Gastrointestinal stromal tumors (GISTs): Diagnostic value of multi-detector computed tomography

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Abstract  Background: GISTs are considered the commonest mesenchymal neoplasms of the GIT originating from the gastrointestinal tract, mesentery, omentum, or retroperitoneum. They arise within the gut musculosa having exophytic growth pattern. They characteristically have hemorrhage, necrosis, or cyst formation that appears as focal areas of low attenuation on computed tomographic images. With multidetector CT (MDCT) capabilities, the exact origin of the GIST can be easily confirmed to differentiate it from other mesenchymal origin tumors.

Materials and methods: Retrospective search for GIST cases in the digital archives of our institute, during a 15 months duration (April 2010 to July 2011). Workstation reviewing of their imaging features.

Results: This study included 24 pathologically proved GISTs (12 gastric, 8 small intestinal, two colonic, one mesenteric and one anorectal) demonstrating the radiologic features of GISTs depending on tumor size and organ of origin.

Conclusion: MDCT with its multiplanar capabilities and isotropic z-axis resolution allows the radiologist to examine the detailed relation of the mass to the surrounding bowel wall, vessels and other structures. It also helps to map the vascular pedicle in cases of hypervascular GIST’s, which may be crucial for trans-catheter embolization in cases presenting with acute gastrointestinal bleeding.

1. Introduction

Gastrointestinal stromal tumors (GISTs) comprise a group of mesenchymal neoplasms that are distinct from true smooth muscle and neural tumors and considered the commonest mesenchymal neoplasms of the gastrointestinal tract. (1) GISTs, leiomyomas, and leiomyosarcomas are distinctly different neoplasms that arise with variable frequency throughout the gastrointestinal tract. GISTs are the most common and may occur from the esophagus to the anus. They may also occur primarily in the omentum, mesentery, and retroperitoneum. The esophagus is the only site where leiomyomas
predominate (75% of esophageal mesenchymal tumors are leiomyomas; 25% are GISTs) (1,2).

In the stomach, small intestine, colon, and anorectum, GISTs account for almost all mesenchymal tumors, as leiomyomas and leiomyosarcomas in these sites are very rare (2).

Previously, it was referred to these tumors as smooth muscle tumors, leiomyomas and leiomyosarcomas because these tumors were believed to originate from the smooth muscle layers of the wall of the gastrointestinal tract, which led to profound diagnostic confusion and is indicative of the diverse radiologic and histologic manifestations of mesenchymal neoplasms (2).

The best defining feature of GISTs is the expression of KIT (CD117), a tyrosine kinase growth factor receptor. Immunoreactivity for KIT distinguishes GISTs from true leiomyomas, leiomyosarcomas and schwannomas. Pharmacologically targeting this receptor with a KIT tyrosine kinase inhibitor (STI-571, Imatinib) has been shown to be of clinical utility in treating patients with GISTs (3).

The clinical manifestation of GISTs is highly variable with wide spectrum of radiologic appearances. For small benign looking GISTs, they are discovered incidentally during radiologic evaluation or surgery for another condition. In contrast, other patients present with profound symptoms that reflect large or highly aggressive GISTs that invade adjacent organs and metastasize (4,5).

2. Materials and methods

This article summarizes the current literature and our recent experience with the help of MDCT in the diagnosis of 24 cases of GIST (12 gastric, 8 small intestinal, two colonic, one mesenteric and one anorectal).

Data was collected from the digital archives of our institute, during a 15 months duration (April 2010 to July 2011).

The scans were performed using a 16-slice MDCT machine (Siemens, Erlangen, Germany). The patients were prepared with neutral oral contrast (iso-osmotic mannitol) except for three patients that ingested positive oral contrast prior to the examination. The study included a non-contrast series, followed by a dual-phase scan after automatic IV injection of 120 ml non-ionic contrast (Ultravist, Schering). The phases were: Enteric phase at 45 s following the start of contrast injection; portal phase at 70 s. Although this may constitute an added radiation load, we believe it adds additional data in cases of GIT bleeding to detect the source of hemorrhage.

