A Pictorial Review of Gastrointestinal Stromal Tumors throughout the GI Tract

Poster No.: C-2557
Congress: ECR 2015
Type: Educational Exhibit
Authors: A. Dixit, A. Hartery, R. Gullipalli; St. John's, NL/CA
Keywords: Cancer, Education, MR, Fluoroscopy, CT, Gastrointestinal tract, Abdomen
DOI: 10.1594/ecr2015/C-2557

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

Upon completion of this education exhibit, the learned should be able to:

1. Describe the epidemiology, pathophysiology, clinical presentation and management of gastrointestinal stromal tumours (GISTs).
2. Be aware of the cytological and histological markers used in the diagnosis of GISTs.
3. Confidently describe the radiological findings of GISTs depending on tumour location and imaging modality utilized.
4. Be familiar with the differential diagnoses of GISTs and the radiological findings that can help to differentiate these etiologies.
Background

The term gastrointestinal stromal tumour (GIST) was coined in the early 1980s to describe a type of non-epithelial GI tumour that lacked the traditional features of smooth muscle and neural tumours (1). GISTs arise from a precursor of the interstitial cells of Cajal, which are normally present in the myenteric plexus, and are clearly distinct from other mesenchymal tumours, such as leiomyomas and leiomyosarcomas (2). The interstitial cells of Cajal normally express a transmembrane receptor tyrosine kinase encoded by the KIT gene. Identifying KIT (CD117) is key to making a diagnosis of GIST in the vast majority of patients (3).

GISTs are the commonest GI mesenchymal tumour, however, they account for only 1-3% of all GI neoplasms. GISTs can occur anywhere along the GI tract as well as in the omentum and mesentery (Fig. 1). The most common locations for GISTs to occur are the stomach (60%), small bowel (30%), colon and rectum (5%), extra-gastrointestinal (5%), oesophagus (<2%) and appendix (<1%); a very small percentage of GISTs can be multicentric (4). The annual incidence of clinically detected GISTs is roughly 10 cases per million in Europe (5).

GISTs are most commonly seen in the 50 to 60 year old age range with no gender bias (6). Most GISTs are sporadic and have no established risk factors. However, some GISTs arise in the setting of specific tumour syndromes and these typically present at an earlier age (<40 years). Such syndromes include Familial GISTs, Carney’s triad (association of gastric GIST, paraganglioma, and pulmonary chondroma), Carney-Stratakis syndrome and type 1 neurofibromatosis (NF-1) (7).

The clinical presentation is vague and depends on tumour site and size. The most common symptom is abdominal pain and/or distension. Other symptomatology includes GI bleeding, occult bleeding, anemia, dyspepsia or a palpable abdominal mass. Ascites is rare in the presentation of GISTs. Duodenal GISTs can present with obstructive jaundice, however, this is uncommon. Major complications include haemorrhage and spontaneous rupture endoluminally or into the peritoneal cavity (8). Occasionally small asymptomatic GISTs are discovered incidentally during a procedure performed for other reasons (9).

GISTs can be either benign or malignant. Clinical risk of malignancy is determined by tumor size, location and mitotic index. Radiological characteristics of a GIST cannot be reliably used to determine its malignant potential (10). The mainstay of management is complete surgical resection when the tumor is well defined and without metastatic spread. For recurrent or GISTs that are not amenable to surgery, treatment is with Imatinib (11).
**Fig. 1:** Incidence of GISTs by location [stomach (60%), small bowel (30%), colon and rectum (5%), extra-gastrointestinal (5%), oesophagus (<2%) and appendix (<1%)].

Findings and procedure details

The term gastrointestinal stromal tumour (GIST) was coined in the early 1980s to describe a type of non-epithelial GI tumour that lacked the traditional features of smooth muscle and neural tumours (1). GISTs arise from a precursor of the interstitial cells of Cajal, which are normally present in the myenteric plexus, and are clearly distinct from other mesenchymal tumours, such as leiomyomas and leiomyosarcomas (2). The interstitial cells of Cajal normally express a transmembrane receptor tyrosine kinase encoded by the KIT gene. Identifying KIT (CD117) is key to making a diagnosis of GIST in the vast majority of patients.

