Received:
27 January 2015

Revised:
2 June 2015

Accepted:
23 June 2015

doi: 10.1259/bjr.20150085

Cite this article as:

Baheti AD, Shinagare AB, O'Neill AC, Krajewski KM, Hornick JL, George S, et al. MDCT and clinicopathological features of small bowel gastrointestinal stromal tumours in 102 patients: a single institute experience. *Br J Radiol* 2015; **88**: 20150085.

FULL PAPER

MDCT and clinicopathological features of small bowel gastrointestinal stromal tumours in 102 patients: a single institute experience

^{1,2}A D BAHETI, MD, ^{1,2}A B SHINAGARE, MD, ^{1,2}A C O'NEILL, MD, ^{1,2}K M KRAJEWSKI, MD, ³J L HORNICK, MD, PhD, ⁴S GEORGE, MD, ^{1,2}N H RAMAIYA, MD, and ^{1,2}S H TIRUMANI, MD

¹Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

²Department of Imaging, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

³Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

⁴Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Address correspondence to: Dr Akshay D Baheti

E-mail: akshaybaheti@gmail.com

Objective: Small bowel (SB) is the second most common site of gastrointestinal stromal tumours (GISTs). We evaluated clinical presentation, pathology, imaging features and metastatic pattern of SB GIST.

Methods: Imaging and clinicopathological data of 102 patients with jejunal/ileal GIST treated at Dana-Farber Cancer Institute and Brigham and Women's Hospital (Boston, MA) between 2002 and 2013 were evaluated. Imaging of treatment-naïve primary tumour (41 patients) and follow-up imaging in all patients was reviewed.

Results: 90/102 patients were symptomatic at presentation, abdominal pain and lower gastrointestinal blood loss being the most common symptoms. On pathology, 21 GISTs were low risk, 17 were intermediate and 64 were high risk. The mean tumour size was 8.5 cm. On baseline CT ($n = 41$), tumours were predominantly well circumscribed, exophytic and smooth/mildly lobulated in contour. Of 41 tumours, 16 (39%) were homogeneous, whereas 25 (61%) were heterogeneous. Of the 41 tumours, cystic/necrotic areas (Hounsfield units < 20) were seen in 16 (39%) and calcifications in 9 (22%). CT demonstrated complications in 13/41 (32%) patients in the form of tumour-bowel fistula (TBF) (7/41), bowel

obstruction (4/41) and intraperitoneal rupture (2/41). Amongst 102 total patients, metastases developed in 51 (50%) patients (27 at presentation), predominantly involving peritoneum (40/102) and liver (32/102). 7/8 (87%) patients having intraperitoneal rupture at presentation developed metastases. Metastases elsewhere were always associated with hepatic/peritoneal metastases. At last follow-up, 28 patients were deceased (median survival, 65 months).

Conclusion: SB GISTs were predominantly large, well-circumscribed, exophytic tumours with or without cystic/necrotic areas. Complications such as TBF, bowel obstruction and intraperitoneal perforation were visualized at presentation, with patients with perforation demonstrating a high risk of metastatic disease. Exophytic eccentric bowel wall involvement and lack of associated adenopathy are useful indicators to help differentiate GISTs from other SB neoplasms.

Advances in knowledge: SB GISTs are predominantly large, well-circumscribed, exophytic tumours, and may present with complications. They often are symptomatic at presentation, are high risk on pathology and metastasize to the peritoneum more commonly than the liver.

INTRODUCTION

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours involving the gastrointestinal (GI) tract. They arise from the interstitial cells of Cajal, the intestinal pacemaker cells present in the myenteric plexus in the muscularis propria, which likely accounts for their more commonly exophytic rather than intraluminal growth.¹⁻⁴ GISTs are classified as spindle cell, epithelioid, and mixed spindle and epithelioid type on histopathology.^{3,5} The pathogenetic signature of GIST is the presence of

activating mutations in the tyrosine kinase receptor KIT or in platelet-derived growth factor receptor alpha (*PDGFRA*), and GIST's hallmark is the response to tyrosine kinase inhibitors (TKIs) such as imatinib mesylate. The mutations occur in "hot spots" within these genes; KIT exon 11 mutations are the most common and show a better response to imatinib than do exon 9 mutations.^{6,7} The risk stratification of GIST depends on its mitotic index (MI), size and anatomic site of origin, with MI being the strongest predictor of recurrence.⁸⁻¹⁰

GISTs may originate anywhere along the GI tract, with small bowel (SB) being the second most common site of involvement (30–45%) after gastric GIST (50–70%). SB GISTs have worse prognosis than tumours of equivalent size and MI elsewhere.^{8,10} Furthermore, exon 9 mutant GISTs, which are relatively resistant to imatinib, arise predominantly in the SB.¹¹

Imaging features of GISTs arising at different sites of the GI tract have been conventionally described in the literature as a single cohort without site-specific analysis.^{12–15} In the past, our group has published the imaging features of GISTs arising at uncommon sites such as the oesophagus, duodenum and anorectal region.^{16–18} To the best of our knowledge, there is no literature focusing dedicatedly on the imaging features of SB GISTs (excluding duodenal GISTs, which have a risk stratification different from jejunal and ileal GISTs).^{8,19} Accordingly, the purpose of our study was to evaluate the clinical, pathological and imaging features of SB GISTs at presentation and their metastatic pattern.

