European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 9, Issue 4, Winter 2022

ROLE OF CROSS-SECTIONAL IMAGING IN DIAGNOSIS AND MANAGEMENT PLANNING OF GASTROINTESTINAL STROMAL TUMORS

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Abstract :

Background information -Gastrointestinal stromal tumors (GISTs)arise from the interstitial cell of Cajal are the most common mesenchymal neoplasms of the gastrointestinal tract. The imaging features of GISTs have only been described in very limited studies. Hence the present study was designed to evaluate CT/MRI findings of Gastrointestinal stromal tumors and to identify appropriate biopsy options. Further To identify the criteria on cross sectional imaging, which determine operability and non-operability of gastrointestinal stromal tumors.

Methods- 36 clinically suspected GIST and subsequent histopathologically proven cases were selected. Based on imaging findings appropriate biopsy options were considered i.e., percutaneous image guided CT/ ultrasound guided/ Endosonological/Laparoscopic or open biopsies. Lesions which are classified as operable are subjected to surgical excision if other conditions are favorable for surgery. Intraoperative findings were studied for correlation and agreement with findings on cross sectional imaging. Inoperable cases were planned for imatinib therapy and close follow-up.

Results and conclusion - We found that the cross-sectional imaging findings were accurate in predicting the operability of GISTs. In this study cross sectional imaging (CT/MRI) had sensitivity of 95.83%, PPV was 100% and Diagnostic Accuracy was 95.83% for GISTs.Cross sectional imaging findings were very helpful in characterizing the tumor, deciding the appropriate biopsy option and operability and non-operability in cases of GISTs.Overall, Cross sectional imaging played a vital role in deciding the best therapeutic options for the patients.Pre-operative staging is incredibly important to see the operability of tumor. It also helps to search for lymph nodal involvement and metastasis preoperatively.It also helps in post-operative follow-up or follow-up in patients on imatinib to look for therapeutic response and in detection of local recurrence and metastasis.

Keywords -GIST (Gastrointestinal stromal tumors); CT (Computed Tomography); MRI (Magnetic resonance imaging)

ISSN 2515-8260 Volume 9, Issue 4, Winter 2022

Introduction:

Gastrointestinal stromal tumor was once considered obscure tumor entity with poor prognosis, now it's considered as most common mesenchymal origin tumors of GIT, originating from interstitial cells of Cajal. They show strong association with Immunohistochemical staining for KIT (receptor for a tyrosinase kinase growth factor) [1].

Cross sectional imaging plays a vital role in diagnosis of GIST and staging of tumor. Contrast enhanced CT is used for evaluation, staging and to access the treatment response. MRI gives high soft tissue contrast which allows visualizing the tumor extent. MRI allows visualization of central necrosis and hemorrhage. Diffusion weighted MRI also plays a crucial role in assessing tumor response to targeted molecular therapy [2].

Relatively rare tumor not very extensively studied, radiological literature continues to be lacking. GISTs usually present at 6th to 7th decades and are asymptomatic in 10-30%. Clinical features include abdominal pain, abdominal mass, ileus, GI bleeding and weight loss. Gastrointestinal stromal tumors displace adjacent organs and vessels [3]. Direct invasion of adjacent structures is rare and typically seen in advanced disease.

Most of gastrointestinal stromal tumors have absence or low local invasiveness; they reach considerable size without producing symptoms like pain, bleeding or signs of obstruction. Most of the tumors are benign or low-grade malignancy and slowly growing, hence highly amendable for treatment, so accurate diagnosis and pre therapeutic workup is vital [4].

Cross-sectional imaging is helpful at initial presentation, for diagnosis, characterization of type, staging and evaluation of treatment outcome in GIST, which helps in planning patient management and better outcome. It also helps in identifying the appropriate biopsy options [5]. Especially CT plays an important role in detection of malignant gist and in detection of local recurrence and metastasis.

