
PICTORIAL ESSAY

Gastrointestinal Stromal Tumours of the Small Bowel — Computed Tomography Appearance, Angiographic Features, and Potential Pitfalls in Digital Subtraction Angiography

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ABSTRACT

Gastrointestinal stromal tumours are neoplasms that were formerly misnamed as smooth muscle tumours of the gastrointestinal tract (leiomyomas and leiomyosarcomas). The diagnosis and localisation of these tumours as a cause of bleeding from the small bowel is often difficult. This article reviews the characteristics of gastrointestinal stromal tumours, with emphasis on their computed tomography appearance and angiographic features, as well as the potential pitfalls in digital subtraction angiography.

Key Words: Angiography, digital subtraction, Computed tomography, Gastrointestinal hemorrhage, Gastrointestinal neoplasms, Intestine, small

INTRODUCTION

Gastrointestinal stromal tumours (GISTs) of the small bowel, although uncommon, often create diagnostic problems for clinicians, radiologists, and pathologists. These neoplasms are usually diagnosed after a prolonged delay, preceded by a number of negative investigations. Because of their concealed nature, GISTs frequently result in significant morbidity and mortality before the correct diagnosis is made. Early diagnosis requires a high index of suspicion and dedicated investigations; more liberal use of CT and angiographic examination can contribute significantly in this respect.

PATHOGENESIS

The pathology of GIST has been the source of much confusion and controversy during the past 2 decades. Formerly described as smooth muscle tumours of the gastrointestinal tract, GISTs were recently renamed to take into account the lack of unequivocal evidence of differentiation along the smooth muscle line.¹ These

unique neoplasms are mesenchymal tumours of the gastrointestinal tract composed of spindled and/or epithelioid stromal cells that are neither mature Schwann cells nor smooth muscle cells (i.e. they exhibit neither a complete Schwannian nor myoid immunophenotype).² Gastrointestinal stromal tumours are immunophenotypically vimentin-, Kit-, and/or CD34-positive.³ Of late, there has been increasing evidence to suggest that these tumours may originate from, or differentiate towards, interstitial cells of Cajal. The latter form a complex network within the gut wall where they function as a pacemaker system for peristalsis; hence the names of interstitial cell of Cajal tumours or gastrointestinal pacemaker cell tumours have been put forward for GISTs.³⁻⁷ The occurrence of GISTs outside the gastrointestinal tract (i.e. in the mesentery, omentum, and retroperitoneum) has led to the idea that they may originate from multipotential stem cells that can differentiate into Cajal cells. Tumourigenesis could be related to 'gain of function' mutation of the c-Kit proto-oncogene located in chromosome 4q 11-21, which encodes a type III tyrosine kinase receptor for stem cell factor/growth factor.⁴

Approximately 10 to 30% of GISTs are malignant.⁸ Factors that have been used to predict metastatic risk or mortality include mitotic count, atypical mitoses, tumour

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necrosis, tumour size, cellularity, tumour grade, Ki-S5 score, tumour infiltration, mutation in the c-Kit gene, p53 overexpression, and gender.⁹⁻¹¹ Nevertheless, many of these lesions are classified as being of indeterminate malignant potential, with a clinical behaviour that is difficult to predict. To confuse the issue further, malignant tumours often contain areas that are histologically benign, whereas benign tumours sometimes contain regions that are histologically malignant.¹² Malignant lesions tend to metastasise to peritoneal surfaces, the liver, and the lungs.¹ Approximately 3% of GISTs are multiple.^{13,14}