METHODS AND MATERIALS

Subjects

In this Health Insurance Portability and Accountability Act-compliant retrospective study approved by the institutional review board with waiver of informed consent, 868 consecutive patients with histopathologically confirmed GIST between 2002 and 2013 were identified from the pathology database at Dana-Farber Cancer Institute and Brigham and Women's Hospital (Boston, MA). One of the radiologists (ADB) searched the electronic medical records of these patients to identify the patients with SB GIST and the picture archiving and communication system (PACS) database to identify patients who had imaging studies available for review. There were 102 patients who fulfilled these criteria and were included in the study cohort.

Clinical and histopathological data

Detailed clinical and histopathological information was extracted from the electronic medical records, including demographic data, date of diagnosis of primary tumour, clinical features at presentation, date of diagnosis of metastases, management of the primary tumour and metastases, duration of follow-up and final outcome. The median follow-up for all the patients was 48 months (range, 1–179 months). The histopathology of all the cases was confirmed at the pathology department. The following details were noted: tumour subtype (spindle cell, epithelioid or mixed), MI per 50 hpf/5 mm², risk stratification, the presence or absence of necrosis and the mutational status (where available). Immunohistochemistry for KIT was performed in all cases.

Imaging

Imaging was performed on a 16-slice (Siemens Medical Solutions, Forchheim, Germany) or 64-slice multidetector CT (MDCT) (Aquilion 64; Toshiba America Medical Systems, San Francisco, CA) scanners with 5-mm thick axial images and 4-mm coronal reconstructions. Iopromide (300 mg I/ml, Ultravist® 300; Bayer HealthCare Pharmaceuticals, San Francisco, CA) was administered as intravenous contrast using an automated injector (Stellant®; Medrad Inc., Warrendale, PA) at a rate of 2–3 ml s⁻¹, with a scan delay of 60 s. The imaging was reviewed on a commercially available workstation (Centricity PACS RA1000; GE Healthcare, Barrington, IL).

Imaging analysis

Baseline MDCT of the treatment-naïve primary tumour was available in 41 patients and follow-up imaging was available in all 102 patients. A systematic review of all pre-treatment and follow-up CT studies was performed in consensus by two oncoradiology fellowship-trained radiologists (ADB and SHT) with 5 and 8 years' experience. A total of 803 CTs were reviewed (mean 5; range, 2–20). Imaging features of the primary tumour that were recorded included the site of origin in SB, largest dimension, margin (well circumscribed or ill defined/infiltrative), outline (smooth/undulating or irregular/lobulated), growth pattern (exophytic, intraluminal or combined), tumour heterogeneity (homogeneous or heterogeneous), presence and percentage of cystic/necrotic component (Hounsfield units ≤ 20), presence of calcifications and complications [tumour–bowel fistula (TBF), bowel obstruction or intraperitoneal rupture]. The presence of local recurrence and of metastases at presentation or during follow-up, their site, number (whether single or multiple) and imaging features were also noted. Metastatic lesions were confirmed either at histopathology (15 patients) or by the presence of unequivocal progression or response to treatment on serial follow-up imaging (36 patients).

RESULTS

The study consisted of 53 males and 49 females with a mean age of 55 years (range, 19–83 years). 64 patients had proximal (jejunal) tumours while 38 had distal (ileal) tumours. The clinicopathological findings are summarized in Table 1.

Clinical presentation

Majority of the patients were symptomatic at presentation (90/102), with the most common presentation being abdominal pain/discomfort (35/102), melena/haematochezia (28/102) and symptoms of anaemia such as early fatigue and breathlessness (12/102). 6/102 patients had symptoms of obstruction such as vomiting, while 1 each presented with altered bowel movements

Table 1. Summary of clinicopathological findings

Characteristic	Finding
Mean age (years)	55 (range, 19–83)
Jejunal vs ileal	64 vs 38
Symptomatic at presentation	90/102 (88%)
Metastases at presentation	27 (26%)
Overall metastases	51 (50%)
Mean tumour size (pathology) (cm)	8.5 (range, 2–28)
Low vs intermediate vs high risk	21 vs 17 vs 64
Spindle cell vs mixed vs epithelioid	65 vs 36 vs 1
Mutational status (<i>n</i> = 32): exon 11 vs 9 vs 13	16 vs 14 vs 2
Median follow-up (months)	48 (1–179)
Alive vs dead vs lost to follow-up	54 vs 28 vs 20
Median survival for patients with metastases at presentation (months)	57 (10–115)
Overall median survival (months)	65 (22–179)

and enterococcal sepsis. The remaining 12/102 patients were asymptomatic with the tumours detected incidentally. Five patients had neurofibromatosis Type I (NF1).

