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Case Series

Unusual Presentation of Gastrointestinal Stromal Tumors – A Case Series

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Conflict of interest: Nil

Abstract:

Background: Gastrointestinal stromal tumours (GISTs) represent approximately 1-3% of all gastrointestinal tumours. Gastrointestinal stromal tumours (GISTs) are a type of soft tissue sarcoma that primarily occurs in the gastrointestinal (GI) tract, which includes the stomach and small intestine. These tumours originate from specialized cells called interstitial cells of Cajal, which regulate digestive tract movements. Most GISTs are associated with mutations in the KIT or PDGFRA genes. While some are benign, others can be malignant and potentially spread to other parts of the body. Symptoms of GISTs may include abdominal pain, gastrointestinal bleeding, and a palpable mass. Diagnosis often involves imaging studies, such as CT scans, and a biopsy to confirm the presence of GIST cells. Treatment approaches for GISTs include surgical removal of the tumour, targeted therapy using tyrosine kinase inhibitors like imatinib, and in some cases, chemotherapy. Regular monitoring and multidisciplinary collaboration are crucial for managing GISTs effectively.

Case Series: Here we describe a series of cases of incidentally found GIST and their management. The first patient was a 45-year-old female with an incidentally found GIST in the ilium following an emergency laparotomy. The second patient was a 33-year-old female who presented with pain associated with difficulty in micturition and difficulty in passing stools. h/o generalised weakness, nausea, and fatigue present. h/o blood transfusion present. In the third case 71-year-old male presented pain abdomen dull aching abdominal pain for 2 days associated with difficulty in micturition and difficulty in passing stools

Discussion: Gastrointestinal stromal tumors (GISTs) demand tailored treatment strategies based on individual factors. Primary management involves surgical resection, aiming for complete tumour removal. However, GISTs often harbour mutations, guiding the use of targeted therapies such as imatinib, sunitinib, or regorafenib. These medications, inhibiting specific molecular pathways, play a pivotal role, especially in unresectable or metastatic cases. The choice of therapy is influenced by tumour size, location, and mutation profile. Regular monitoring and collaboration with oncologists are crucial for adapting treatment plans, ensuring optimal outcomes for patients with GISTs.

Introduction

Gastrointestinal stromal tumours (GISTs) represent a unique subset of soft tissue sarcomas originating in the gastrointestinal (GI) tract, specifically from interstitial cells of Cajal, crucial for GI tract movement regulation. Activating mutations in KIT (CD117) or PDGFRA genes result in uncontrolled cell proliferation. Comprising 1-3% of GI tumors. GISTs can occur at any age with a median occurrence at 60 to 65 years. GISTs have a wide variety of clinical presentations depending on the site of involvement. The most common site is the stomach (60-70%), followed by the small intestine (20-30%), colon, rectum (5%), and oesophagus (<5%) [1]. CD117-positive GISTs stem from KIT or PDGFRA mutations. Clinical symptoms range from GI bleeding to abdominal discomfort. The outward growth of many GISTs within the gastrointestinal wall is one of the reasons why several are diagnosed relatively late, either as major abdominal masses or as causes of gastrointestinal bleeding, hemoperitoneum, and perforations. Therefore, as many as one-fourth of GISTs are diagnosed in a clinical emergency, often leading to surgical explorations resulting in the unexpected finding of the disease. One-fourth of GISTs are discovered incidentally during diagnostic assessments (whether an endoscopic procedure, ultrasound, or computed tomography [CT] scan) done for other reasons. The remaining are diagnosed because of symptoms of compression from an abdominal mass, chronic anaemia, fatigue, and the like and complete surgical excision with clear margins remains the primary curative approach. Adjuvant therapy with C-kit inhibitor Imatinib mesylate enhances overall and progression-free survival. The prognosis hinges on tumour size, location, and mitotic activity. The progression of asymptomatic to symptomatic disease remains unclear, suggesting potential indolent GISTs without progression to

