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## Case Report

# Multifocal gastrointestinal stromal tumor: A case report with CT, surgical, and histopathologic correlation

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## ABSTRACT

Multifocal gastrointestinal stromal tumors (GISTs) are rare conditions that are usually associated with other syndromes or reported in pediatric cases. The sporadic form represents only 11% of GISTs. The imaging features on a contrast-enhanced computed tomography examination, surgery and histopathology of a rare case of a sporadic multifocal small bowel GISTs in an emergency setting are described. This case highlights how GISTs appearances on an imaging computed tomography may vary. Radiologists can have difficulty in defining the point of origin of large lesions. In our case, laparotomy open surgery was mandatory to figuring out the correct diagnosis.

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## Introduction

Gastrointestinal stromal tumors (GISTs) represent rare entities that are made up of a heterogeneous group of mesenchymal tumors that originated from interstitial cells of Cajal or their precursors [1,2]. They can arise anywhere in the gastrointestinal (GI) tract. They account for only 0.1%–3% of all tumors in the GI tract [3]. The stomach is the most common

location followed by the small intestine. The median age at presentation is around 60 years old [1,3]. The most common symptoms during diagnosis are usually chronic bleeding or in an emergency they may be diagnosed with acute abdominal pain. Small bowel GISTs may be asymptomatic and are usually found incidentally on abdominal computed tomography (CT) scans, during endoscopy or surgical procedures for other manifestations. GISTs usually appear as solitary well-circumscribed masses [1,2,4]. Sporadic multifocal GISTs in

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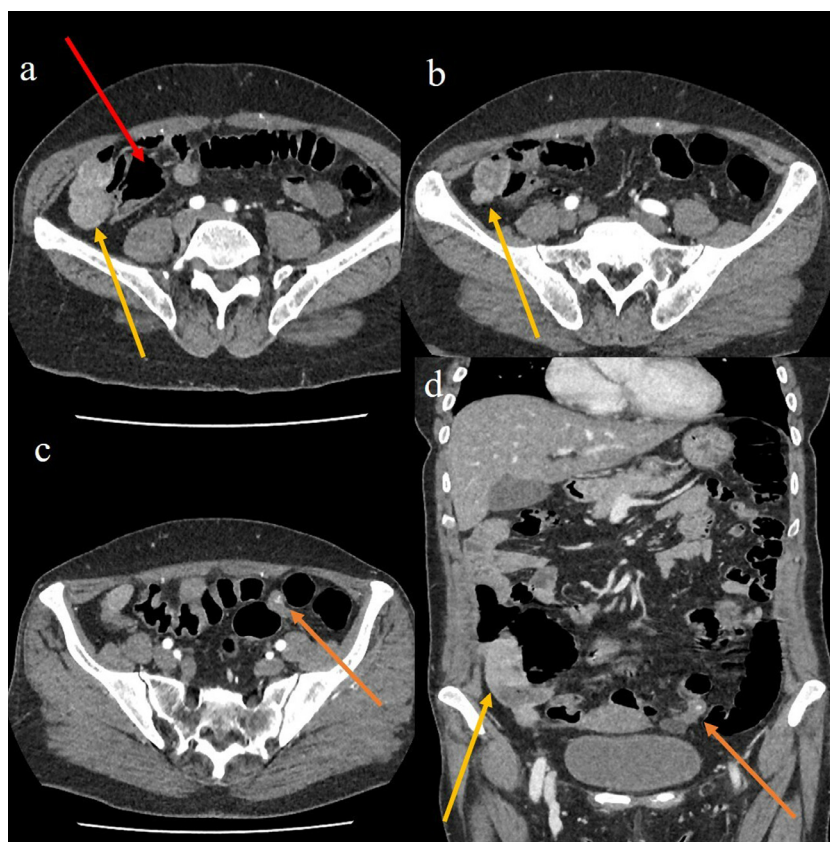
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**Fig. 1** – The multinodular appearance of the multifocal intestinal GISTs (yellow arrow) found on the right iliac fossa (a and b). It was difficult to establish the exact point of origin on the CT. The mass was located near some intestinal loops and the cecum (red arrow). The other nodule with some calcifications and poor enhancement was misinterpreted as a nodule of carcinomatosis (c and d, orange arrow). MPR image on the coronal plane (d): multilobular tumor on the right iliac fossa (yellow arrow) and the other nodule on the left iliac fossa (orange arrow). (Color version of figure is available online.)