Imaging of the primary tumour ($n = 41$)

The mean size of the primary tumour on imaging was 6.8 cm (range, 2–22 cm). Tumours had well-circumscribed margins in 35/41 (85%) patients and ill-defined infiltrative margins in 6/41 (15%) patients (Table 2). 30/41 (73%) tumours were smooth/undulating in outline, while 11/41 (27%) tumours were irregular/lobulated. Tumours that had ill-defined margins (6/41) were difficult to accurately measure but had a larger mean size (10.2 cm) than tumours with well-defined margins (6.2 cm). Similarly, tumours with irregular outline (10 cm) were larger than tumours with smooth outline (5.7 cm). 22/41 (54%) tumours were exophytic, 16/41 (39%) had both exophytic and intraluminal components and 3/41 (7%) were intraluminal (Figures 1 and 2). The exophytic component was greater than 50% in all except one of the 16 tumours having both the components. 16/41 (39%) tumours were homogeneous while 25/41 (61%) were heterogeneous, with cystic/necrotic component seen in 16 of the latter. Calcifications were visualized in 9/41 (22%) tumours, in the form of single or multiple specks of stippled calcification.

Among the five patients in our cohort having NF1, imaging of the primary was available in three. The tumour in the first patient was seen on CT as a single mildly lobulated tumour involving a short segment of the jejunum, but found on pathology to have multiple small subcentimetre tumours. The second patient demonstrated TBF (Figure 2) while the tumour in the third patient was a heterogeneously enhancing exophytic mass. All these tumours were <5 cm.

Complications on CT at presentation

CT demonstrated complications in 13/41 (32%) patients in the form of TBF ($n = 7$), bowel obstruction ($n = 4$) and intraperitoneal perforation ($n = 2$). The mean tumour size in these patients was 7 cm (range, 4.6–11.0 cm). TBF manifested in the form of presence of intratumoral air specks in all seven patients, with oral contrast also seen in two of them. The fistulous tract was directly visualized in one patient, who presented with aneurysmal dilatation of the jejunum (Figure 3). Bowel obstruction was present in 4/41 patients, with volvulus visualized in 1 of them (Figure 4). All of the patients with obstruction had an exophytic tumour without an intraluminal component and did not have peritoneal disease at presentation. Two patients had intraperitoneal rupture (confirmed on surgery), and intratumoral haemorrhage with haemorrhagic ascites was seen

Figure 1. 43-year-old male presenting with abdominal pain and vomiting. (a) Axial CT demonstrates a heterogeneous solid-cystic exophytic pelvic mass with a calcific speck within (arrow). Note the adjacent dilated fluid-filled bowel loops (arrowhead), suggestive of obstruction. (b–d) The mass was resected and histopathology confirmed it to be a gastrointestinal stromal tumour. Gross pathology image reveals a large mural mass with a fleshy cut surface (b). High power microscopy image (c) shows fascicles of spindle cells with uniform nuclei and pale eosinophilic, fibrillary cytoplasm (haematoxylin and eosin; original magnification $\times 400$). Immunohistochemistry for KIT (d) demonstrated strong, diffuse cytoplasmic staining, confirming the diagnosis (original magnification $\times 400$). (e, f) The patient had multiple ill-defined hepatic metastases at presentation (e) and was started on imatinib. Restaging scan after 6 months of treatment demonstrates response (f), with the metastases becoming smaller, well defined and hypodense, along with the development of calcifications within.

Figure 2. 57-year-old male with neurofibromatosis type I presenting with abdominal pain. Axial CT images show a predominantly exophytic gastrointestinal stromal tumour with tumour–bowel fistula demonstrated by the presence of air and oral contrast within the tumour (arrow in a). Note the intraluminal component of the tumour on the coronal CT image (arrow in b).

in one of them (Figure 5). Apart from the patient with haemorrhagic ascites, four other patients had minimal free fluid in the pelvis at the time of presentation and only one of them developing metastatic disease later on.

Imaging of recurrent/metastatic disease

Local recurrence on follow-up imaging was seen in 7/102 (7%) patients; four of them developing distant metastases as well. Locally recurrent tumours presented as homogeneously or heterogeneously enhancing nodular masses at the site of surgery. In total, 51/102 (50%) patients developed metastatic disease. 27 (26%) patients had metastases at presentation (18 with peritoneal and 12 with hepatic metastases), while the remaining 24 patients developed metastatic disease at a median interval of 20 months (range, 7–84 months). Pathologically proven regional mesenteric nodal metastasis was present in one patient at presentation.

Peritoneum (40/102, 39%) and liver (32/102, 31%) were overall the most common sites of metastases (Table 3). None of the patients had extra-abdominal disease without hepatic and/or peritoneal metastases. Other sites of metastases included subcutaneous or

intramuscular metastases (9/102), lungs (7/102), bones (6/102) and kidneys (1/102).

Peritoneal metastases (40/102) presented as multiple heterogeneously enhancing, discrete peritoneal implants (peritoneal sarcomatosis picture) in 39 patients. Peritoneal nodularity and omental caking similar to peritoneal carcinomatosis was seen in a single patient. Associated ascites was present in five patients. The mean size of the largest peritoneal nodule was 8.9 cm (range, 1.5–29.0 cm). While on treatment, one patient developed TBF whereas another developed spontaneous intratumoral bleed involving these lesions, with fluid–fluid levels seen on imaging.