The clinical, pathologic, and radiologic spectrum of GISTs throughout the gastrointestinal tract are presented and summarized in view of these cases.

3. Clinical features

The exact prevalence of GISTs is difficult to determine. Miettinen and Lasota (6) estimated the frequency of GISTs as 10–20 cases per million persons. No association between geographic location, ethnicity, race, or occupation has been established. Most individuals are over 50 years of age at the time of presentation, and GISTs are rarely seen in patients younger than 40 years of age (7,8).

Although some studies in the literature show a slight male predominance, others show no gender predilection (7).

Patients with neurofibromatosis type 1 (NF1) have an increased prevalence of GISTs. Classically, patients with NF1 have multiple small intestinal GISTs (9,10). GISTs are likely a feature of the Carney triad, which is a rare condition referring to the association of an epithelioid leiomyosarcoma with paraganglioma and pulmonary chondroma (11).

Presenting signs and symptoms depend on the size and anatomic location of the tumor. GISTs most frequently occur in the stomach (60–65% of cases), followed by the small intestine (30–35%), anorectum (7%), colon, and esophagus (12).

The most common clinical manifestation for symptomatic GISTs is gastrointestinal bleeding from mucosal ulceration (13). Patients may present with hematemesis, melena, hematochezia, or signs and symptoms of anemia caused by occult bleeding. Other signs and symptoms include nausea, vomiting, abdominal pain, weight loss, abdominal distention, and intestinal obstruction.

Occasionally, small asymptomatic GISTs are discovered incidentally during a radiologic evaluation or surgical procedure performed for other reasons. Asymptomatic anorectal tumors may be discovered as a palpable mass during routine digital rectal examination (14).

4. Pathologic features (15,16)

GISTs range in size from several millimeters to greater than 30 cm (15). They are typically well-circumscribed masses that compress adjacent tissue and lack a true capsule. Cut sections of specimens have a pink, tan, or gray surface. Focal areas of hemorrhage, cystic degeneration, and necrosis may occur, particularly in large lesions.

GISTs of the hollow gastrointestinal tract most commonly involve the muscularis propria of the intestinal wall. Mesenchymal tumors that involve the muscularis mucosae most frequently arise in the colon and occur as polyps. Such tumors are thought to uniformly represent true leiomyomas (16).

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 intestinal wall and projecting into the abdominal cavity (16). Often, a component of the tumor distends to the mucosal surface of the involved segment of intestine. Mucosal ulceration is seen on the luminal surface of the tumor in up to 50% of cases (15).

Cavities form from extensive hemorrhage or necrosis and may communicate with the intestinal lumen. Aneurysmal dilatation of the involved segment of the colon is an uncommon feature of colonic GISTs (15).

Small intestinal GISTs may have a more aggressive course compared with that of gastric GISTs of the same size. Therefore, the size threshold for estimating recurrent or metastatic risk in small intestinal GISTs may be smaller than that for gastric GISTs. The majority of esophageal, colonic, and anorectal GISTs are malignant (16).

5. Radiologic features

5.1. Stomach

Considered the commonest site for origin of GISTs which make up 2–3% of all gastric tumors. In our series of 24 GISTs,
12 cases (50%) were located in the stomach, two of them (17%) was confined to the cardia and fundus of the stomach, six (50%) were in the body, and four (33%) were in the antrum.

Regarding the size, the tumors ranged from 3.4 to 22 cm (mean is 11.3 cm) in maximal dimension with the largest GIST mass of all our cases reached down to the pelvic cavity (Fig. 1).

In our study, no correlation between radiologic appearance and malignant potential could be established with regard to the size, degree of necrosis, hemorrhage, cyst formation, or contrast enhancement on computed tomographic (CT) images.

CT showed an intramural component in three cases of 12 cases gastric GIST (25%) that we reviewed (Fig. 2).