Multidisciplinary approach is important in deciding the management of the patient which involves a team of the radiologists, medical oncologist, medical gastroenterology and operating onco-surgeon. Pre-operative staging is incredibly important to see the operability of tumor [6]. It also helps in searched for lymph nodal involvement and metastasis preoperatively. Cross sectional imaging also helps in follow from cases to look for recurrence post operatively and used for follow up after surgery or post chemotherapy. Limited number of publications on GIST, there is a need for further radiological research. Hence the present study was planned toevaluate cross sectional imaging findings of Gastrointestinal stromal tumors.

Materials and methods :

Study details

The study population included 36 patients of gastrointestinal stromal tumors who presented for CT/ MRI imaging in department of Radio diagnosis were histopathologically confirmed between January 2020 to June 2021.

Type of study: Prospective observational study

Imaging details and analysis:

Triphasic CT was performed on 34 out of 36 patients with Siemens Somatom Definition AS 128 slice Multi-detector CT scanner with 5 mm collimation and a gantry speed of 0.05 sec and pitch of 1.2 sec, 120kvP and 345 effective mAs. First a non-contrast axial cuts were obtained, thereafter contrast was administered (Omnipaque (Iohexol) ---350 mg I/ml), typical doses of 1.5 mg/kg (60-90 ml) through pressure injector (Imaxeon, SW version- 1.5-.12) using smart prep software (RCU manager) and arterial, venous and delayed phase were obtained. The typical scan parameters involved 5 mm and 1 mm slice thickness, coronal, axial and sagittal reconstruction, with 120 MA and 60-80 Kvp. The CT examinations were analyzed on dedicated workstations, this included Aquarius systems (Aquaris Nutrition Edition Ver.4.4 TERARECON Protected by U.S Patent 6,826,297 @1998-2009 TeraRecon, Inc. All rights reserved) or Syngovia (127.0.0.1@ 2009-2016 Siemens Healhcare dedicated workstation. The analysis was performed of the axial cuts (5mm), thin section reconstructions (1 mm). Multiplanar reformats were performed and image analysis was done in multiple planes for the details of the lesion and the involvement of the adjacent structures [7,8].

In a few selected cases (2 out of 36) CEMRI was performed (on Philips 1.5 T MR Systems Achieva Release 3.2.3.5 2018-09-27 SRN:32389 @ KONINKLIJKE PHILIPS ELECTRONIS N.V.2018 All rights reserved) for better delineation of certain lesion, these findings will be described.

Inclusion criteria:

All patients who presented for CT /MR imaging in department of radiology with clinically suspected GIST, imaging features of involvement of GI tract and subsequent histopathologically proven cases.

Exclusion criteria:

1. Cases in whom histopathological confirmation could not be done or in whom it is repeatedly negative or suggestive of other tumors.

2. Cases which were not ready for any further treatment following imaging diagnosis.

3. Patients in whom adequate follow-up is not available.

4. Patient allergic to contrast media.

5. Patients with high creatinine value secondary to renal failure.

Methods of Data Collection

Patients referred to department of radiology with clinically suspected GIST, imaging features of involvement of GI tract and subsequent histopatholoically proven cases after taking written informed consent.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Results :

Age and sex distribution

A total of 36 patients who presented for CT /MR imaging in department of radiology with clinically suspected GIST underwent triphasic CT/ CE MRI scanning and in whom ultimately proved by histopathology were analyzed.Mean age of subjects was 49.19 ± 12.924 years. Majority of subjects were in the age group 41 to 50 years (33.3%).In the study 58.3% were males and 41.7% were females. This included 21 males and 15 female patients. In our study majority of male patients compared to female.100% of them were elective presentation. All patients presented electively, none of the patients presented with acute symptoms or emergency.

Imaging details

In the study most common symptom was Abdominal pain (83.3%), followed by Malena (25%), Anemia (16.7%) and others as shown in above table. Majority of patients presented with more than one symptom. The chief complaints of the patients were pain abdomen, abdominal mass, abdominal distension, symptoms of GI bleed [melena and hematemesis], symptoms of anemia. In only one patient incidental detection was there, patient was being evaluated for varicose veins, on USG abdomen peripancreatic lesion was detected incidentally for which patient underwent CECT abdomen, and diagnosed stomach GIST, which was further proven histopathologically.In the study 80.6% had new onset, 16.7% had recurrent and 2.8% had residual lesion.