We review the pathological, histological and radiological findings of GISTs by presenting cases from our tertiary-level hospitals.

Pathologically, GISTs appear as well-circumscribed exophytic masses that project outwards into the abdominal cavity and cause mass effect on surrounding structures (Fig. 2). The tumour surface can be smooth with the overlying mucosa being intact or there can be ulceration of this mucosa. GISTs can vary in size from millimetres to over 30 cm (12). When surgically resected, GISTs can have a grey, tan or pink surface and can contain variable regions of necrosis and haemorrhage (12).

Histologically, there are two main categories of GISTs - epithelial (round or polygonal cells) and spindle cell (cigar-shaped cells) types (Fig. 3). The majority of GISTs are of the epithelioid type, however roughly 75% of gastric GISTs are spindle cell type. Occasionally, GISTs can be composed of a mixture of both cell types (13).

In terms of immunohistochemistry, GISTs stain positive for the KIT (CD117) marker (Fig. 4). KIT (CD117) is a transmembrane receptor tyrosine kinase and GISTs are defined by their expression of this receptor (3, 14). The majority of GISTs also stain positive for the CD34 marker (Fig. 5), which is a hematopoietic progenitor cell antigen that is expressed in normal as well as neoplastic endothelial cells (14). More recently, there has been discovery of a third marker that is expressed by GISTs known as DOG1 (Fig. 6), which is a chloride channel protein. Studies show that the sensitivity of this marker is comparable to that of KIT (CD117) indicating that it is an important part of the diagnostic panel for GISTs (15).

GISTs have a variety of radiological appearances, however, there are three broad categories - intraluminal, extraluminal and dumbbell types. The dumbbell type refers to large tumours with both intraluminal and exophytic components. Imaging helps in the diagnosis as well as the localization, characterization and staging of GISTs. The modality
used depends on both the clinical presentation and the local availability. Cross-sectional studies are the most useful. Conventional radiography, sonography and barium studies have a limited role.

The remainder of this section will discuss radiological findings based on the modality and tumor location within the GI tract.

Conventional radiography does not play a role in the diagnosis of small or asymptomatic GISTs. Occasionally, the suggestion of a large GIST can made by the radiologist due to signs of mass effect such as displacement of abdominal viscera or separation of bowel loops. There can also be visualization of calcification and/or air-fluid levels depending on the gross pathology of a given GIST (Fig. 7).

Barium studies will show typical features of submucosal masses. They are well-circumscribed rounded tumours that form obtuse angles with the adjacent GI tract (Fig. 8). The overlying mucosa is typically intact but can occasionally ulcerate giving rise to the classic "bull's-eye" appearance on barium studies (9). Differentiation from other submucosal masses is not possible via barium studies and requires further investigation with cross-sectional imaging and laboratory testing.

Trans-abdominal ultrasound has a limited role and is only used for the characterization of GIST internal contents. Sonographically, GISTs appear as well-defined hypoechoic masses that are intimate with the GI tract. Larger tumours tend to be irregular whereas smaller GISTs are typically well rounded (Fig. 9). Larger GISTs have a variable degree of heterogeneity depending on the extent of necrosis and internal haemorrhage. Ultrasound also has a role in the percutaneous needle biopsy of GISTs (16).

Magnetic resonance (MR) imaging is commonly used as an adjunct to computed tomography (CT) to determine the origin of large GISTs and relationships to nearby soft tissue and vascular structures. MR is especially helpful for large exophytic tumours and anorectal GISTs. The MR imaging characteristics are variable and depend on the degree of tumour necrosis and internal haemorrhage. Solid aspects of the tumour display low signal intensity on T1-weighted images, high signal on T2-weighted images and enhancement after gadolinium administration (Fig. 10). Post-gadolinium administration images can serve to delineate regions of tumour necrosis. Regions of internal haemorrhage can range from high to low signal intensity on both T1 and T2-weighted images depending on the age of haemorrhage (9).