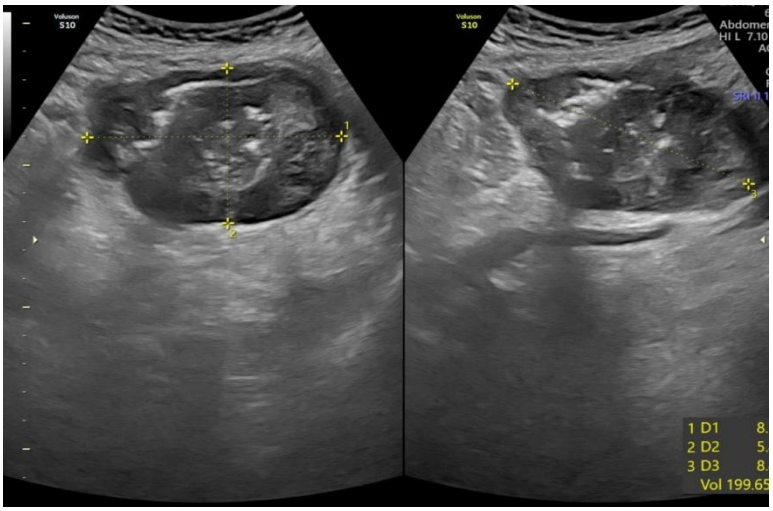
symptomatic stages. Here we describe a series of cases of incidentally found GIST and their management.

Case-1

A 45-year-old woman, GP came to the emergency department with acute pain abdomen for 2 days. ultrasound (US) showed a solid hypoechoic pelvic mass, with irregular margins, vascularized in power Doppler (colour score 3), not fixed to surrounding structures. Because of the site and the proximity to the ovarian vessels it was considered as a right ovarian mass of 11.2*5.4*7.3cm in diameter.

The woman was counselled to perform a hysterectomy and bilateral salpingo-oophorectomy with an intraoperative frozen section on the right adnexa. Thus, the patient underwent surgery.

The explorative laparotomy shows a round-shaped, reddish, easily bleeding mass that originated from one ileal loop displaced in the pelvis. The right ovary was normal and covered by the mass, peritoneal surfaces and organs were free from disease and no enlarged retroperitoneal lymph nodes were detected. intraoperatively surgeons were called and the Patient was submitted to removal of the mass with ileal loop resection and ileal anastomosis without stoma. At the macroscopic examination, the pathological examination revealed an ileal tumour mass measuring 11*6*4.5 cm over the antimesentric border and it is covered by a slough. the cut section shows an ulcer measuring 2*2*1.8cm over the antimesenteric border. Microscopic examination of the small bowel tumour showed circumscribed proliferation of intersecting fascicles of spindle cells with moderate atypia. Mitoses numbered LESS THEN 5 mitotic figures/5mm2 *High Power Field* (HPF); occasional atypical mitotic figures were noted. Immunohistochemistry showed strong and diffuse positivity for DOG-1 and c-kit leading to the diagnosis of GIST. The final diagnosis was GIST (spindle cell type) of the small bowel. appropriate clinical management and follow-up done. A daily treatment with imatinib at the standard dose of 400 mg was then started, with a surveillance program by CT-scan every 4 months. At the last follow-up, the patient is still free of disease



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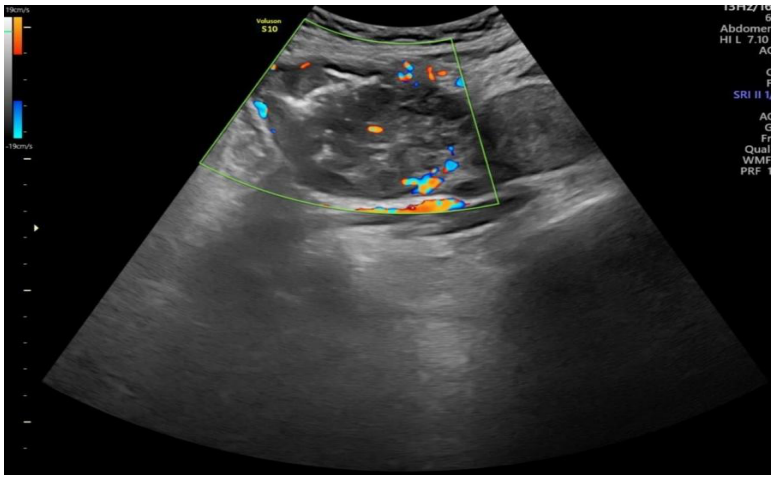

