhage. They may appear as intramural masses or intraluminal polyps, and may show extension into adjacent mesentery (Fig. 5). Small intestinal GISTs demonstrate similar features of peripheral enhancement and central areas of low attenuation. Encasement of adjacent small bowel, colon, and bladder can be seen. Extension into the adjacent small bowel mesentery and encasement of noncontiguous segments of small intestine, colon, bladder, ureter, and abdominal wall may occur. The differential diagnosis for small intestinal GISTs includes adenocarcinoma and lymphoma. Adenocarcinoma typically manifests as an annular lesion in the proximal small intestine; thus, its appearance usually does not overlap with that of GISTs. Lymphoma, however, has many features similar to those of GISTs. The presence of associated lymphadenopathy, however, would favor the diagnosis of lymphoma [14].

Anorectal GISTs most commonly present as well-defined, eccentric mural masses that expand the rectal wall and may contain mucosal ulceration. The mass spreads via extension into the ischiorectal fossa, prostate, or vagina. As in GISTs at other locations, central areas of hemorrhage can be seen [15].

Colonic GISTs are described as transmural tumors that involve the intraluminal and extraserosal surfaces of the colon. Other features include cystic change, hemorrhage, necrosis, or calcification. Colonic GISTs have been seen to exhibit circumferential growth and secondary dilatation of the affected colonic segment.

![Fig 2. Small intestine GIST. Axial contrast-enhanced CT scans (a, b) of mid abdomen show a large inhomogeneous mass arising from small bowel with large exophytic component and necrotic hypodense areas.](image2)

![Fig 3. GIST arising from the lesser curvature of the stomach in a 60 year old man that was incidentally discovered. CT scan shows a homogeneous mural-based extraluminal mass along the lesser curvature. The mass extends into the gastrohepatic ligament (arrows).](image3)
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GISTs may originate from the mesentery and secondarily involve the small intestine. The presence of hemorrhage, necrosis, and cystic change in these tumors results in the appearance of a complex mass on cross-sectional imaging. The imaging appearance of mesenteric and omental GISTs is indistinguishable from that of other sarcomas that may arise in these locations [16] (Fig 6).

Signs of high-grade GIST include liver metastasis, GI wall infiltration, large volume, irregular surface, ill-defined margins, inhomogeneous enhancement and peritoneal spread (Figs. 6, 7). No definite correlation between radiologic appearance and malignant potential has been established with regard to the degree of necrosis, hemorrhage, cyst formation, or contrast material enhancement on CT images.

On MR imaging (MRI) solid portions of tumors typically show low signal intensity on T1-weighted images, intermediate to high signal intensity on T2-weighted images, and enhancement after administration of gadolinium (Figs. 8, 9). The marked high signal seen on T2-weighted MRI should be considered as a feature strongly indicating diagnosis of GIST [17]. The multiplanar capability of MRI may be helpful in determining the organ of origin in large tumors (Fig. 10).

Nearly 50% of patients with GISTs present with metastasis. Most metastases of GISTs involve the liver and peritoneum by hematogeneous spread and peritoneal seeding, respectively. Less commonly, metastases are found in the soft tissue, lungs, and pleura. Unlike gastrointestinal adenocarcinomas, GISTs metastasizing to the lymph nodes are extremely rare.

The CT characteristics of metastatic lesions of GISTs are similar to those of primary tumors: enhancing masses that can be heterogeneous because of necrosis, hemorrhage, or cystic degeneration [18].

The primary treatment goal for localized primary GIST is complete resection, without the need for lymphadenectomy or wide resection margins. Thus, gastric wedge resections...
and segmental resections of the small bowel are the most common surgical procedures. Until recently, the only therapy that has proved effective for GISTs has been surgical resection. In 2001, Jonsuu et al [19] published a case report about a nonresectable, widely metastatic GIST that showed a very dramatic response to a tyrosine kinase inhibitor, STI571 (Gleevec, Novartis). This drug is a molecular targeted therapy, and acts on the c-kit growth factor receptor, which is the most important diagnostic marker of GISTs.

In general practice, contrast-enhanced CT is routinely used to monitor tumor response. The degree and pattern of enhancement observed on CT scans are useful for identifying post treatment changes. On contrast-enhanced CT, a response to imatinib is characterized by rapid transition from a heterogeneously hyperattenuating pattern to a homogeneously hypoattenuating pattern with resolution of the enhancing tumor nodules and a decrease in tumor vessels. The density of hepatic metastases decreases after treatment to approximately 20–25 H, which is near to, but greater than that for a true cyst (<15 H). This Hounsfield unit range...
Gastrointestinal stromal tumors may be helpful in differentiating true cysts from metastases after treatment with Gleevec (Fig. 11). Similarly on MRI the metastatic lesions after treatment become bright on T2 images and remain unenhanced on post contrast images (Fig. 12).

**Fig 12.** Hepatic metastasis 4 years after radical resection small bowel GIST. a) Axial T2W image shows a high signal target like metastasis in the right liver lobe. (b) after the administration of contrast medium a ring like peripheral enhancement is seen. (c) 6 weeks after therapy the lesion became cystic with homogeneous high signal intensity on T2W image. (d) on post contrast image the lesion remain unenhanced.

In conclusion, a reduction in tumor size, extensive cystic changes, and calcification in primary and metastatic GISTs on CT or MRI indicate a disease response. The early detection of focal solid or new solid lesions after maximal dose of imatinib mesylate suggests disease progression and might be helpful in early intervention such as surgery or new tyrosine kinase inhibitors [20].

**Conflicts of interest**

None to declare.

**References**