In the Stomach, 38.9% were body lesion, 5.6% were fundus lesion and 2.8% was Antropyloric Region lesion. In Small intestine, 5.6% was duodenal lesion, 13.9 % was jejunal lesion and 8.3% was ileal lesion. In the study 2.8% had Ascending colon lesion. 2.8% had Extraintestinal - Mesenteric lesion.In the study out of 6 subjects with recurrent lesion, 33.3% were at ileum, and 16.6% were at Duodenum and Paracecal Region, Ileum and Mesentery of Small Bowel, Jejunum and Peritoneal lesion.

CT/MRI Findings:

In the study size of the lesion was <5 cm in 11.1%, >5cm to ≤10cm in 30.6% and >10 cm in 58.3%.In the study 77.8% had exophytic, 5.6% had intraluminal and 16.7% had combined growth pattern.In the study 94.4% had lobulated, 2.8% had smooth and 2.8% had irregular margins.In the study 100% had arterial phase enhancement. In our study all lesions demonstrated arterial phase enhancement showing arterial feeders of the tumour.In the study 97.2% had heterogeneous and 2.8% had homogeneous enhancement pattern.

Majority of the tumors showed heterogeneous enhancement. As discussed, earlier lesion < 2cm shows homogeneous contrast enhancement, as the size increases heterogeneous attenuation of the tumor increases due to areas of necrosis and hemorrhage, as majority of the cases in our study have size > 5 cm which explains most cases showing heterogeneous attenuation tumor.

Internal characteristics of lesion

In the study 22.2% had calcification, 66.7% had necrosis and 5.6% had Fistulous Communication. In the internal characteristics of most of the lesions showed necrosis which appears as hypodense, non-enhancing areas in post contrast images, it is due to loss of blood supply to the tumour cells as the tumour increases in size. Second most common finding was intralesional calcific foci. Two of the lesions showed fistulous communication. One patient with residual jejunal GIST on imaging had a thickened enterocutaneous fistulous tract, extending from the jejunum, through the mesentery till the abdominal wall. Other case of inoperable stomach GIST showed well-defined, exophytic heterogeneously enhancing lesion arising from the greater curvature of the stomach with evident luminal communication.

In the study 55.6% had local adhesion or invasion to adjacent organs. Local adhesions to adjacent organs or invasion are important predictors of operability of the lesion. It tells about the fat planes between the adjacent structures. If the lesion is seen invading adjacent structures like pancreas, involve multiple bowel loops. The operability of the lesion becomes difficult. In our study majority of patients showed local adhesion or invasion to the adjacent structures.

In the study 33.3% had liver, 8.3% had mesentery, 5.6% had Omentum and 27.8% had lymph node metastasis. Metastasis was seen in 16 patients at presentation. Liver was most common site for metastasis, followed by lymph nodes, mesentery, and omentum.In the study 72.2% underwent ultrasound guided biopsy, 25% Endosonological in gastroenterology and 2.8% by Percutaneous CT guided biopsy. Appropriate biopsy options were decided based on the size, location and vascularity of the lesion, involvement of the adjacent major organs. EUS biopsy is considered in patients presenting with small endoluminal growth pattern, esophageal/ gastric/duodenal GISTs. Large exophytic lesions, peritoneal lesions were sampled using ultrasound guidance. The liver metastatic lesions and the peritoneal deposits were sampled using ultrasound guidance. The tissue sampling of the uncommon, rarer lesions with

significant vascular encasements, adjacent bowel involvements individualized based on the CT appearance.

In case of deep lesions with high suspicion of tumor capsule rupture/ significant bleeding complications or in cases preoperative biopsy is contraindicated were considered for intraoperative biopsy. However, we did not encounter such cases.

In the study 86.1% had spindle, 5.6% had epithelioid, 8.3% had mixed pathology.27.8% had low grade, 38.9% had intermediate grade and 33.3% had high grade.63.9% had <5/50hpf mitoses and 36.1% had >5/50hpf mitoses.100% were positive for Immunohistochemistry.In the study 66.7% were operable and 33.3% were non-operable.After detailed analysis of the imaging features and the histopathological confirmation, the operability was discussed in a multidisciplinary team consisting of radiologists specializing in interventions (Dr Salil Pandey, and Dr Muthu Subramanian), medical oncologist, medical gastroenterology and operating onco-surgeon team, based on the criteria listed above 24 tumors were considered operable and 12 tumors were inoperable.