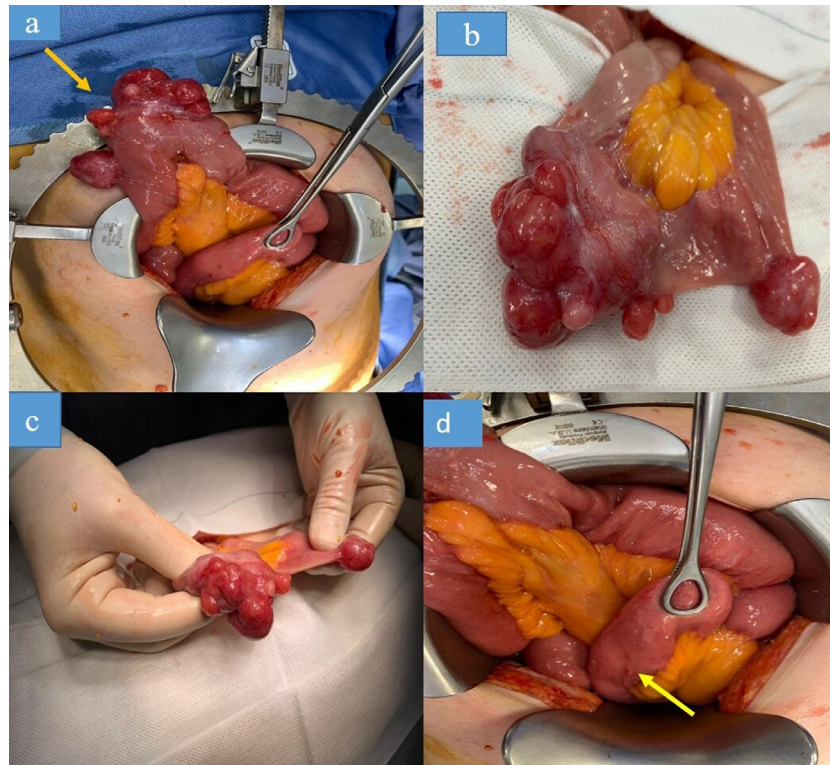
adults represent only 11% of all multifocal diseases [5,6]. The grading of malignancy is based on the assessment of the tumor size, the mitotic index, and the tumor localization [1,7]. GISTs can be a diagnostic challenge in an emergency setting. Surgery remains the treatment of choice for patients with nonmetastatic diseases. Only the histopathology can make the diagnosis conclusive [2].

### Case report

A 56-year-old woman came into the emergency room of our hospital due to having dark tarry stool for 3 days that changed to dark red in the hours prior to her admission. She was accompanied by her relatives that informed us that the patient also had a history of alcohol abuse. She did not report any previous surgical interventions. During the physical examination, she suffered from right abdominal pain at deep palpation. A digital rectal exam revealed cherry red stool mixed with blood clots. The results of laboratory testing performed when the patient was admitted to the Emergency Department

revealed the following values: low hemoglobin value (Hb) of 6 g/dL; mean cell volume of 90.8 fL and normal white blood cell count of 6400/mm<sup>3</sup> with a low platelet count of 126,000/mm<sup>3</sup>. An emergency CT was requested that showed a mass measuring 2.7 × 2.3 × 8 cm with a multinodular appearance and homogeneous enhancement on the right iliac fossa (Fig. 1a and b). It seemed to involve some ileal loops but a cecal origin was not excluded. No abdominal obstruction was seen. During imaging our first suspicion was an intestinal tumor with an exophytic growth. Another differential diagnosis was a cecal adenocarcinoma. A nodule of about 1 × 1.3 cm was also visible on the left iliac fossa and was contiguous to the peritoneal surface of an intestinal loop. It showed calcifications with poor enhancement and it was misinterpreted as possible being carcinomatosis (Fig. 1c and d).

Multiplanar reconstruction was also used to delineate the lesions localizations better (Fig. 1d). The patient was initially treated with 2 blood transfusions. A colonoscopy was done 4 days later but the results were negative. However, an explorative laparotomy was necessary to figure out the diagnosis and it was also used as a therapeutic procedure. A large multinodular mass was found arising at the level of the right