Hepatic metastases were solitary in three patients and multiple in the remaining 29 patients. They presented as well-defined heterogeneously enhancing lesions with mean tumour size of

Table 2. Imaging features of gastrointestinal stromal tumour at presentation

Characteristic	Number (<i>n</i> = 41)
Well circumscribed <i>vs</i> ill defined	35 <i>vs</i> 6
Smooth/mildly lobulated <i>vs</i> irregular	30 <i>vs</i> 11
Exophytic <i>vs</i> intraluminal	38 <i>vs</i> 3
Homogeneous <i>vs</i> heterogeneous	16 <i>vs</i> 25
Calcifications	9
Complications	13
Tumour–bowel fistula	7
Bowel obstruction	4
Intraperitoneal rupture	2

Figure 3. 59-year-old male with an incidentally palpated abdominal lump during routine check-up. Axial CT image reveals aneurysmally dilated bowel loop (arrows) with the presence of tumour–bowel fistula (arrowhead). The mass was resected and the patient was started on adjuvant imatinib. The patient is disease-free on 5 year follow-up.

Figure 4. 63-year-old female presenting with abdominal pain and vomiting. Coronal CT image shows a predominantly cystic pelvic mass in close association with the bowel loops and the presence of calcific specks within (arrow in a), confirmed to be arising from the ileum at surgery. The patient had small bowel obstruction secondary to the development of volvulus (arrows in b). The patient is on adjuvant imatinib and is disease-free on 2 year follow-up.

5.6 cm (range, 1–25 cm). One of the lesions developed extensive calcification as treatment response when the patient was started on TKIs (Figure 6).

Pulmonary metastases were multiple and bilateral in all the patients, with the mean size being 1.7 cm (range, 0.9–4.3 cm). None of the nodules demonstrated cavitation. Other forms of pulmonary involvement such as lymphangitic spread and consolidation were not seen in any patient. 2/6 patients with bony metastases had a solitary bone lesion, while the remaining four had multiple lesions. The metastases were lytic in three patients and mixed lytic and sclerotic in the other three. Nine patients

had subcutaneous and intramuscular metastases in the form of well-defined hypervascular nodules, with six of them having involvement of the anterior abdominal wall suggestive of tumour seeding. Metastatic adenopathy developed in four patients and included the retroperitoneal, epicardiac, mediastinal and hilar nodal stations. Both the patients with mediastinal and hilar nodal involvement had metastatic pulmonary involvement, whereas the two patients with retroperitoneal and epicardiac nodal involvement had peritoneal disease.

Overall, out of the 102 patients, 8 (8%) had intraperitoneal perforation of the primary tumour as per operative notes and pathology (7 on presentation and one intraoperatively). 7 (87.5%) of these developed metastatic disease, 4 at presentation. These included five patients with peritoneal metastases (three had concurrent hepatic metastases) and two patients with hepatic metastases without peritoneal involvement.

Figure 5. 75-year-old man with abdominal pain and vomiting. Axial CT image demonstrates an ill-defined heterogeneous pelvic mass (arrow) with hyperdense peritoneal fluid, consistent with haemorrhagic ascites. Surgery confirmed intraperitoneal perforation of gastrointestinal stromal tumour.

Histopathological findings

The mean tumour size of all the 102 patients on pathology was 8.5 cm (range, 2–28 cm). It was 9 cm for ileal tumours and 8 cm for jejunal tumours. There was no significant difference in the size of tumours in asymptomatic patients nor in that of patients with complications. On pathological risk stratification, 21 tumours were low risk, 17 were intermediate risk and 64 were high risk. 65 tumours were spindle cell, 36 were mixed spindle cell and epithelioid and a single tumour was purely epithelioid. Tumours that were ill-defined or had irregular margins were all moderate/high risk. Metastases developed in 2/21 (9%) low-risk, 5/17 (29%)

Table 3. Metastatic disease

Metastases	Liver	Peritoneum	Total
At presentation	12 (12%)	18 (18%)	27 (26%)
Overall	32 (31%)	40 (39%)	51 (50%)
Jejunal (64)	23 (36%)	24 (37%)	31 (48%)
Ileal (38)	9 (24%)	16 (42%)	20 (53%)

Figure 6. 62-year-old male with history of resected small bowel gastrointestinal stromal tumour 8 years ago. (a) Restaging axial CT while the patient was on imatinib revealed multiple homogeneously and heterogeneously enhancing peritoneal masses, consistent with peritoneal sarcomatosis. The patient was started on sunitinib. (b) Restaging scan after 2 months shows the development of a tumour-bowel fistula involving one of the peritoneal masses (arrow). The patient remained asymptomatic and treatment was continued.

intermediate-risk and 44/64 (69%) high-risk tumours. All five patients with NF1 had jejunal tumours that were low risk, with two patients having multifocal tumours. Mutational analysis was performed in 32 patients and revealed KIT exon 11 mutations in 16 patients, exon 9 mutations in 14 and exon 13 mutations in two patients. No significant correlation was found between the imaging findings and type of mutation.

Management and final outcome

The primary tumour was resected in all patients. Medical management was with molecular-targeted therapy (MTT) including TKIs and vascular endothelial growth factor inhibitors such as imatinib, sunitinib, regorafenib, sorafenib and pazopanib, along with clinical trials. Metastectomy was performed in patients with low volume hepatic or peritoneal disease (11 patients).