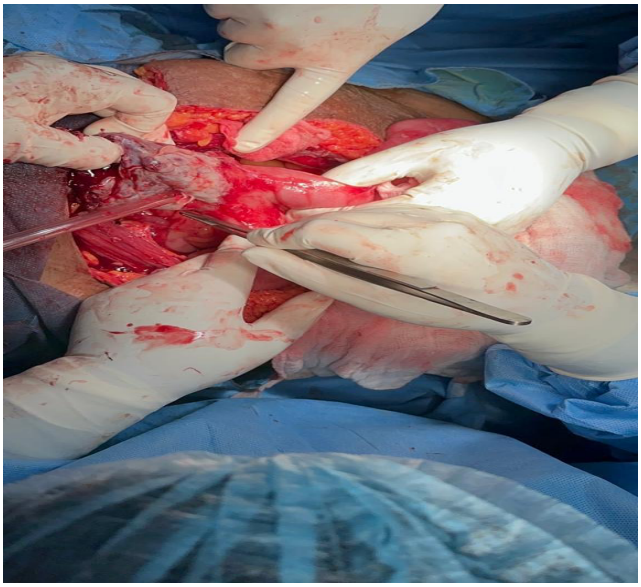

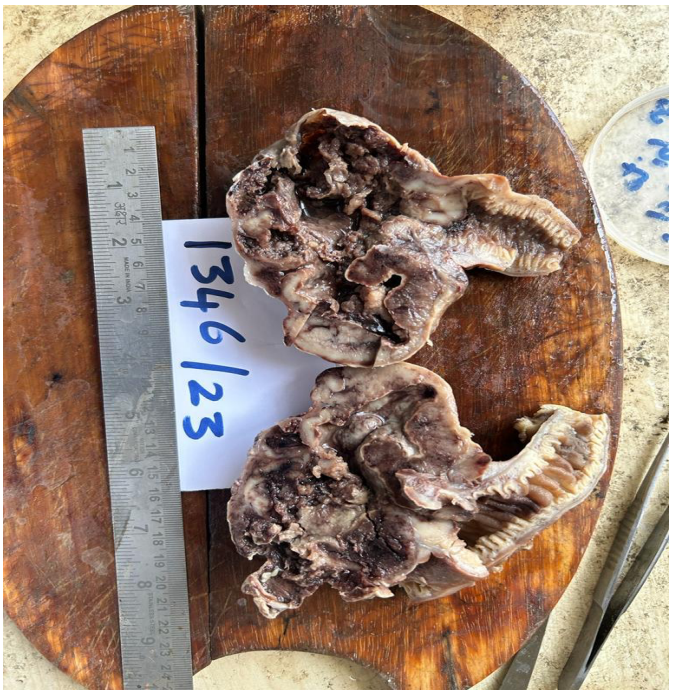
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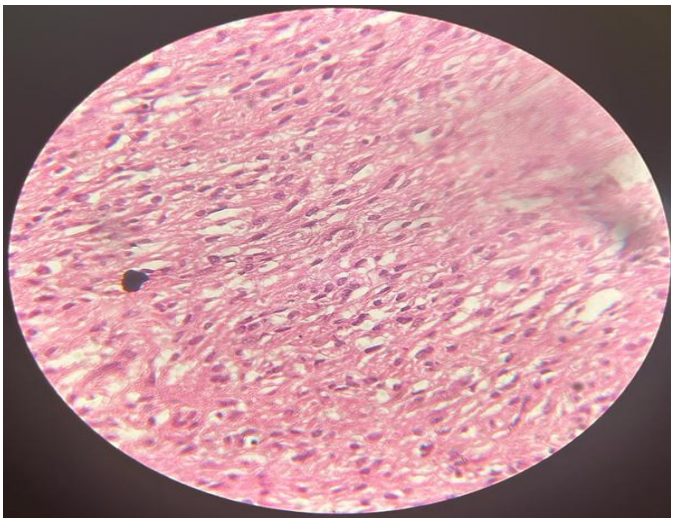
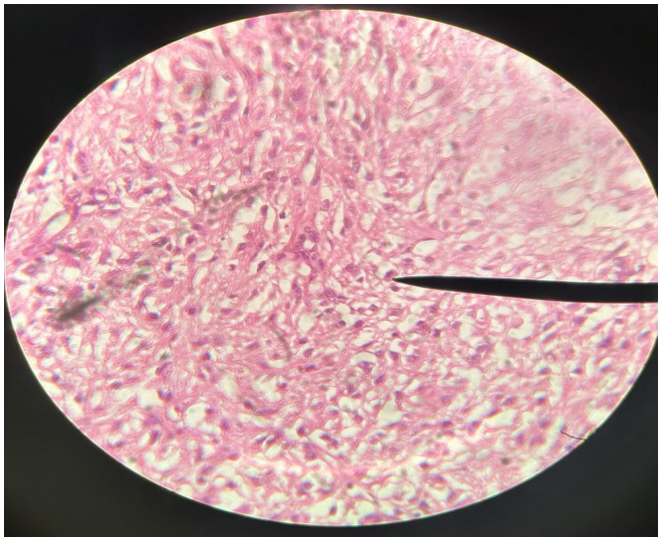