Extragastric extension was present in 75% of cases. Extension may occur in the direction of gastrohepatic ligament (Fig. 3), into the gastrospenic ligament (Fig. 4), or posteriorly into the lesser sac.

In many cases, the bulk of the tumor was in an extragastric location, which makes it difficult to appreciate the origin of the tumor from the gastric wall on CT images. Reviewing all images on the work station in the three planes as well as the oblique direction helps in assessing the origin of the lesion and the direction of growth (17,18).

The tumor may be attached to the gastric wall by a thin pedicle. Careful evaluation of the gastric wall in these cases may reveal subtle wall thickening that will help establish the stomach as the origin of the mass (17).

A peripheral enhancement pattern was present in the majority (75%) of our cases on intravenous contrast-enhanced CT images (Fig. 3) whereas homogeneous enhancement, in small sized cases, presented in a minority (25%) of cases (Fig. 2).

Correlation of this appearance with gross pathologic findings demonstrates that this pattern represents enhancement of peripheral areas of viable tumor. Central areas of low attenuation correspond to hemorrhage, necrosis, or cyst formation.

Lesions with extensive hemorrhage or necrosis may form large cystic spaces or cavities. The cavities may communicate with the gastric lumen and contain air, air-fluid levels, or oral contrast media (19).

Calcification is an unusual feature of GISTs, seen in only one (3%) of our gastric cases. It may occur in a mottled pattern or be present extensively throughout the tumor. CT may also demonstrate evidence of adjacent organ invasion, ascites, omental and peritoneal spread of tumor, or liver metastasis. Metastatic lymphadenopathy is not a feature in patients with GISTs. None of our cases presented with focal or multicentric calcification (20).

The differential diagnosis (18) for gastric GISTs includes other neoplastic growths from gastric wall which simulate
imaging features of GIST tumors as other mesenchymal neoplasms such as true leiomyomas, leiomyosarcomas, schwannomas, neurofibromas, and neuroendocrine neoplasms (e.g., solitary gastric carcinoids). Solitary gastric carcinoids are most commonly seen in the antrum and characteristically have a central ulceration.

Other common neoplastic growths include gastric adenocarcinoma and lymphoma rarely demonstrate marked exophytic growth. However, they may occasionally have a radiologic appearance similar to that of GISTs—that is, a predominantly mural location or an intraluminal component.

Advanced gastric carcinomas and lymphomas commonly have associated perigastric, hepatoduodenal ligament, and celiac lymphadenopathy, which are not seen in malignant GISTs and are considered as a respectable differentiating point.

Lymphoma may be associated with bulky adenopathy or adenopathy that extends into the lower abdomen and pelvis. Adenopathy is not usually observed in cases of gastric GISTs.

5.2. Small intestine

GISTs may occur throughout the small intestine. Of the eight small intestinal GISTs in our series, three were located in the duodenum, three in the jejunum, and two in the ileum. The tumors ranged from 2.2 to 16 cm in maximal dimension, with a mean size of 8.6 cm.

Regarding the behavior of intestinal GIST, like gastric GISTs, many intestinal tumors often have an extra-serosal component. These tumors may exhibit significant mass effect on the affected segment of intestine or adjacent segments. Cavity and fistula formation may occur, but less frequently, resulting in luminal enlargement and communication of the cavity or fistula with the intestinal lumen (21).

Mass effect on surrounding structures with large masses is also noted as for example obstructive jaundice with a case of gastric GIST compressing CBD (Fig. 5).

The intraluminal, mural, and extra-serial components of small intestinal GISTs are well depicted on MDCT images. GISTs may appear as an intramural mass or intraluminal polyp. Three cases (33%) of the small intestinal GISTs in our series were primarily in an extra-serosal location such that a small bowel origin was not readily evident at CT.

Following intravenous administration of contrast media, GISTs are typically enhancing masses with areas of low attenuation from hemorrhage, necrosis, or cyst formation (22). A homogeneous pattern of attenuation is less common and was present in two of our cases (Fig. 7).