At the time of last follow-up, 54 (53%) patients were alive, 28 (27%) were deceased while the remaining 20 (20%) were lost to follow-up. Out of the 28 patients who expired, 15 had metastases at presentation. Excluding one patient who died owing to post-operative complications, the median survival for the patients was 65 months (range, 22–179 months). The median survival for the 27 patients with metastases at presentation was lower at 57 months (range, 10–115 months), with 40% (15/27) being deceased. 12 patients were asymptomatic at presentation, with four developing metastases and one having expired (8%). Among the 9 patients who had calcifications on CT, 3 (33%) developed metastatic disease and eight are alive with a single death (after 32 months) at the time of last follow-up.

DISCUSSION

SB GISTs are the second most common anatomic localization of GIST and show a mild male preponderance, similar to our study.^{10,20,21} GISTs are usually sporadic, but may be associated with familial syndromes including NF1 (usually SB), Carney triad (gastric GIST, paraganglioma and pulmonary chondroma), Carney–Stratakis syndrome (gastric GIST and paraganglioma) and familial GIST.⁸ We found jejunal tumours (63%) to be more common than ileal tumours, consistent with prior reports.^{10,20} Miettinen *et al.*, in a retrospective clinicopathological study of

906 patients, found 62% of the tumours to involve the jejunum. They described the clinical presentations in 622 patients, out of which 256 patients (42%) had GI bleeding, 185 (30%) presented with acute or chronic abdominal pain while 116 patients (19%) were asymptomatic.¹⁰ We found overall 40/102 (39%) patients to have some form of GI blood loss in the form of melaena, haematochezia or anaemia, 48/102 (47%) to present with acute or chronic abdominal pain and 12/102 (12%) to be asymptomatic. Miettinen *et al.*¹⁰ found the mean tumour size to be 7 cm with ileal tumours tending to be larger than jejunal tumours without reaching statistical significance, similar to our study. Another series including 27 SB GISTs had a mean tumour size of 8.5 cm.²²

SB GISTs were predominantly well circumscribed and smooth/undulating exophytic tumours in our study. They were either homogeneously enhancing or heterogeneous in appearance with hypodense areas within. These findings are similar to the appearance of GISTs elsewhere. Tumour heterogeneity develops owing to the hypervascular tumour outgrowing its blood supply and developing intratumoral necrosis or haemorrhage or owing to development of cystic degeneration.^{12,22,23} Calcifications were seen in 22% cases at presentation. This is much higher than in previous radiology reports, with a prior series of 64 patients of GISTs throughout the GI tract having a single patient with calcification (3%) and another series of 24 patients of gastric and SB GISTs not reporting a single patient with calcification.^{14,22} Miettinen *et al.*¹⁰ reported 10.5% patients with SB GIST to demonstrate calcifications on pathology in their series of 906 patients.

GISTs associated with NF1 reveal certain unique features. SB is the most commonly affected site in patients with NF1. A review of 45 patients of NF1 by Miettinen *et al.*²⁴ showed 34 patients to have dominant SB tumours, 10 to have duodenal tumours and a solitary patient to have a dominant gastric mass along with multiple SB tumours. Jejunum is the most commonly affected site, and multifocal tumours are common (62% in the former study). There is no association between multifocal tumours and aggressive disease. Overall, GISTs associated with NF1 have a comparatively lower MI and a better prognosis. These concur

with our findings. GISTs associated with NF1 did not appear different from sporadic GISTs in our study, consistent with a previous report of six patients.²⁵

CT demonstrated associated complications in one third (32%) of the patients in our series. TBF either developed spontaneously owing to ulceration of the tumour into the subjacent bowel mucosa or subsequently while the patient was treated with MTT and is depicted on CT as the presence of air or oral contrast within the tumour or visualization of a communication with the bowel lumen.^{22,26,27} A previous study of 51 patients with TBF revealed majority of the patients to have GIST (27%), followed by colorectal cancer.²⁷ Aneurysmal dilatation of the bowel without associated obstruction is considered a classic sign of lymphoma, but can be rarely seen in GIST as well, with two similar cases having been reported previously. Tumour cavitation leading to enlargement of the apparent bowel lumen as also the tumour's origin from the myenteric plexus may be responsible for the aneurysmal dilatation.¹⁴ The lack of associated lymphadenopathy and visualization of heterogeneously enhancing hepatic metastases (if present) may help differentiate between the two.^{14,15,28,29} Four patients presented with bowel obstruction in our series. None of them demonstrated intraluminal tumours or peritoneal disease, indicating that the obstruction was not owing to direct luminal narrowing by the tumour or owing to peritoneal involvement. Although the exact mechanism is unknown, associated volvulus was present in one of them. We believe that the origin of GIST from the intestinal pacemaker cells in the myenteric plexus may also be another possible etiological factor for the obstruction.¹⁴ Intraperitoneal rupture is the third complication visualized in our series and may be associated with haemorrhagic ascites.