Table 1 – Distribution of parameters

	Count	**%**
Age		
<30 years	3	8.3%
31 to 40 years	7	19.4%
41 to 50 years	12	33.3%
51 to 60 years	7	19.4%
61 to 70 years	5	13.9%
>70 years	2	5.6%
Gender		
Male	21	58.3%
Female	15	41.7%
Presentation distribution		
Elective	36	100%
Lesion onset Distribution		
New Onset	29	80.6%
Recurrent	6	16.7%
Residual	1	2.8%
Location of Recurrent Lesion		
Duodenum and Para cecal Region	1	16.6%
Ileum	2	33.3%
Ileum and Mesentery of Small Bowel	1	16.6%
Jejunum	1	16.6%
Peritoneal	1	16.6%

Size of Greatest Dimension		
<5 cm	4	11.1%
>5cm to ≤10cm	11	30.6%
>10 cm	21	58.3%
Growth pattern		
Exophytic	28	77.8%
Intraluminal	2	5.6%
Combined	6	16.7%
Type of tumor margin		
Lobulated	34	94.4%
Smooth	1	2.8%
Arterial phase enhancement	36	100.0%
Homogeneous	1	2.8%
Heterogeneous	35	97.2%
Operability of lesion		
Yes	24	66.7%
No	12	33.3%

Intraoperative Finding

For the tumors considered operable, a comparison of intraoperative findings was done with the cross-sectional imaging findings. The CT/MRI findings were accurate in predicting operability in 24 cases and correlated well with intraoperative findings. There was non-correlation noted in 01 case. In this case the peritoneal deposits were not seen on the cross-sectional imaging, which was seen intraoperatively. Overall, the diagnostic accuracy of CT/MRI in predicting operative feasibility in GISTs was found to 95.83%.

In the study type of lesion, necrosis, Local adhesion or invasion to adjacent organs, Metastasis, Grade and No of Mitoses were significant factors associated with Operability of lesion. Among New onset lesion, 75.9% were operable, 16.7% of recurrent lesions were operable, 100% of residual lesions were operable. Among subjects with Necrosis, 54.6% were operable and among subjects without necrosis, 91.7% were operable. Among subjects with Local adhesion or invasion to adjacent organs, 45% were operable and among subjects with Local adhesion or invasion to adjacent organs, 93.8% were operable. Among subjects with metastasis, 31.2% were operable and among subjects without metastasis, 95% wereoperable. Among subjects with low grade, 100% were operable, among subjects with intermediate, 61.5% were operable and high-grade lesions, 41.7% were operable. Among subjects with <5/50hpf mitoses, 78.3% were operable and among subjects with >5/50hpf, 46.2% were operable.

Operability:

As the tumour size increases the heterogeneity and invasiveness of the tumour increases and shows invasion to the adjacent major organs with or without metastasis. As the tumour size increases the operability becomes low.

According to tumour grade based on histopathology, low grade tumours were more operable followed by intermediate grade, in case of high-grade type of tumour the patients had metastatic disease at presentation or invasion of major adjacent organs / vascular structures and majority are considered inoperable.

Lesion with low mitotic count is slow growing and benign in nature, as the number of mitoses increases the invasiveness of the tumour increases, more chances of recurrence and metastasis, which is also seen correlating with our study.In our study majority of patients had low mitosis [< 5 / 50 hpf] were operable, compared to high mitoses.