Case 2

33 year year-old nulligravida female presented diffuse dull aching abdominal pain for 3 months associated with mass per abdomen which is insidious in onset and gradually progressive in nature associated with difficulty in micturition and difficulty in passing stools History of generalised weakness, nausea, fatigue present History of blood transfusion present No HISTORY OF other comorbidity Abdomen examination shows mass extending from right lumber to right iliac fossa diffuse tenderness present local rise of temperature present.

On Cect Abdomen and Pelvis

A large fairly well-defined heterodyne intraabdominal mass lesion measures 12 x 18 x 16cm (AP xTR X CC) epicentre in the mesentery of the umbilical region most likely originating from distal ileum segment shows peripheral post-contrast enhancement in the arterial phase and there is centripetal contrast filling on successive delayed phases. Multifocal ill-defined non-enhancing foci are seen within the above mass lesion which represents necrosis.

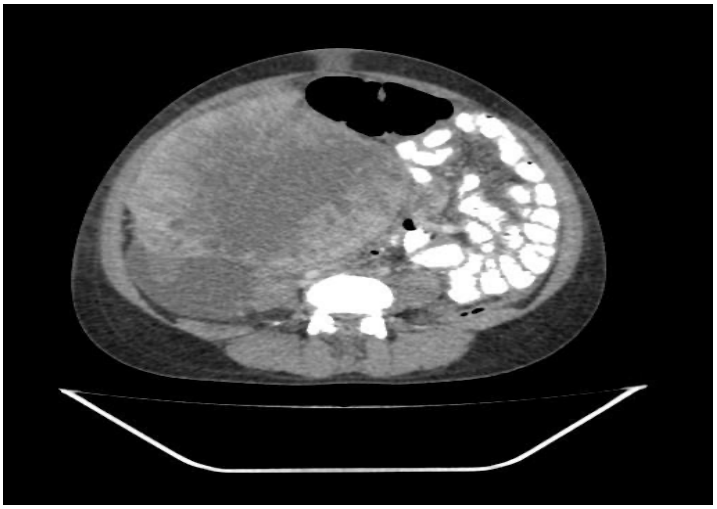
The lesion shows mass effects in the form of displacing small bowel loops towards the left side, ileocecal junction and cecum inferiorly, ascending colon posteriorly and transverse colon superiority.

The lesion shows multiple exophytic components, predominantly along the inferior aspect of the lesion and shows loss of fat plane posterior surface of anterior abdominal walls on the right side.