CLINICAL FEATURES

Gastrointestinal stromal tumours are usually difficult to clinically diagnose. They can occur at any age, but are distinctly unusual in children and teenagers. The peak frequency is between the fifth and seventh decades of life. The signs and symptoms of GISTs are often vague and non-specific. They include abdominal pain, occult gastrointestinal bleeding with anaemia, melaena, obstructive symptoms, palpable abdominal mass, and weight loss. Gastrointestinal stromal tumours can sometimes present acutely due to massive gastrointestinal bleeding, perforation, and intussusception. Asymptomatic tumours found incidentally during laparotomy had an average size of 1.5 cm, while symptomatic tumours had an average size of 6 cm.¹⁵ In their report of 45 cases and review of the literature, Bruneton et al found no significant differences in the clinical presentation of benign and malignant tumours, except that a palpable mass was encountered in nearly half of the malignant tumours, presumably due to their large size.¹⁶ Delay in diagnosis was fairly common. In general, many patients have symptoms for more than 6 months before the diagnosis is made.¹⁷

RADIOLOGICAL FEATURES

Plain films of GISTs are usually unrewarding, but occasionally may show calcifications in the form of flecks or dense plaques. Conventional barium studies exhibit a variable (0 to 50%) success rate in the radiological diagnosis of small intestinal tumours. Enteroclysis gives better results, but those tumours that are small and mainly exophytic are difficult to identify in barium studies.¹⁸

Angiography has been shown to be useful in the diagnosis of GISTs with negative barium study results.¹⁹ The angiographic appearance of GISTs is rather typical (Figure 1).^{16,20,21} Almost all lesions are hypervascular masses, with dense homogeneous capillary staining that

is both rapid and fairly prolonged. The majority of lesions have prominent feeding arteries and enlarged draining veins (Figure 2). It is not always possible to differentiate between benign and malignant lesions based on an angiogram, but there is usually a good correlation between angiographic and pathological measurement of tumour size.²⁰ Occasionally, these tumours undergo cystic degeneration or haemorrhage, which presents as an avascular area in the lesions. Due to these angiographic characteristics, GISTs are readily identified by angiogram even if the lesion is as small as 1.5 cm in size. Hypovascular lesions also occur, although they can only be detected from their mass effect on angiogram.¹⁴

Emergency angiography can be performed for critically ill patients with acute, profuse gastrointestinal bleeding. This will not interfere with urgent surgery or other radiological examinations of the abdomen that may follow. Compared with radioisotope study, angiography can be performed quickly, give the exact localisation of the lesion, and suggest possible cause(s) of bleeding. No contrast extravasation is needed for the diagnostic localisation of GISTs because of their characteristic angiographic appearance. In a study by Tillotson et al, 26 of 64 patients with small bowel haemorrhage had no contrast extravasation during angiography,²² but other angiographic findings suggested the source of bleeding. On the other hand, radioisotope study is more



Figure 1. Digital subtraction angiogram of the superior mesenteric artery of a 35-year-old man who presented having passed tarry stools. After admission, he passed 500 mL of fresh melaena and developed hypovolaemic shock. Emergency superior mesenteric arteriography showed a very hypervascular tumour (arrow) in the distal part of the duodenum. An emergency operation confirmed the presence of an 8 cm gastrointestinal stromal tumor in the fourth part of the duodenum.