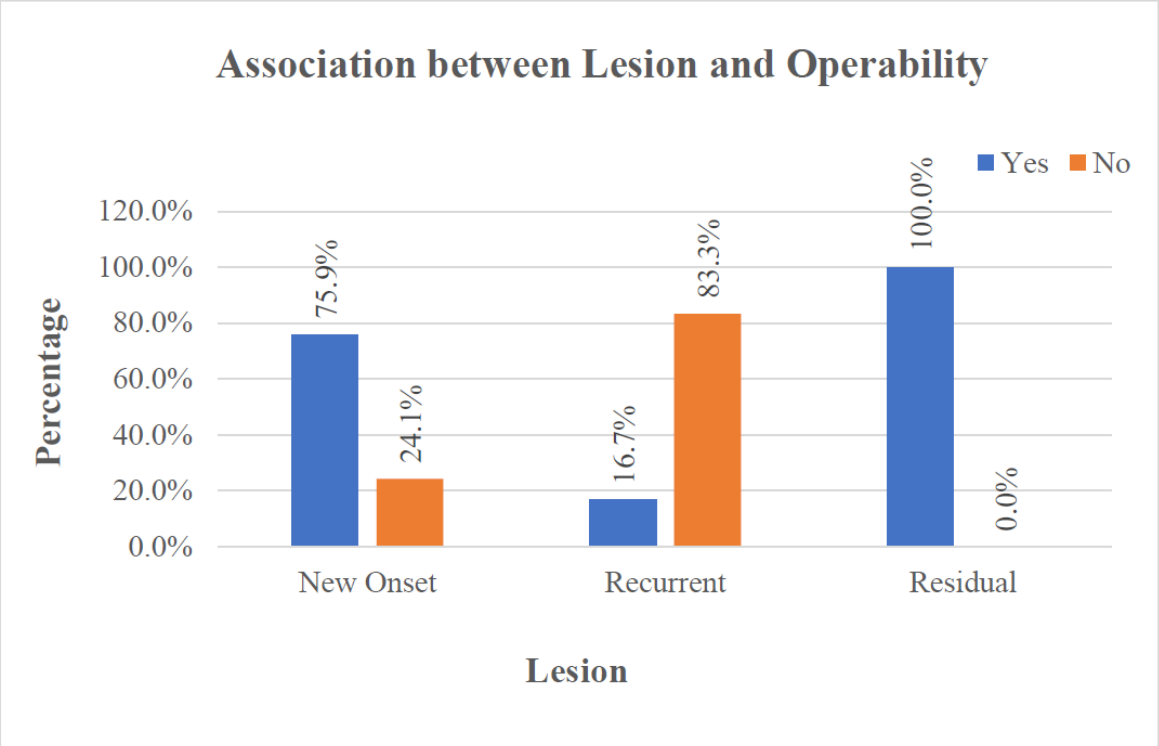

Figure 1 - Bar diagram showing Association between Lesion and Operability

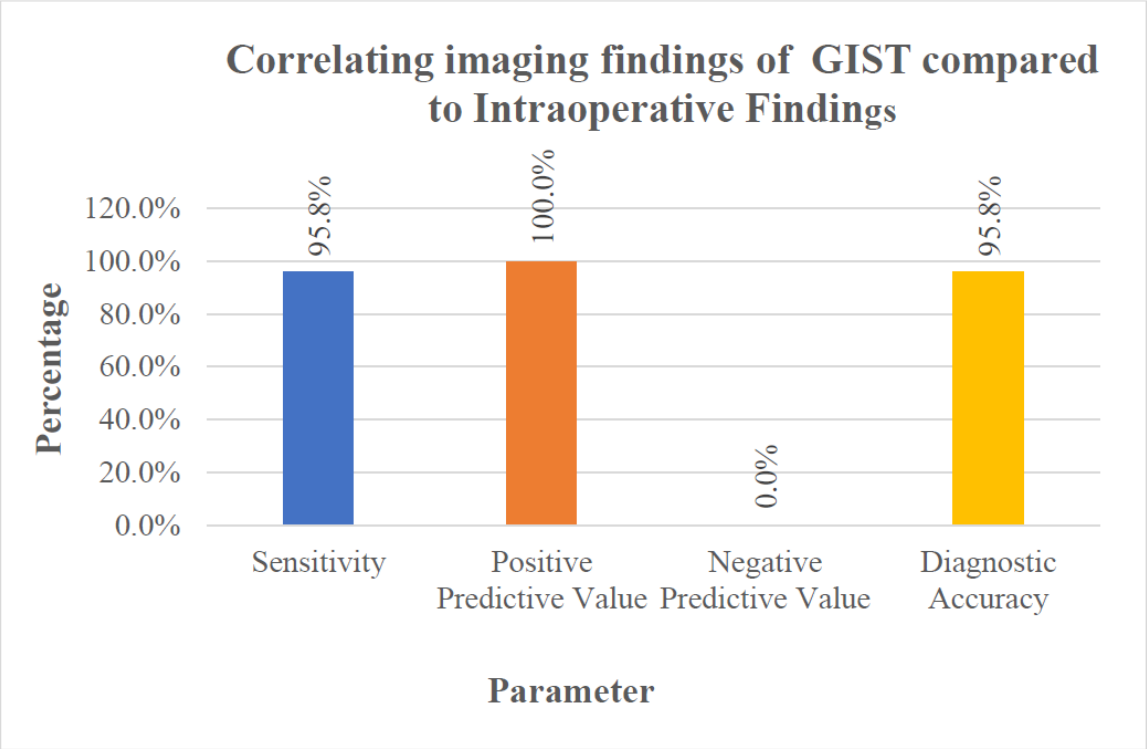

Figure 2 - Bar diagram showing correlation of imaging findings compared to Intraoperative Findings

Discussion :

Our study aimed to evaluate the role of the role of cross-sectional imaging in diagnosis and management planning of GIST.With the study group of 36 patients with GIST underwent Triphasic CT scanning or CE MRI was further confirmed histopathologically.Cross sectional imaging helps to identify appropriate biopsy options- Percutaneous image guided CT/ ultrasound guided/ Endosonological/Laparoscopic or open biopsies. Pre-operative staging is very important to decide the operability of tumor. Cross sectional imaging also helps in look for lymph nodal involvement and metastasis preoperatively.

We observed that Triphasic CT/ CEMRI imaging was very accurate in deciding operability and non-operability in gastrointestinal stromal tumors. It also helps in follow up of cases to look for recurrence post operatively and used for follow up after surgery or post chemotherapy.Our goal of the study to assess the role of cross-sectional imaging in diagnosis and management planning of gastrointestinal stromal tumors was achieved. We found that cross sectional imaging played a very vital role in in deciding the best therapeutic management options for the patients.

Cross sectional imaging also helps in monitoring treatment-related complications. It also helps in the early detection of imatinib-related complications, such as gastrointestinal tract bleeding or intra tumoral bleeding and retention of fluid including ascites pleural effusion and pulmonary edema. Hepatitis, pancreatitis, cholecystitis, and infections are other common toxicities associated with targeted therapies. Radiologists should also be aware of the intestinal complications likeperforation of bowel, formation of fistulas and pneumatosis associated with targeted therapies [9,10].