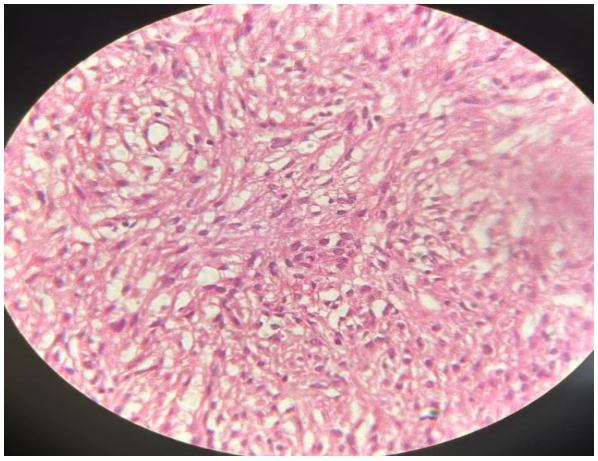
Multiple enhancing omental deposits are seen, the largest measuring 14 x 12 mm at the right lateral aspect of the transverse colon.

Diffuse mesenteric fat stranding and oedema along with peritoneal thickening and omental caking.

The liver is normally sized and shows hypodense focus measures 6.4 x 5.1 x 3.8cm (AP x TR x CC) seen in segment VIll of the right hepatic lobe shows exophytic component, central and centripetal delayed post-contrast enhancement and ill-defined hyperdense focus seen within the lesion which represents hemorrhagic component. Gross ascites noted. Ill-defined hyperdense foci seen with fluid-dependent areas of the pelvic cavity- represent a hemorrhagic component.



Patient HB is optimized before taking to surgery Then explorative laparotomy shows a round-shaped, reddish, easily bleeding mass that originated from a distal ileal loop displaced The lesion shows mass effects in the form of displacing small bowel loops towards the left side. peritoneal surfaces are thickening and omental deposits are seen. a hemorrhagic mass measures 5 x 3.5cm (TR x CC) seen in segment VIII of the right hepatic lobe. The patient was submitted to the removal of the mass with ileal loop resection and ileal anastomosis without a stoma. At the macroscopic examination, the pathological examination revealed an ileal tumour mass measuring cm over 12*18*16 cm and it is covered by slough. the cut section shows an ulcer measuring 3*4cm. Microscopic examination of the small bowel tumour showed circumscribed proliferation of intersecting fascicles of spindle cells with moderate atypia.



Mitoses numbered LESS THEN 5 mitotic figures/5mm2 *High Power Field* (HPF); occasional atypical mitotic figures were noted. Immunohistochemistry showed positivity for DOG-1 and c-kit leading to the diagnosis of GIST. The final diagnosis was GIST (spindle cell type) of the small bowel. appropriate clinical management and follow-up done. A daily treatment with imatinib at the standard dose of 400 mg was then started, with a surveillance program by CT-scan every 4 months. At the last follow-up, the patient is still free of disease

Case-3

A 71-year-old male presented pain abdomen dull aching abdominal pain for 2 days associated with a mass per abdomen which is insidious in onset and gradually progressive in nature associated with difficulty in micturition and difficulty in passing stools