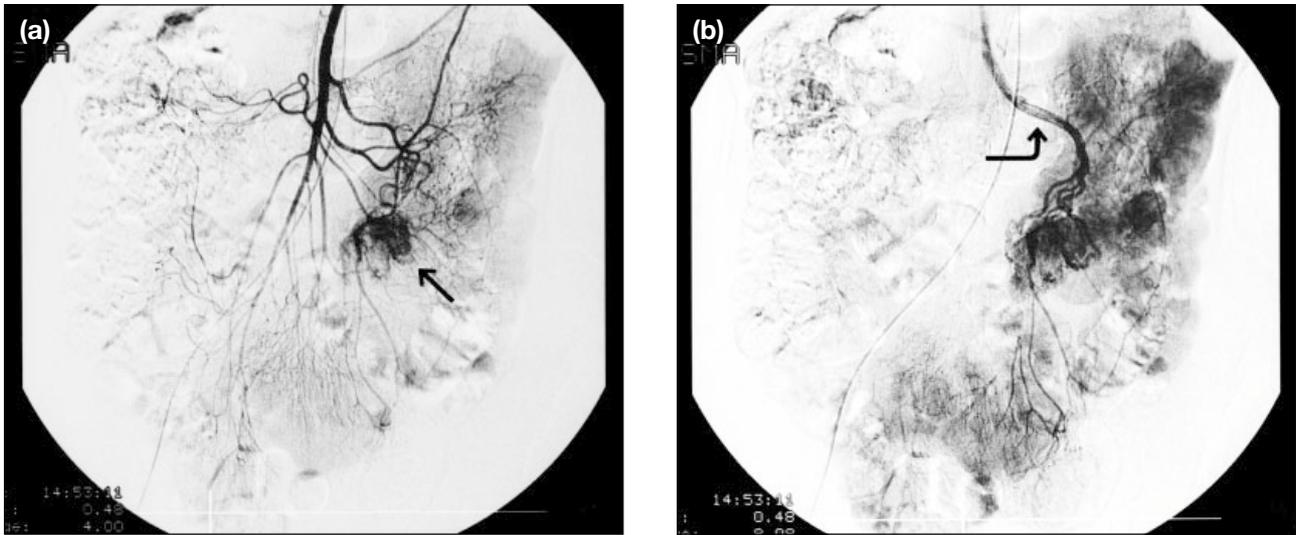


Figure 2. Digital subtraction angiogram of the superior mesenteric artery of a 53-year-old woman admitted with a 3-year history of recurrent gastrointestinal bleeding. Upper gastrointestinal endoscopy, barium meal and follow through, small bowel enema, and colonoscopy were all negative. Superior mesenteric arteriography was performed for an episode of profuse gastrointestinal bleeding and rapid decrease in haemoglobin level. The arterial phase images (a) showed a hypervascular lesion (arrow) in the jejunum. In the early venous phase (b), an enlarged draining vein (curved arrow) was noted. At operation, a 7 cm malignant gastrointestinal stromal tumour was found in the jejunum, 20 cm distal to the duodenojejunal junction.

sensitive in detecting slow rates of arterial bleeding, and can demonstrate venous bleeding not visualised by arteriography.¹⁴ Angiography can facilitate the identification of GISTs at laparotomy, which reduces bowel handling and shortens operating time(s). In addition, angiographic examination offers opportunities for embolisation in lesions not requiring surgery or in patients in too critical a state to withstand emergency surgery. Because of the unique advantages of angiography, some authors even suggest that this technique should be the first-line imaging procedure for evaluating gastrointestinal bleeding in patients with negative upper and lower endoscopy.²⁰

Other lesions of the small bowel with abnormalities on angiography include arteriovenous malformations, neurogenic tumours, and carcinoid tumours. Arteriovenous malformations appear as a tangle of abnormal vessels but, unlike GISTs, they are not associated with a significant mass effect. Carcinoid tumours show a stellate or sunburst vascular pattern, which reflects mesenteric thickening and retraction. Angiography is of limited value in distinguishing neurogenic tumours from GISTs, since both exhibit similar hypervascular patterns.

CT is sometimes used to investigate the lower gastrointestinal tract and, in 73 to 80% of patients, can show a small bowel tumour (if present).²³ It is useful for detecting both hypervascular and hypovascular tumours, or CT may provide evidence of another pathology as the cause of

gastrointestinal symptom(s). GISTs appear as spherical or ovoid masses with early enhancement, which may be uniform or show a central area of diminished attenuation. Small foci of calcification may be detected. Benign lesions are usually uniform in density, have smooth margins, and show uniform enhancement. Malignant lesions, on the other hand, are more commonly lobulated, irregular, infiltrating, inhomogeneous in density, and enhancing with central necrosis.²⁴ The area of necrosis may be so big in large tumours, that the lesion appears as a cystic neoplasm (Figure 3). These large necrotic tumours are more prone to rupture, a rare complication that leads to acute abdomen and haemoperitoneum.^{25,26} Air or air-fluid level might be present, indicating communication with the gut lumen through deep ulceration/invasion (Figure 4). However, interpretation is sometimes difficult if bowel preparation and distension are suboptimal.