CT is the modality of choice for the detection, staging, surgical planning and follow-up of GISTs. Smaller tumours will appear on CT as sharply margined, smooth walled, homogenous soft-tissue attenuation with moderate contrast enhancement. Larger GISTs
have the classic appearance of large and irregular exophytic tumours. Peripheral contrast enhancement represents viable tumour, whereas the central low attenuation corresponds to cystic change, necrosis and haemorrhage. While the aforementioned CT appearance of GISTs is uniform throughout the GI tract, there are unique features that can be seen depending on the anatomic location of the tumour.

Oesophageal GISTs are rare and typically arise from the distal third of the oesophagus. They are well rounded with clearly defined margins. CT attenuation is typically hypo-intense or iso-intense to the comparable smooth muscle with mild enhancement on contrast-enhanced imaging (Fig. 11). Similar to other GISTs, there can be regions of necrosis, cystic change or haemorrhage (17).

The gastric body is the most common location for a gastric GIST to present followed by the antrum and fundus (9). Gastric GISTs frequently display extension into the gastrohepatic ligament, gastrospenic ligament, and lesser sac. Additionally, the bulk of the tumor is in an extragastric location. Most show peripheral enhancement indicating viable tumor in these areas. Air-fluid levels may be seen indicating cystic or necrotic components that communicate with the gastric lumen. Calcification is unusual in gastric GISTs (Fig. 12).

GISTs of the small bowel most commonly arise from the jejunum (9). They display peripheral enhancement with central areas of low attenuation. Homogenous enhancement is uncommon. They can appear as intraluminal polyps or intramural masses with extension into the mesentery. Encasement of non-contiguous segments of small intestine, colon, abdominal wall, ureter and bladder structures can also be seen (Fig. 13-15). Malignant small bowel GISTs may metastasize to the peritoneum, omentum and liver.

Colonic GISTs appear as transmural tumours that involve the intraluminal and extraroserosal surfaces of the colon. Tumour margins may be smooth or multinodular. Additional features can include cystic change, haemorrhage, necrosis, or calcification (12).

Anorectal GISTs typically appear as well defined, eccentric, mural masses that expand the rectal wall and may contain mucosal ulceration. There can be central regions of haemorrhage and extension into the ischiorectal fossa, prostate, or vagina (Fig. 16).

Extra-gastrointestinal GISTs are most commonly found in the mesentery and omentum. These appear as complex heterogeneous tumours with variable amounts of cystic change, necrosis and haemorrhage. Contrast enhancement is in a peripheral pattern (Fig. 17). Differentiation from other smooth muscle tumours arising in these regions cannot be made solely on cross-sectional imaging (9).
The differential diagnoses for GISTs primarily consists of other epithelial tumours of the GI tract and although the radiologic features of GISTs are often distinct from these epithelial tumours, definite diagnosis depends on immunological and histological testing. Examples of these tumours include leiomyomas, leiomyosarcomas, schwannomas and neurofibromas. Other etiologies include lymphoma, carcinoid, adenocarcinomas and cystic mesenteric formations.
Fig. 2: Flythrough of a 3D-MIP MRCP reconstruction showing a lobulated lesion arising from the proximal gastric wall of the lesser curvature. This was a pathologically proven gastric GIST (See Fig. 10 for multiplanar MR images of this gastric GIST).

© Radiology, Memorial University, Health Sciences Center - St. John’s/CA
Fig. 3: Histologic specimen of a duodenal GIST showing spindle shaped cells arranged in short fascicles.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA

Fig. 4: Histologic specimen of a duodenal GIST showing positive staining for the CD117 (c-kit) marker.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
**Fig. 5:** Histologic specimen of a duodenal GIST showing positive staining for the CD34 marker.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA

**Fig. 6:** Histologic specimen of a duodenal GIST showing positive staining for the DOG1 marker.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
Fig. 7: Single erect radiograph of the abdomen shows a 9 cm soft tissue density in the right lower quadrant that appears to be separate from the overlying liver and kidney. There is a focus of calcification within this. Follow-up cross sectional imaging showed this to represent a jejunal GIST (see Fig. 14)

© Radiology, Memorial University, Health Sciences Center - St. John’s/CA
Fig. 8: Selected images from an upper GI series show a well-circumscribed round submucosal lesion within the cardia of the stomach. This was a pathologically proven gastric GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
Fig. 9: Selected trans-abdominal sonographic images of the abdomen and pelvis show a solid ovoid hypoechoic mass in the left peri-aortic region that is separate from the left ovary. This was a pathologically proven extra-gastrointestinal GIST.