No HISTORY OF other comorbidity

p/a-

- suprapubic region tenderness present
- local rise of temperature present

On Cect Abdomen and Pelvis-

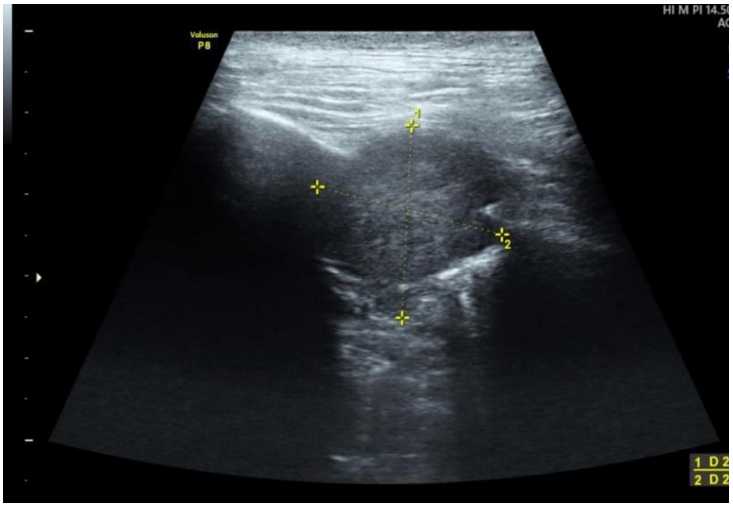
Findings: A well-defined peripherally enhancing solid-cystic lesion measuring - 7.5 x 8.4 × 6.3 cms (AP x TR x CC) is noted in the left lower lumbar region. It shows central non-enhancing fluid attenuation areas with multiple enhancing thin internal septations. The lesion shows lobulated contours. Superiority is abutting the transverse colon with loss of intervening fat planes. Antero-medially, it is abutting the small bowel loops (ejunal loops). Anteriorly, it is abutting the transverse colon with loss of intervening fat planes. Posteriorly. it is abutting the left psoas muscle and the portion of the transverse colon. Mild perilesional fat stranding is noted. The lesion shows continuity with the transverse colon. The lesion is causing significant narrowing of the transverse colon lumen.

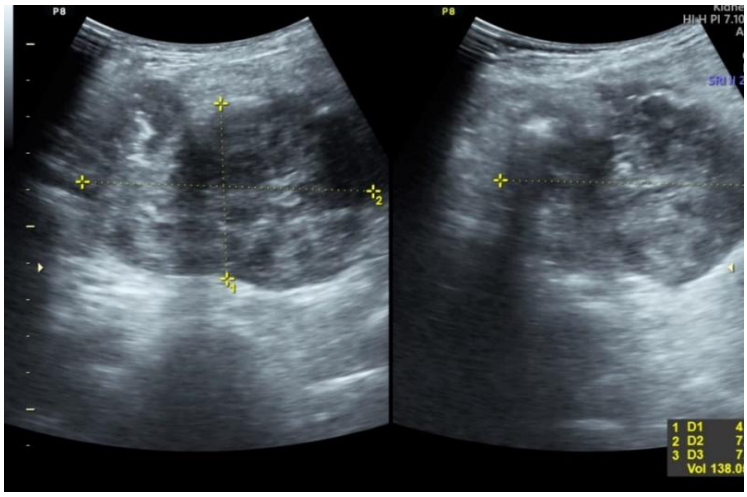
There is acute angulation of the duodenal-jejunal flexure with a rightward deviation of the jejunal loops. Most of the jejunal loops are noted on the right side of the abdomen.

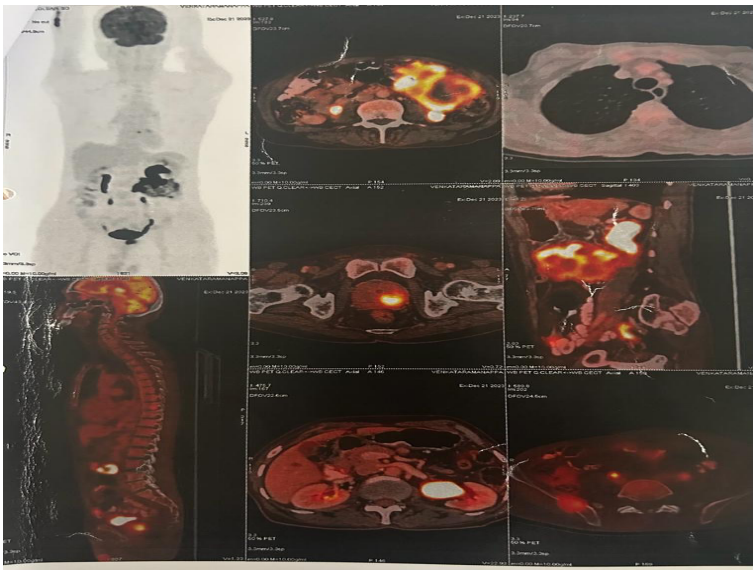
A well-defined enhancing, expansile lytic lesion measuring - 21 x 25 x 27 mm (AP × TR x CC) is noted in the right iliac blade - suggestive of a metastatic lesion.