POTENTIAL PITFALLS WITH DIGITAL SUBTRACTION ANGIOGRAPHY FOR DIAGNOSIS OF GASTROINTESTINAL STROMAL TUMOURS

Digital subtraction angiography (DSA) is gaining in popularity for the evaluation of the abdominal vasculature. DSA reduces the mean examination time for acute gastrointestinal bleeding by 20%.²⁷ However, there are limitations and pitfalls in using DSA for the evaluation of the lower gastrointestinal tract because of bowel

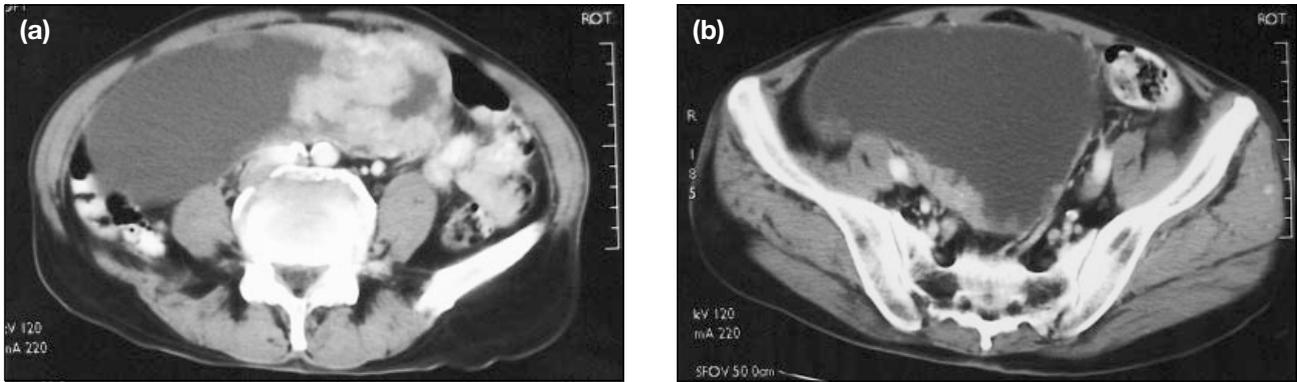


Figure 3. Enhanced axial computed tomography sections of the pelvis in a 71-year-old man with a 3-year history of gastrointestinal bleeding and anaemia. Upper gastrointestinal endoscopy, colonoscopy, and small bowel enema were all negative. A large cystic tumour in the pelvis was found incidentally during transrectal ultrasound examination of the prostate gland for acute retention of urine. At the level of the iliac crests, the tumour had an eccentric enhancing solid component (a). At the mid-pelvic level, the lesion was largely cystic in appearance. An emergency operation was performed for acute abdominal pain due to tumour rupture 2 days after the computed tomography study. This revealed a 20 cm malignant gastrointestinal stromal tumour arising from the proximal jejunum at 20 cm from the duodenojejunal flexure. Pathological examination revealed that the cystic component of the tumour was due to tissue necrosis.

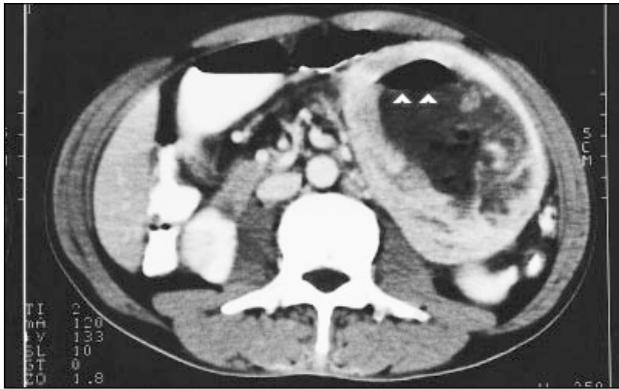


Figure 4. Enhanced axial computed tomography section of the abdomen in a 54-year-old man who complained of passing tarry stools. A large tumour was noted over the left side of the abdomen. Approximately 25 x 15 cm in size, with an air-fluid level (arrowheads) within the lesion. Operation showed a malignant gastrointestinal stromal tumor just distal to the duodenojejunal junction.