The differential diagnoses for GIST includes SB adenocarcinoma, SB lymphoma, metastases and carcinoid. Primary SB adenocarcinomas are rare, but most commonly involve the jejunum and are usually annular and cause narrowing of the lumen with associated obstruction, unlike GIST which is exophytic and eccentric. Associated lymphadenopathy is common. SB lymphomas may present as homogeneously enhancing concentric bowel wall thickening or as polypoid intraluminal masses or less commonly as an exophytic mass. Associated bowel obstruction is uncommon. Although they may sometimes be difficult to differentiate from GIST, they are usually associated with bulky adenopathy, which helps differentiate them from the other lesions. Carcinoids are the most common SB tumours, most commonly affecting the ileum. They appear on imaging as a small intraluminal enhancing nodule and show associated mesenteric puckering and desmoplastic reaction owing to metastatic spread, often with associated adenopathy. There may be associated kinking of bowel loops, leading to obstruction/ischaemia. Metastases may be distinguished from the patient's history and visualization of the primary mass.^{14,22,30–32}

Recurrent/metastatic disease developed in half the patients in this study. Peritoneal and hepatic metastases were the most common sites of metastatic disease. We found peritoneal involvement to be more common than hepatic spread both at presentation and

overall. Two earlier studies of 50 and 39 patients each of SB GIST had described hepatic metastases as more common than peritoneal involvement, whereas Miettinen et al¹⁰ reported "abdominal" metastases to be more common than liver metastases.^{20,21} Overall however, GISTs have been described to metastasize more commonly to liver than to peritoneum.^{1,12,16} DeMatteo et al¹ studied 200 patients with GIST including 63 with SB GISTs and reported 94 (47%) of them to have metastatic disease, with the liver being involved in 61 and the peritoneum in 20 patients.

7/8 (87.5%) patients who had intraperitoneal rupture of tumour developed metastatic disease. Although it would be logical to expect all these patients to develop peritoneal disease, there were two patients who developed hepatic metastases without peritoneal involvement, indicating that meticulous surgery with peritoneal lavage may indeed successfully remove the peritoneal contamination. The high incidence of extraperitoneal metastases in this group also indicates that perforated tumours tend to be high risk with a high likelihood of developing recurrent disease. Our findings concur with a recent study of 23 patients with ruptured primary GIST, which concluded that perforated GISTs have a high risk of recurrent disease (78%), with 9 patients developing peritoneal metastases, 6 having peritoneal plus hepatic disease and 3 developing only hepatic disease.³³ Metastatic locoregional mesenteric adenopathy was present in only one patient, consistent with prior studies which demonstrate that GIST rarely metastasizes to lymph nodes.^{1,10,14} Distant metastatic adenopathy, however, was observed in four patients, in the setting of advanced disease.

The differential diagnosis for metastatic GIST varies depending on the site of metastatic disease. Differentials for a SB mass along with hepatic metastases include neuroendocrine tumour, adenocarcinoma and metastases (particularly melanoma).^{34,35} On the other hand, the presence of associated peritoneal metastases would include various differentials for peritoneal carcinomatosis including GI malignancies and neuroendocrine tumours (carcinoid), metastatic ovarian cancer, lymphoma and infections such as tuberculosis.^{36,37}

Limitations of our study include the retrospective study design and the referral bias owing to ours being a tertiary cancer centre in that a higher proportion of our patients likely had more aggressive tumours. Statistical analysis was limited owing to the relatively small number of patients with baseline imaging available who developed metastatic disease and died.

In conclusion, SB GISTs were often symptomatic at presentation, high risk on pathology and metastasized to the peritoneum more commonly than the liver in our study. On CT, they were predominantly large, well circumscribed, exophytic tumours with or without cystic/necrotic areas. Complications such as TBF, bowel obstruction and intraperitoneal perforation were visualized on CT at presentation, with patients with perforation demonstrating a high risk of metastatic disease. Exophytic eccentric bowel wall involvement and lack of associated adenopathy are useful indicators to help differentiate GISTs from other SB neoplasms.