Vascular supply of the lesion as well as the course of vascular pedicle easily demonstrated with CT angiography, MIP (maximum intensity projection) as well as CPR (curved planer reconstruction) of the arterial supply (Fig. 6).

Extension into the adjacent small bowel mesentery and encasement of noncontiguous segments of small intestine, colon, bladder, ureter, and abdominal wall may occur (22). Patients with malignant GISTs may present with metastases to the liver, omentum, and peritoneum (23,24).

In those patients who presented with signs and symptoms of small intestinal obstruction, abdominal radiography showed evidence of small intestinal dilatation or a soft-tissue mass. Irregular gas collections were evident on abdominal radiographs in those patients who had cavitary masses containing air (25).

Small luminal or mural based GISTs have high mobility potentials and can be demonstrated in changeable locations during serial phases or scans (Fig. 8).

The differential diagnosis (25) for small intestinal GISTs includes primary and metastatic small intestinal neoplasms. Adenocarcinoma is the most common primary malignancy of the small bowel. It typically manifests as an annular lesion in the proximal small intestine; thus, its appearance usually does not overlap with that of GISTs. However it has many features similar to those of GIST.

Lymphoma produces large masses within the small intestine that may ulcerate, cavitate, and extend into the adjacent mesentery. In these cases, lymphoma may be indistinguishable from a GIST on radiologic images. The presence of associated lymphadenopathy, however, would favor the diagnosis of lymphoma (26).
Primary colonic GISTs are much less common than gastric, small intestinal, and equal in presentation to anorectal and esophageal GISTs, although GISTs metastatic from other sites commonly involve the external aspect of the colon. We had two cases of a colonic GIST in our series, one of them presented in (Fig. 9). In the literature, they are described as transmural tumors that involve the intraluminal and extraserosal surfaces of the colon (27).

They may be smooth or multinodular in contour and may contain central areas of hemorrhage, cystic change, necrosis, or calcification. A circumferential growth pattern with aneurismal dilatation of the affected colonic segment has been observed in a colonic GIST (27).
The radiographic and cross-sectional imaging appearances of colonic GISTs are similar to those of leiomyosarcomas. Small lesions are typically confined to the wall of the colon and appear as mural or submucosal masses at barium examination.

Mucosal ulceration may be present. The lesions in our series ranged from 10–18 cm and are seen as large exophytic masses, with central necrosis, that extended beyond the serosal surface of the colon on CT images.

The radiologic differential diagnosis for colonic GISTs includes adenocarcinoma, lymphoma, metastatic melanoma, and leiomyosarcoma. Retroperitoneal sarcomas such as malignant fibrous histiocytoma, fibrosarcoma, and liposarcoma arising adjacent to the colon may appear to have a colonic origin and may also be confused with a GIST (19).

6. Anorectum

Focal well-circumscribed mural mass is the most common finding on CT and MRI images. Unfortunately, the only case we met during this study for anorectal GIST had MRI and not CT study.

Mucosal ulceration may be present. External spread frequently occurs with extension of the mass into the ischiorectal fossa, prostate, or vagina.

The least common appearance is a focal intraluminal polypoid mass. The CT attenuation of anorectal GISTs is similar to that of GISTs in other locations of the gastrointestinal tract. Low-attenuation areas of hemorrhage are commonly present (28).

On T1-weighted MR images, anorectal GISTs have uniform, intermediate signal intensity; on T2-weighted images they have heterogeneous high signal intensity, with heterogeneous enhancement following gadolinium administration (Fig. 10).

The differential diagnosis for anorectal GISTs includes both epithelial and nonepithelial neoplasms of the anorectal region. Rectal adenocarcinoma, anal squamous cell carcinoma, lymphoma, malignant melanoma, carcinoid, leiomyoma, and leiomyosarcoma may have imaging appearances similar to that of GISTs, although leiomyosarcoma may have a dominant polypoid intraluminal component (27,28).

Carcinomas tend to have irregular margins and may be associated with perirectal lymphadenopathy, whereas GISTs tend to have well-defined margins and lack perirectal adenopathy (29).