A small non-enhancing fluid attenuation lesion measuring - 7 × 8 mm (AP xTR) is noted in segment V of the liver. The rest of the liver shows normal attenuation.

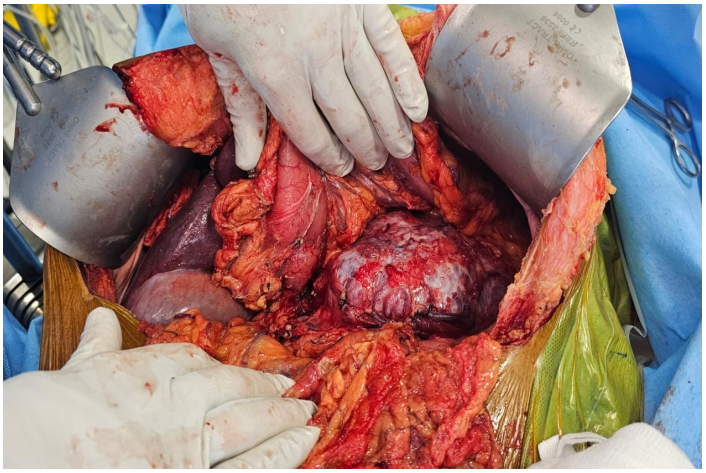
Impression: A well-defined peripherally enhancing solid-cystic lesion in the left lower lumbar region. It shows central non-enhancing fluid attenuation areas with multiple enhancing thin internal septations. The lesion shows lobulated contours. Superiorly, posteriorly and anteriorly, it is abutting the transverse colon with loss of intervening fat planes - features are suggestive of neoplastic aetiology.



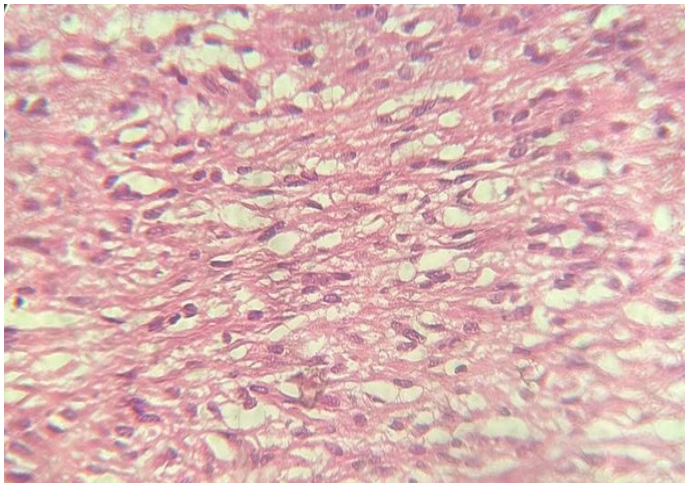




Then explorative laparotomy shows a round-shaped, reddish, easily bleeding mass that originated from the transverse colon displacing small bowel loops towards the right side. peritoneal surfaces are thickening and omental deposits are seen. a hemorrhagic lesion measuring - 7 × 8 mm (AP xTR) is noted in segment V of the liver. The patient was submitted to the removal of the mass with transversal colon resection and anastomosis with a stoma. macroscopic examination, the pathological examination revealed a transverse colon tumour mass measuring cm over 7 x 8 × 6.3 cms (AP x TR x CC) and it is covered by slough. the cut section shows an ulcer measuring 1*2cm



Microscopic examination of the transverse colon tumour showed circumscribed proliferation of intersecting fascicles of spindle cells with moderate atypia. Mitoses numbered LESS THEN 5 mitotic figures/5mm2 *High Power Field* (HPF); occasional atypical mitotic figures were noted.