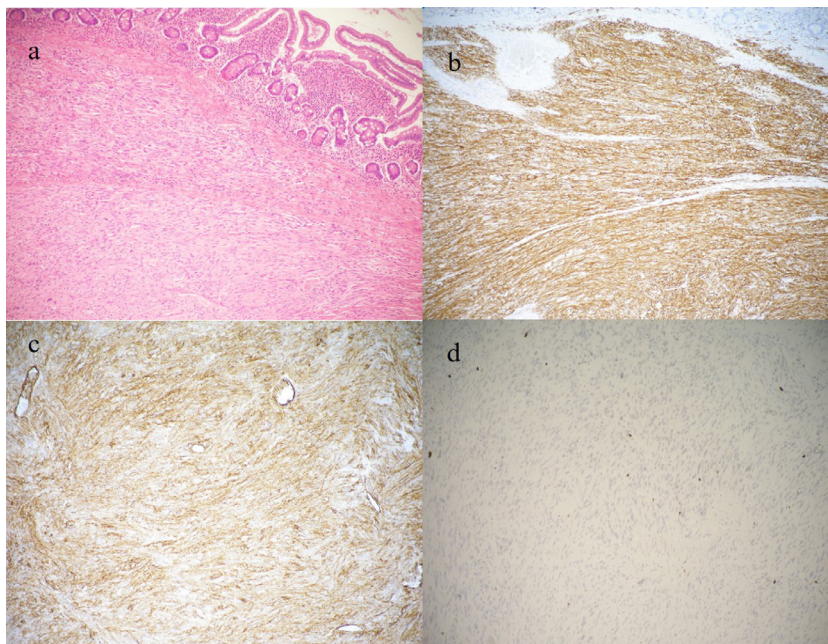


**Fig. 2 – The surgical specimen revealed a multinodular mass with solid, whitish-yellow parenchyma (a-c). Other small lesions of about 1.2 mm were present within 40 cm from the Treitz ligament (d). (Color version of figure is available online.)**

iliac fossa at about 150 cm from the ileocecal valve with a hard-elastic consistency (Fig. 2). It showed an extra luminal and intraluminal growth. A resection of the small intestinal tract, including the large lesion, the corresponding mesentery, and the corresponding vessels, with safety margins of 2 cm was performed. The continuity of the gastrointestinal tract was reinstated with side-to-side anastomoses of the small intestine. At about 100 cm from the ileocecal valve, another nodular lesion was found. It was located on the outer wall of an ileal loop at the level of the left iliac fossa and was compatible with the second lesion shown on the CT. The consistency of the second lesion was identical to that of the first. The lesion was excised with the underlying intestinal wall with safety margins of 1 cm. Other small lesions of about 1.2 mm were present within 40 cm of the Treitz ligament (Fig. 2). Their excisions were not useful and could have resulted in a high rate of postoperative complications. The postoperative course was normal and the patient had 5 generally good postoperative days. The results of the pathologic and histologic examinations of the surgical specimens revealed a spindle-shaped multifocal GIST with some round cells and mitotic activity of less than 5 per 50 high power fields and the surgical margins were intact. The results also showed immunohistochemically stains that were strongly positive for CD117+, CD34+, and S100–, SMA–. The proliferation index (Ki-67) was as low as 5% (Fig. 3). The largest tumor was categorized under intermediate risk category. Her case was followed by oncologist and adjuvant therapy with Imatinib was indicated

## Discussion

GISTs are mesenchymal tumors that arise from the interstitial cells of Cajal, which are the pacemaker cells located in the myenteric plexus of the GI tract. The histopathology of GISTs shows spindle-shaped (most common) or round cells (epithelioid type) or a mixture of both and are commonly stained positive for CD117 and DOG-1(1,2). Identifying KIT (CD117), a tyrosine kinase receptor in the interstitial cells of Cajal, is the key to diagnosing a GIST. A multifocal disease is a poor prognosticator and it usually occurs with specific syndromes like Neurofibromatosis and Carney-Stratakis Syndrome, in familial GISTs and in pediatric cases [5,6]. A sporadic multifocal disease is a rare condition and an underestimated entity. The nature of the tumor multiplicity still needs to be clarified. It may be the result of the metastatic spreading of a single primary GIST or it may have an independent origin. Some authors suggested that multifocal disease lesions are caused by different somatic KIT mutations [5,8]. However, this case shows that GISTs can come in various forms and detecting them can be a diagnostic challenge due to their rarity and the absence of characteristic features [9,10]. Their appearance also makes it difficult to understand the real origin of the tumors [9]. Diagnosis of small bowel GISTs is often made after there are complications such as a hemorrhage, an obstruction, or a perforation and are generally associated with less favorable outcomes than those arising from the stomach. None of the