GISTs that have significant perirectal extension may be mistaken as tumors arising from adjacent structures such as prostatic adenocarcinoma or sarcomas of the prostate and perineum. Anorectal lymphoma is seen in patients with AIDS (acquired immunodeficiency syndrome) and manifests radiographically as an eccentric or annular mural mass that may be associated with mucosal ulceration or perianal fistulization (29).

7. Mesentery and omentum

Primary GISTs may occur in any of the mesenteric or omental structures within the peritoneum. We had one case in our series measuring 8 × 10 cm (Fig. 11). In the series reported by Miettinen et al. (6), the median size of primary omental and mesenteric GISTs was 16.5 cm.

The presence of hemorrhage, necrosis, and cystic change in these tumors results in the appearance of a complex mass on cross-sectional images. The cystic component of the tumor may be the dominant feature. The peripheral solid portions of the tumor enhance during intravenous contrast material administration (1).

The only case in our study presents the typical features of pre-sacral centrally necrotic mass with mildly enhancing peripheral solid component, having lobulated well defined outer margins and proved pathologically to be mesenteric GIST.

The imaging appearance of mesenteric and omental GISTs is indistinguishable from those of other sarcomas that may arise in these locations, such as leiomyosarcoma, malignant fibrous histiocytoma, fibrosarcoma, and liposarcoma (18).

GISTs from the gastrointestinal tract may metastasize to the omentum and mesentery; however, they typically result in multiple masses throughout the peritoneal cavity. In these instances, the differential diagnosis includes peritoneal carcinomatosis, lymphomatosis, and the benign condition leiomyomatosis peritonealis disseminata; the latter typically manifests as innumerable small nodules measuring only a few millimeters each (18,19).
Esophageal GISTs are relatively uncommon, and we had no cases of an esophageal GIST in our series. GISTs accounted for approximately 25% of esophageal mesenchymal neoplasms studied by Miettinen et al. (6).

In contrast, leiomyomas are the most common mesenchymal neoplasm of the esophagus (75% of cases) and occur in a younger population (median age, 35 years) compared with GISTs (for whom the median patient age is 63 years) (6).

Esophageal GISTs are reported to range up to 25 cm in size and are most commonly located in the distal third of the esophagus (30,31). Small lesions tend more to be esophageal polyps than GIST.

Barium studies of the esophagus may show a smooth intramural mass or a large, ulcerative mass that extends into the esophageal lumen. Distal lesions may extend into the proximal stomach. On CT images, these lesions may be homogeneous or heterogeneous in attenuation. They may contain central areas of low attenuation from hemorrhage, necrosis, or cystic degeneration (30).

The use of endoluminal ultrasonography with fine-needle aspiration biopsy has been reported as a useful technique to aid in characterization, diagnosis, and management of submucosal lesions of the esophagus (32).

Papilloma, adenoma, inflammatory polyp, fibrovascular polyp, and esophageal carcinoma manifest as intraluminal polypoid masses and are considered in the differential diagnosis (30).

9. Conclusions

GISTs most commonly involve the muscularis propria of the stomach or intestinal wall and extend to involve extramural, mural, and intraluminal surfaces of the stomach and intestine.

The extramural component of GISTs may be extensive such that the bulk of the tumor is outside the organ of origin. GISTs occurring in the gastrointestinal tract and mesentery characteristically have hemorrhage, necrosis, or cyst formation that appears as focal areas of low attenuation on CT images. Although the radiologic features of GISTs are often distinct
from those of epithelial tumors, criteria to separate GISTs radiologically from other nonepithelial tumors have not yet been fully developed.

Multislice CT with its multiplanar capabilities and isotropic z-axis resolution allows the radiologist to examine the detailed relation of the mass to the surrounding bowel wall, vessels and other structures. It also helps to map the vascular pedicle in cases of hypervascular GIST’s, which may be crucial for trans-catheter embolization in cases presenting with acute gastrointestinal bleeding.

References