Immunohistochemistry showed positivity for DOG-1 and c-kit leading to the diagnosis of GIST. The final diagnosis was GIST (spindle cell type) of the transverse colon. appropriate clinical management and follow-up done. A daily treatment with imatinib at the standard dose of 400 mg was then started, with a surveillance program by CT-scan every 4 months. At the last follow-up, the patient is still free of disease

Investigations

	Case1	Case2	Case3
HB (mg/dl)	10	5	9.3
TC	15000	6400	9000
PLATELETS	530000	338000	608000
TOTAL PROTIEN	4.8	6.1	5.0
ALB	2.1	3.0	3.0
A:G RATIO	0.78	0.97	
NA/K/CL	138.4/3.61/97.9	135.1/4.1/105.1	133/4.42/100.7
UREA	27	20	31
CREATININE	0.70	1.11	1.36
CA125		167.5 U/ml	
C-KIT	POSITIVE	POSITIVE	POSITIVE
DOG-1	POSITIVE	POSITIVE	POSITIVE
PREGNENCY	NEGATIVE	NEGATIVE	--------

Discussion

It's vital to remember that not every patient will have the same symptoms, and GISTs can present with a broad range of clinical presentations. Furthermore, certain GISTs may not present any symptoms at all or only cause a few, which makes diagnosis difficult. A precise diagnosis of GIST frequently requires a combination of imaging investigations, endoscopy, and biopsy if the condition is suspected. For those with GISTs, early identification and effective management can greatly improve results [2]

When an abdominal mass is seen on an abdominal contrast-enhanced CT scan or magnetic resonance imaging (MRI), the diagnosis of GIST is frequently considered. Additionally, imaging helps determine the size of the tumour and determine whether metastases are present [3]. To assess whether the mass has affected the luminal region, endoscopy can be used. Nonetheless, endoscopic ultrasonography (EUS) can distinguish between intramural and extramural lesions, describe the mass further by pinpointing its origin layer, and enable the acquisition of an ultrasound-directed fine needle aspiration (FNA) biopsy for a conclusive diagnosis [4].

Surgical removal of the tumour in its entirety is the conventional treatment for localized GISTs; clinically negative lymph nodes are not dissected. Following all guidelines for oncological surgery should be done if a laparoscopic (including robotic) excision is planned. In patients with big tumours, a laparoscopic or robotic approach is explicitly discouraged due to the possibility of tumour rupture, which is linked to an extremely high chance of relapse. endoscopic excisions may be explored for specific presentations (small tumours in the upper or lower GI tract). R0 excision, or an excision whose margins are free of tumour cells at least at the site of origin in the GI tract, is the desired outcome in any scenario. Since there is no official evidence linking R1 surgery to a lower overall survival (OS), patients with low-risk GISTs in unfavourable locales may choose to accept potentially R1 (microscopically positive) margins. It is not advised to perform an R1 excision again if one has already been done. Note that adjuvant treatment should not be determined by the microscopic margin status [5].

As Per GEIS Guidelines for Gastrointestinal Sarcomas (GIST), the following are recommended

(1) Genotype is mandatory for treating advanced/metastatic GIST patients.

(2) Imatinib 400 mg/day is the recommended dose in the first line in advanced/metastatic GIST. Evidence I, A.

(3) In exon 9 mutants, Imatinib 800 mg/day is the recommended dose. Evidence II, A.

(4) In PDGFR/KIT WT GIST is not clear enough that Imatinib should be the standard. In these patients, enrolment in specific clinical trials should be encouraged (ie. Regorafenib for WT GIST; NCT02638766).

(5) In Imatinib-resistant D842V mutant, alternative treatments other than Imatinib could be taken into account (i.e. Dasatinib). (IV, B). But, if available, a clinical trial should be the first option in this subset of patients (ie. the forthcoming trials with the PDGFRa D842V inhibitors Crenolanib or BLU-285 (NCT02508532) [6].

Conclusion

In this article, we have discussed about 3 different cases of gist with each having a presentation different from the other. This emphasizes the importance of excluding another possible differential diagnosis which can mimic other common diseases. rarity of gist and impractical screening procedures prevent getting diagnosed early and awareness of such rare diseases should be inevitable .it often requires a multidisciplinary approach which includes surgeries

targeted therapy and regular follow-up to ensure complete recovery, prolonged survival and minimal reoccurrence rate.

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