REFERENCES

- DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumours: recurrence patterns and prognostic factors for survival. *Ann Surg* 2000; **231**: 51–8. doi: [10.1097/0000658-200001000-00008](https://doi.org/10.1097/0000658-200001000-00008)
- Corless CL, Heinrich MC. Molecular pathology of gastrointestinal stromal sarcomas. *Annu Rev Pathol* 2008; **3**: 557–86. doi: [10.1146/annurev.pathmechdis.3.121806.151538](https://doi.org/10.1146/annurev.pathmechdis.3.121806.151538)
- Ludwig DJ, Traverso LW. Gut stromal tumours and their clinical behavior. *Am J Surg* 1997; **173**: 390–4. doi: [10.1016/S0002-9610\(97\)00064-0](https://doi.org/10.1016/S0002-9610(97)00064-0)
- Kindblom LG, Remotti HE, Aldenborg E, Meis-Kindblom JM. Gastrointestinal pacemaker cell tumour (GIPACT): gastrointestinal stromal tumours show phenotypic characteristics of the interstitial cells of Cajal. *Am J Pathol* 1998; **152**: 1259–69.
- Tirumani SH, Jagannathan JP, Krajewski KM, Shinagare AB, Jacene H, Ramaiya NH. Imatinib and beyond in gastrointestinal stromal tumours: a radiologist's perspective. *AJR Am J Roentgenol* 2013; **201**: 801–10. doi: [10.2214/AJR.12.10003](https://doi.org/10.2214/AJR.12.10003)
- Heinrich MC, Corless CL, Demetri GD, Blanke CD, von Mehren M, Joensuu H, et al. Kinase mutations and imatinib response in patients with metastatic gastrointestinal stromal tumour. *J Clin Oncol* 2003; **21**: 4342–9. doi: [10.1200/JCO.2003.04.190](https://doi.org/10.1200/JCO.2003.04.190)
- Marrari A, Wagner AJ, Hornick JL. Predictors of response to targeted therapies for gastrointestinal stromal tumours. *Arch Pathol Lab Med* 2012; **136**: 483–9. doi: [10.5858/arpa.2011-0082-RA](https://doi.org/10.5858/arpa.2011-0082-RA)
- Grover S, Ashley SW, Raut CP. Small intestine gastrointestinal stromal tumours. *Curr Opin Gastroenterol* 2012; **28**: 113–23. doi: [10.1097/MOG.0b013e32834ec154](https://doi.org/10.1097/MOG.0b013e32834ec154)
- Joensuu H. Risk stratification of patients diagnosed with gastrointestinal stromal tumour. *Hum Pathol* 2008; **39**: 1411–19. doi: [10.1016/j.humpath.2008.06.025](https://doi.org/10.1016/j.humpath.2008.06.025)
- Miettinen M, Makhlof H, Sobin LH, Lasota J. Gastrointestinal stromal tumours of the jejunum and ileum: a clinicopathologic, immunohistochemical, and molecular genetic study of 906 cases before imatinib with long-term follow-up. *Am J Surg Pathol* 2006; **30**: 477–89. doi: [10.1097/0000478-200604000-00008](https://doi.org/10.1097/0000478-200604000-00008)
- Antonescu CR, Sommer G, Sarraf L, Tschernyavsky SJ, Riedel E, Woodruff JM, et al. Association of KIT exon 9 mutations with nongastric primary site and aggressive behavior: KIT mutation analysis and clinical correlates of 120 gastrointestinal stromal tumours. *Clin Cancer Res* 2003; **9**: 3329–37.
- Burkill GJ, Badran M, Al-Muderis O, Meirion Thomas J, Judson IR, Fisher C, et al. Malignant gastrointestinal stromal tumour: distribution, imaging features, and pattern of metastatic spread. *Radiology* 2003; **226**: 527–32. doi: [10.1148/radiol.2262011880](https://doi.org/10.1148/radiol.2262011880)
- King DM. The radiology of gastrointestinal stromal tumours (GIST). *Cancer Imaging* 2005; **5**: 150–6. doi: [10.1102/1470-7330.2005.0109](https://doi.org/10.1102/1470-7330.2005.0109)
- Sandrasegaran K, Rajesh A, Rydberg J, Rushing DA, Akisik FM, Henley JD. Gastrointestinal stromal tumours: clinical, radiologic, and pathologic features. *AJR Am J Roentgenol* 2005; **184**: 803–11. doi: [10.2214/ajr.184.3.01840803](https://doi.org/10.2214/ajr.184.3.01840803)
- Ulusan S, Koc Z, Kayaselcuk F. Gastrointestinal stromal tumours: CT findings. *Br J Radiol* 2008; **81**: 618–23. doi: [10.1259/bjr/90134736](https://doi.org/10.1259/bjr/90134736)
- Cheng JM, Tirumani SH, Shinagare AB, Jagannathan JP, Hornick JL, Raut CP, et al. MDCT of primary, locally recurrent, and metastatic duodenal gastrointestinal stromal tumours (GISTs): a single institution study of 25 patients with review of literature. *Clin Radiol* 2014; **69**: 137–44. doi: [10.1016/j.crad.2013.09.002](https://doi.org/10.1016/j.crad.2013.09.002)
- Koch MR, Jagannathan JP, Shinagare AB, Krajewski KM, Raut CP, Hornick JL, et al. Imaging features of primary anorectal gastrointestinal stromal tumours with clinical and pathologic correlation. *Cancer Imaging* 2013; **12**: 557–65. doi: [10.1102/1470-7330.2012.0048](https://doi.org/10.1102/1470-7330.2012.0048)
- Shinagare AB, Zukotynski KA, Krajewski KM, Jagannathan JP, Butrynski J, Hornick JL, et al. Esophageal gastrointestinal stromal tumour: report of 7 patients. *Cancer Imaging* 2012; **12**: 100–8. doi: [10.1102/1470-7330.2012.0017](https://doi.org/10.1102/1470-7330.2012.0017)
- Agaimy A. Gastrointestinal stromal tumours (GIST) from risk stratification systems to the new TNM proposal: more questions than answers? A review emphasizing the need for a standardized GIST reporting. *Int J Clin Exp Pathol* 2010; **3**: 461–71.
- Crosby JA, Catton CN, Davis A, Couture J, O'Sullivan B, Kandel R, et al. Malignant gastrointestinal stromal tumours of the small intestine: a review of 50 cases from a prospective database. *Ann Surg Oncol* 2001; **8**: 50–9. doi: [10.1007/s10434-001-0050-4](https://doi.org/10.1007/s10434-001-0050-4)
- Brainard JA, Goldblum JR. Stromal tumours of the jejunum and ileum: a clinicopathologic study of 39 cases. *Am J Surg Pathol* 1997; **21**: 407–16. doi: [10.1097/0000478-199704000-00006](https://doi.org/10.1097/0000478-199704000-00006)
- Levy AD, Remotti HE, Thompson WM, Sobin LH, Miettinen M. Anorectal gastrointestinal stromal tumours: CT and MR imaging features with clinical and pathologic correlation. *AJR Am J Roentgenol* 2003; **180**: 1607–12. doi: [10.2214/ajr.180.6.1801607](https://doi.org/10.2214/ajr.180.6.1801607)
- Miettinen M, Lasota J. Gastrointestinal stromal tumours—definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. *Virchows Arch* 2001; **438**: 1–12. doi: [10.1007/s004280000338](https://doi.org/10.1007/s004280000338)
- Miettinen M, Fetsch JF, Sobin LH, Lasota J. Gastrointestinal stromal tumours in patients with neurofibromatosis 1: a clinicopathologic and molecular genetic study of 45 cases. *Am J Surg Pathol* 2006; **30**: 90–6. doi: [10.1097/01.pas.0000176433.81079.bd](https://doi.org/10.1097/01.pas.0000176433.81079.bd)
- Levy AD, Patel N, Abbott RM, Dow N, Miettinen M, Sobin LH. Gastrointestinal stromal tumours in patients with neurofibromatosis: imaging features with clinicopathologic correlation. *AJR Am J Roentgenol* 2004; **183**: 1629–36. doi: [10.2214/ajr.183.6.01831629](https://doi.org/10.2214/ajr.183.6.01831629)
- Tirumani SH, Baez JC, Jagannathan JP, Shinagare AB, Ramaiya NH. Tumour-bowel fistula: what radiologists should know. *Abdom Imaging* 2013; **38**: 1014–23. doi: [10.1007/s00261-013-9987-6](https://doi.org/10.1007/s00261-013-9987-6)
- Tirumani SH, Shinagare AB, Jagannathan JP, Krajewski KM, Ramaiya NH. Multidetector-row CT of tumour-bowel fistula: experience at a tertiary cancer centre. *Clin Radiol* 2014; **69**: e100–7. doi: [10.1016/j.crad.2013.09.020](https://doi.org/10.1016/j.crad.2013.09.020)
- Balthazar EJ, Noordhoorn M, Megibow AJ, Gordon RB. CT of small-bowel lymphoma in immunocompetent patients and patients with AIDS: comparison of findings. *AJR Am J Roentgenol* 1997; **168**: 675–80. doi: [10.2214/ajr.168.3.9057513](https://doi.org/10.2214/ajr.168.3.9057513)
- Engin G, Korman U. Gastrointestinal lymphoma: a spectrum of fluoroscopic and CT findings. *Diagn Interv Radiol* 2011; **17**: 255–65. doi: [10.4261/1305-3825.DIR.3332-10.3](https://doi.org/10.4261/1305-3825.DIR.3332-10.3)
- Buckley JA, Fishman EK. CT evaluation of small bowel neoplasms: spectrum of disease. *Radiographics* 1998; **18**: 379–92. doi: [10.1148/radiographics.18.2.9536485](https://doi.org/10.1148/radiographics.18.2.9536485)
- Horton KM, Fishman EK. Multidetector-row computed tomography and 3-dimensional