As there is high incidence of recurrence in GIST in the high-risk patients in the first 3 years following definitive surgery. There is a need intensive image surveillance (at intervals of three to four months) during this period. Interventional radiology has an important role in management of the GISTs, especially in case of imatinib resistant cases. Recent advances include chemoembolization in patients presenting with progressive liver metastases [11].

Also, in patients who present with focal progression of liver disease, Radiofrequency ablation (RFA) is also suggested as a treatment option. In all the methods mentioned interventional radiology has an important role in patient management planning and improve the patient survival. In future we should stratify patients according to the grade of their tumor and other factors like adjacent organ involvement, metastatic disease, and disease progression. MRI can be done instead of CT to reduce the radiation dose [12]. Limitations of our study is small sample size as our study included a sample size of 36 patients. Limited duration of time as we were not able to follow up the patients.

To conclude radiologists should be aware of pros and cons of all imaging modalities in diagnosis of GISTs, with help of multidisciplinary team approach and an appropriate management plan is formulated patient with GISTs.

Conclusion:

Majority of the lesions were operable and underwent open laparotomy and the intraoperative findings correlated excellently with preoperative cross-sectional imaging. The preoperative cross-sectional imaging was also useful in planning the surgical procedure. There was one case in which few additional intraoperative findings were seen in which mesenteric deposits were identified which was not seen on preoperative imaging. In inoperable cases an effective palliative treatment approach is formulated. Once the tumor is decided as non-operable in in multidisciplinary team meetings or multidisciplinary tumor boards (MDTs) along with the relevant clinical profile, patient is referred to medical oncology department for chemotherapy with imatinib.