© Radiology, Memorial University, Health Sciences Center - St. John’s/CA
Fig. 10: MR images of the abdomen show a lobulated T2 hyperintense, T1 hypointense lesion arising from the proximal gastric wall of the lesser curvature. MRCP 3D reconstruction shows the gross architecture of the tumour. There is no significant lymphadenopathy or ascites. This was a pathologically proven gastric GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
Fig. 11: Contrast enhanced CT images of the abdomen and pelvis show a well-circumscribed, fairly homogenous, soft tissue density mass arising from the right lateral wall of the oesophagus. There is no significant lymphadenopathy or ascites. This was a pathologically proven oesophageal GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
Fig. 12: Contrast enhanced CT images of the abdomen and pelvis show an extremely large mass arising from the fundus of the stomach causing significant mass effect on adjacent structures. The majority of this tumour is in an extragastric location. This mass has an irregular thick wall with some peripheral enhancement. The central aspect of the mass is primarily cystic. There is no significant lymphadenopathy or ascites. This was a pathologically proven gastric GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
Fig. 13: Contrast enhanced CT images of the abdomen and pelvis show a large heterogeneous mass arising from the duodenum. This mass is irregularly enhancing with lobulated borders. The central aspect is hypodense, suggesting necrosis. There is no significant lymphadenopathy or ascites. This was a pathologically proven duodenal GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
Fig. 14: Contrast enhanced CT images of the abdomen and pelvis show an amorphous heterogeneous mass arising from the jejunum. This mass has an irregular thick wall and punctate regions of calcification. The central aspect is hypodense and contains foci of air suggesting necrosis. There is no significant lymphadenopathy or ascites. This was a pathologically proven jejunal GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
Fig. 15: Contrast enhanced CT images of the abdomen and pelvis show a lobulated, and irregularly enhancing soft tissue mass arising from the ileum. The central aspect is hypodense, suggesting necrosis. There is no significant lymphadenopathy or ascites. This was a pathologically proven ileal GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
**Fig. 16:** Contrast enhanced and MR images of a lobulated GIST arising from the rectosigmoid junction. On CT, the tumour appears as a subtle heterogeneous mural prominence at the rectosigmoid junction. On MR, this tumour is heterogeneous with decreased T2 signal intensity and T2 hyperintense and is primarily rounded with a short tail that extends into the sigmoid. There is no significant lymphadenopathy or ascites. This was a pathologically proven rectal GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
**Fig. 17:** Contrast enhanced CT images of the abdomen and pelvis show a well-circumscribed heterogeneous mass arising in an extra-gastrointestinal position. The mass is primarily hyperattenuating. There is a small punctate region of calcification within this. There is no significant lymphadenopathy or ascites. This was a pathologically proven extra-gastrointestinal GIST.

© Radiology, Memorial University, Health Sciences Center - St. John's/CA
Conclusion

GISTs are the most common mesenchymal tumours of the GI tract and are defined by a common altered oncogene. Typically arising in the 5th and 6th decades of life, the clinical presentation commonly includes abdominal pain and distension. Treatment is with surgical excision and adjuvant Imatinib therapy. The role of imaging includes the detection, characterisation, staging, prognostic assessment and follow-up during specific treatment. Important features that can assist the radiologist to suggest the diagnosis of GIST include visualizing a voluminous exophytic mass with heterogeneous enhancement. Significant lymphadenopathy, concentric bowel involvement and large-volume ascites are suggestive of an alternative diagnosis.
References