motion and misregistration artifact.²⁷ This problem is nicely illustrated in Figure 5 where, based only on interpretation of the DSA images (Figure 5a), the presence of a large elongated tumour at the proximal jejunum might be suspected. Alternatively, it might represent a misregistration artifact. However, in the non-subtracted images, it is clear that the lesion is a small, round, hypervascular tumour. This example highlights the importance of reviewing the non-subtracted images while interpreting the digitally-subtracted sequence. There are a few ways to improve the quality of the DSA images. Breath-holding is a must for patients who can suspend respiration for 20 seconds or more. Nose pinching may be helpful for some patients, especially the elderly. The use of smooth muscle relaxants may lessen the problem, but cannot

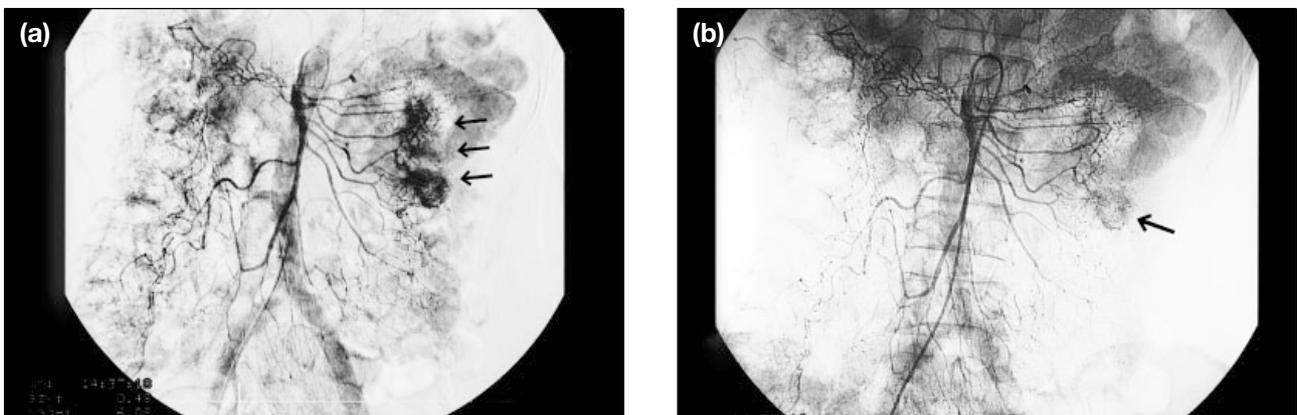


Figure 5. Superior mesenteric arteriogram of a 75-year-old man who first presented in 1996 with melaena and syncope. Upper gastrointestinal endoscopy, colonoscopy, and barium meal and follow through did not reveal the cause of the bleeding. The patient presented again in 1998 after passing tarry stools and a rapid decrease in haemoglobin level. Digital subtraction angiogram of the superior mesenteric artery (a) showed an extensive area of apparent increase in staining (arrows) over the proximal jejunum. Non-subtracted images (b) revealed a 1.5 cm hypervascular nodular lesion (arrow) in the proximal jejunum. Operation confirmed the presence of a gastrointestinal stromal tumour located 25 cm distal to the duodenojejunal junction.

eliminate the misregistration artifact. If the finding is in doubt, performing a selective branch vessel angiogram should be considered.

CONCLUSION

Diagnosis and localisation of GISTs of the small bowel remains challenging; a high index of suspicion is essential. The use of abdominal angiography or CT is important in making an early diagnosis, especially for lesions that are exophytic where other imaging modalities are often negative. Besides suggesting the correct diagnosis, angiography gives the exact location of the tumour and offers an opportunity for intervention. CT is especially useful for hypovascular lesions. Potential pitfalls in using DSA in small bowel angiography include bowel motion and misregistration artifact. Accordingly, concurrent review of the non-subtracted images is important to avoid misinterpretation of the digitally-subtracted images.

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