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ISSN 2515-8260 Volume 9, Issue 4, Winter 2022

SUPPLEMENTARY DATA

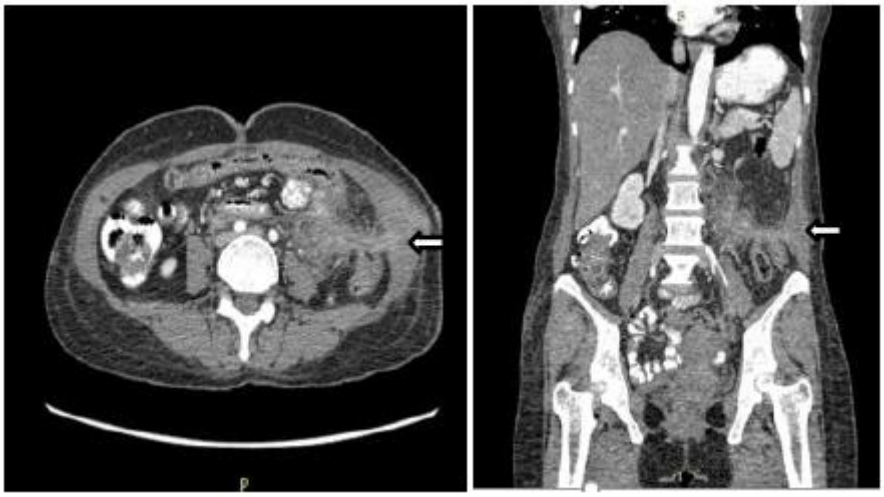
Case 1: 61 Years old male patient came for come for routine health check-up to hospital, on USG abdomen peripancreatic lesion was detected incidentally for which patient has undergone CECT abdomen. CT findings: A large well defined heterogeneously enhancing mass lesion with few non enhancing areas, arising from the lesser curvature of stomach, extending into the lesser sac.

a) CECT axial image showing heterogeneously enhancing mass lesion arising from the lesser curvature of stomach (arrow) b) Microscopy image: Histopathology showing tumor cells composed of spindle cells USG guided biopsy report: Spindle cell type GIST Operability predictively: Operable Intra operative findings- Partial gastrectomy was done. Nodular bulky growth arising from the posterior wall of the stomach.

ISSN 2515-8260 Volume 9, Issue 4, Winter 2022

Case 2

Residual GIST in jejunum with enterocutaneous fistula. 50 years old female patient K/C/O GIST, involving jejunal loops in the left side of abdomen she was operated outside, present to our hospital with symptoms of pain abdomen, with residual lesion and enterocutaneous fistula. CT FINDINGS: Thickened loop of jejunum in the left lumbar and umbilical quadrant, involvement from the DJ flexure, involving adjacent short length with loss of planes with few adjacent loops of jejunum and a focal loss of plane with descending colon. CECT also demonstrates the enterocutaneous fistula.