- computed tomography imaging of small bowel neoplasms: current concept in diagnosis. *J Comput Assist Tomogr* 2004; **28**: 106–16. doi: [10.1097/00004728-200401000-00019](https://doi.org/10.1097/00004728-200401000-00019)
32. McLaughlin PD, Maher MM. Primary malignant diseases of the small intestine. *AJR Am J Roentgenol* 2013; **201**: W9–14. doi: [10.2214/AJR.12.8492](https://doi.org/10.2214/AJR.12.8492)
 33. Hohenberger P, Ronellenfitsch U, Oladeji O, Pink D, Ströbel P, Wardelmann E, et al. Pattern of recurrence in patients with ruptured primary gastrointestinal stromal tumour. *Br J Surg* 2010; **97**: 1854–9. doi: [10.1002/bjs.7222](https://doi.org/10.1002/bjs.7222)
 34. Danet IM, Semelka RC, Leonardou P, Braga L, Vaidean G, Woosley JT, et al. Spectrum of MRI appearances of untreated metastases of the liver. *AJR Am J Roentgenol* 2003; **181**: 809–17. doi: [10.2214/ajr.181.3.1810809](https://doi.org/10.2214/ajr.181.3.1810809)
 35. Namasivayam S, Martin DR, Saini S. Imaging of liver metastases: MRI. *Cancer Imaging* 2007; **7**: 2–9. doi: [10.1102/1470-7330.2007.0002](https://doi.org/10.1102/1470-7330.2007.0002)
 36. Levy AD, Arnaiz J, Shaw JC, Sobin LH. From the archives of the AFIP: primary peritoneal tumours: imaging features with pathologic correlation. *Radiographics* 2008; **28**: 583–607; quiz 21–2.
 37. Levy AD, Shaw JC, Sobin LH. Secondary tumours and tumourlike lesions of the peritoneal cavity: imaging features with pathologic correlation. *Radiographics* 2009; **29**: 347–73. doi: [10.1148/rgr.292085189](https://doi.org/10.1148/rgr.292085189)