**Fig. 3 – Microscopically, the tumor originated from the muscularis propria and extended longitudinally in a multilobular form (H&E, x20) (a). The sliced surface of the tumor was characterized by spindled and some epithelioid mixed tumor cells showing less than 5 mitosis for 50 high-power fields (a); 20x objective magnification positive immunostaining for CD34 (b) and CD117 (c), low proliferation index (Ki-67) at 5% (d)**

diagnostic procedures have a 100% certainty for diagnosis [10]. Therefore, a CT is the best modality for an abdominal emergency and a contrast-enhanced CT can help diagnosis a GIST [2,11–13]. Small GISTs usually present as soft-tissue masses with intraluminal growths and as homogeneous enhancements. Larger lesions normally have inhomogeneous density both on unenhanced and contrast-enhanced CT scans, with combined intraluminal/extra luminal growths or with only extra luminal growths. Sometimes no enhancement is seen. Large GISTs may exhibit areas of necrosis and hemorrhage, but cystic degeneration and calcification are rarely found [9,11–13]. Multiplanar reconstructions can aid in determining the exact anatomic origin, but because of their rarity radiologists can underestimate their diagnosis, especially in emergency settings. Nevertheless, in our case it was also complicated to determine the exact point of the largest mass origin and the multifocal tumors were underestimated and misinterpreted on the CT scan. The nodular appearances, as in our case, and calcifications are also uncommon features of GISTs [9]. On a CT GISTs can be differentiated from other intestinal masses such as adenocarcinoma, lymphoma, peritoneal carcinomatosis, metastases, and abscess [9,12]. However, GISTs are usually not associated with lymphadenopathy such as adenocarcinoma and lymphoma and do not cause intestinal obstructions like adenocarcinoma. A contrast-enhanced CT can be helpful in the initial staging and during the follow-up to evaluate the tumor response. A CT enterography has a high accuracy in the evaluation of GISTs. It improves the visualization of the mucosa and the parietal tumor's involvement and differentiates the extra luminal/intraluminal GISTs growths in

an optimal small bowel distension. A CT enterography can detect and characterize occult gastrointestinal bleeding of vascular or neoplastic origin [14]. Contrast-enhanced ultrasound is a useful tool for the detection of liver metastases. Endoscopic ultrasound is a valuable imaging technique for diagnosing small submucosal GISTs and also for allowing biopsy confirmation [11]. GISTs usually need of a multidisciplinary treatment planning. Complete surgical excision in a laparoscopic approach remains the gold standard for localized GIST > 2 cm [15,16]. The aim is to achieve microscopic negative margins to ensure a R0 resection without a tumor rupture [16–18]. A laparoscopic approach is not recommended for large lesions (>5 cm) that may be associated with tumor ruptures and have a very high risk of relapse [19,20]. In our case, surgical treatment with explorative laparotomy was essential to aid in the diagnosis of the large multinodular tumor found on the right iliac fossa at 150 cm from the ileocecal valve and in the diagnosis of the nodule on the left iliac fossa that was misinterpreted as a nodule of carcinomatosis on the CT. A risk classification was proposed by the Armed Forces Institute of Pathology for tumor recurrences and includes 3 clinical factors: the anatomic location (small intestinal GISTs are more aggressive than gastric GISTs of equal size), the tumor size, and the mitotic rate [20]. In the absence of high-risk features, small lesions with less than 2 cm in diameter may be followed up by annual endoscopic ultrasound or imaging and biopsied or excised if they continue to grow [20,21]. Adjuvant therapy with Imatinib is the standard treatment for GISTs with a significant risk of relapse, in cases of unresectable and metastatic disease [21,22]. In our case adjuvant treatment with Imatinib

was retained appropriate by Oncologists due to the multifocal nature of the disease and the residual small tumors detected at laparotomy explorative surgery. Although the lack of clinical importance of these small lesions, they may be also considered as a metastatic spreading of the largest tumor. However, some GISTs are insensitive to Imatinib and mutational analysis is necessary. A multidisciplinary approach to multifocal GISTs diagnosis and treatment is essential for successful outcomes. Nevertheless, adjuvant treatment with Imatinib remains controversial in patients at intermediate risk and also a strict follow-up with imaging may be used for monitoring the residual small lesions [23].

## Conclusion

The characteristics of GISTs on imaging can vary, especially in the multifocal forms that can be underestimated and misinterpreted. Complete surgical resection is still the primary treatment. Small intestine GISTs cause subtle clinical signs and symptoms. Their diagnosis is often delayed until complications develop. Even if complications occur, exact diagnosis is usually very difficult preoperatively. GISTs should be kept in mind when diagnosing patients with unexplained intra-abdominal pain.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.radcr.2019.05.015](https://doi.org/10.1016/j.radcr.2019.05.015).

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