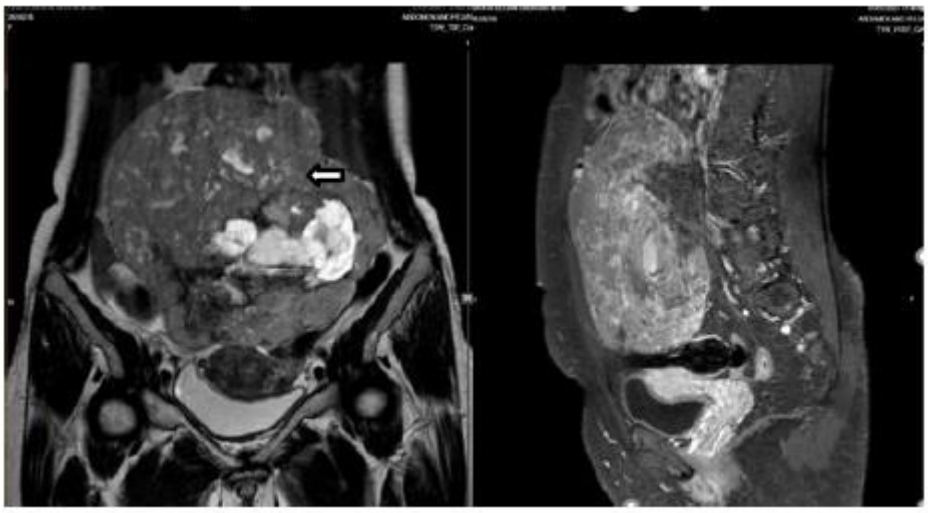
CECT axial image showing thickened loop of jejunum (residual lesion) in the left lumbar region (arrow). B. CECT coronal reformatted image showing thickened enterocutaneous fistulous tract, extending from the jejunum, through the mesentery till the abdominal wall (arrow).

Case 3

Recurrent ileal GIST. A 40 years old female complaints of pain abdomen since 2 months, known case of GIST**.** Postoperative status.

MRI FINDINGS - There is well-defined large multilobulated solid- cystic intraperitoneal lesion with fluid levels and hemorrhage within, in the abdominal cavity involving the umbilical, lumbar and iliac regions on both sides. The lesion shows T1w hypointense with hyperintense areas within (s/o hemorrhage), T2W heterogeneously hyperintense with heterogeneous avid enhancement on post-GAD and restricted diffusion.

ISSN 2515-8260 Volume 9, Issue 4, Winter 2022



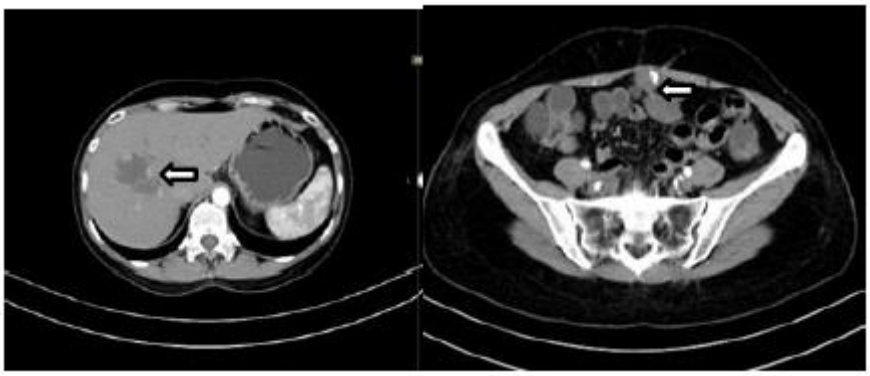
a, b, and c) a. CEMRI T2W coronal images shows, large multilobulated solid- cystic intraperitoneal lesion in the abdominal cavity arising from ileal loops (arrow). B. Post GAD sagittal image showing avid enhancement. C. Image showing gross specimen of the operated recurrent ileal GIST.

Case 4

Recurrent GIST with liver metastasis Clinical details: A 51-year-old female patient is a known case of GIST – Stage IV with liver metastasis. Patient underwent laparotomy and excision in 2015

CT FINDINGS: Ill-defined non- enhancing lesion with specs of calcification noted in the umbilical quadrant adherent to the rectus abdominis muscle. Liver shows irregular elongated hypodense necrotic lesions showing peripheral enhancement**.** USG guided biopsy report: Morphologic features & IHC report are consistent with epithelioid GIST.CD 117, DOG1, CD34 &Vimentin- Immunoreactive, Score 4+ This is a case of recurrent GIST with liver metastasis. Operability predictivity: Inoperable Plan of care- due to inoperability patient is planned for chemotherapy with ImatinibRegular follow up advised.

ISSN 2515-8260 Volume 9, Issue 4, Winter 2022



a. CECT axial image shows irregular hypodense metastatic lesion in liver showing peripheral enhancement (arrow). B. CECT axial image shows Ill-defined recurrent lesion in the umbilical quadrant adherent to the rectus abdominis (arrow).