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Gastrointestinal Stromal Tumour: An Extensive Study Of Clinical And Histological Pathology

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Abstract

Introduction: Gastrointestinal stromal tumours (GISTs) are the predominant type of mesenchymal tumour found in the gastrointestinal tract. Most of these tumours develop in the stomach, with others occurring in the small intestine, colon, rectum, oesophagus, and rarely in the omentum or nearby structures within the abdomen. Stromal tumours make up most of the primary non-epithelial tumours in the stomach.

Objective: To study the clinical, histological, and molecular pathology of GIST.

Materials and Methods: The study of 10 patients who were clinically diagnosed and histologically proven for GIST.

Results: Out of 10 cases, there were 6 (60%) females and 4 (40%) males with the age range spans from 28 to 79 years. The most common symptoms were upper gastrointestinal bleeding (40%), abdominal discomfort (25%), abdominal mass (20%), and asymptomatic incidental discovery (15%). Tumours are mostly located in the stomach, we found two cases of GIST with rare sites (Extra gastrointestinal GIST).

Discussion: While gastric GIST is an uncommon disease, early detection & prompt treatment can potentially save many lives.

Keywords: gastric, gastrointestinal stromal tumour, stomach

Introduction

Gastrointestinal stromal tumor (GIST), originating from Cajal cells or their precursors, is the most common mesenchymal tumor found in the gastrointestinal tract [1]. This tumor can occur anywhere throughout the gastrointestinal tract, from the esophagus to the rectum; however, it predominantly resides in the stomach [2]. Gastrointestinal stromal tumors (GISTs) make up just 0.1% to 3% of all gastrointestinal malignancies, yet they represent 20% of soft tissue sarcomas [3]. These tumors vary widely in their potential for malignancy, ranging from slow growing to aggressive forms, and can occur anywhere along the intestinal tract [4].

GIST primarily arises from an aberrant form of the tyrosine protein kinase, KIT or CD117, which induces uncontrolled cellular proliferation within the gastrointestinal tract. It has an activating mutation in either the kit or platelet derived growth Factor Alpha (PDGTKA). Certain tumors in this category feature mutations within the SDH complex (comprising subunits A, B, C, and D), resulting in negative SDH-B immunohistochemistry testing, irrespective of the mutated SDH subunit [5]. Histopathological examination on surgical specimen and Immunohistochemistry (IHC) can be done to confirm the diagnosis [6]. The aim of this study is to examine instances of GIST exhibiting diverse presentations.

Materials And Methods

After the approval of the Institutional Ethics Committee, a hospital based cross-sectional study of clinically and radiologically diagnosed 10 patients of GIST was carried out in the pathology department, tertiary care hospital, Nagpur, Maharashtra.

The study reviewed medical records to gather patient data including gender, age, symptom onset, primary complaint, history of alcohol consumption and smoking, metastasis, and treatment. Tumor locations were identified using information from endoscopic reports.

All surgically resected specimens underwent comprehensive macroscopic and microscopic examination. The specimens were thoroughly analyzed for size, external appearance, tumor location, extension, consistency, and the presence of hemorrhage and necrosis. Detailed observations were recorded, and representative sections from both the tumor/lesion and adjacent normal tissue were sampled for further analysis. Tissue was processed, paraffin embedded blocks were made, sections were taken, and slides were stained with hematoxylin and eosin stains for studying general histology. Considering the cost of IHC, we made judicious use of IHC markers in feasible cases.

Results

We obtained specimens from 10 patients. Among these, 6 were clinically and radiologically diagnosed with Gastric GIST, while in the remaining 4 cases, one was clinically diagnosed as Meckel's Diverticulum, one as Mesenteric cyst, and the remaining 2 as Cystic masses. (Table 1).

Table 1: Basic characteristics and details of tumour mass.

Case no	Sex	Age (years)	Clinical diagnosis	Tumour location	Size (cm)	Mitotic rate (per 50 HPF)	Histopathological diagnosis
1	Female	40	Meckel's Diverticulum	Loop of small intestine	20 cm	<5	GIST (category 3b)
2	Male	32	Mesenteric cyst	Mesenteric mass	15 cm	<5	GIST- Mixed type (category 3b)
3	Female	28	Cystic mass	Greater curvature of stomach	19 cm	>5	GIST (Category 6b)
4	Female	58	Gastric GIST	Antrum of stomach	7 cm	>5	GIST (Category 6a)
5	Female	79	Cystic mass	Body of stomach	20 cm	<5	GIST (Category 3b)
6	Male	77	Gastric GIST	Greater curvature of stomach	8 cm	<5	GIST (Category 3a)
7	Male	70	Gastric GIST	Cardiac end of stomach	11 cm	<5	GIST (Category 3b)

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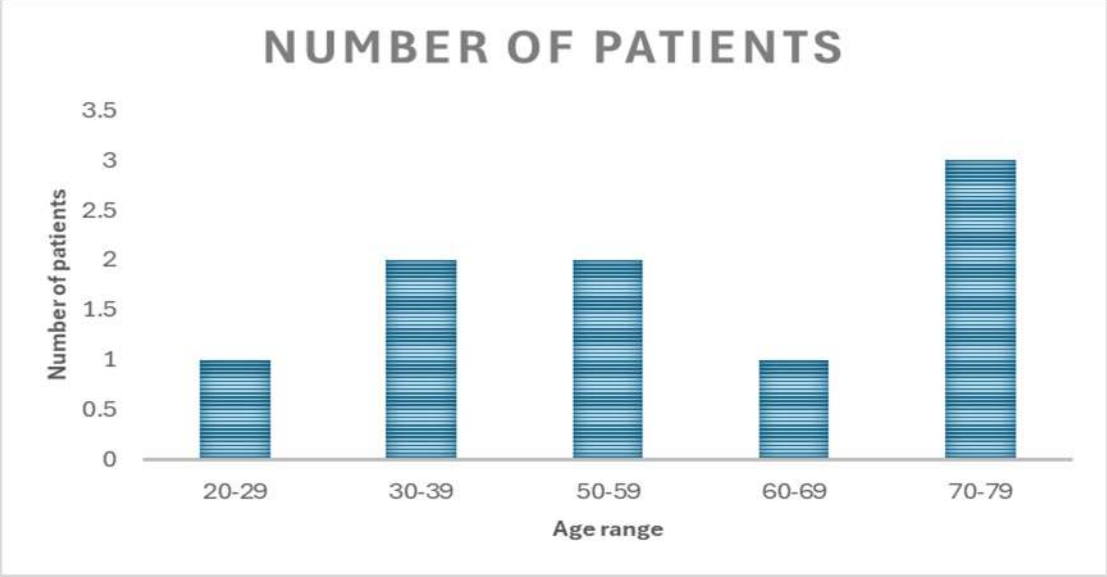
8	Male	33	Gastric GIST	Body of stomach	10 cm	<5	GIST (Category 3a)
9	Female	60	Gastric GIST	Cardiac end of stomach	4 cm	<5	GIST (Category 2)
10	Female	74	Gastric GIST	Growth over fundus	5 cm	<5	GIST (Category 2)

The age range spans from 28 to 79 years, comprising 6 (60%) females and 4 (40%) males. (Figure 1)

Figure 1: Age distribution of the patients



The primary symptoms prompting patients to seek hospital care included upper gastrointestinal bleeding (40%), abdominal discomfort (25%), abdominal mass (20%), and asymptomatic incidental discovery (15%) (Figure 2).

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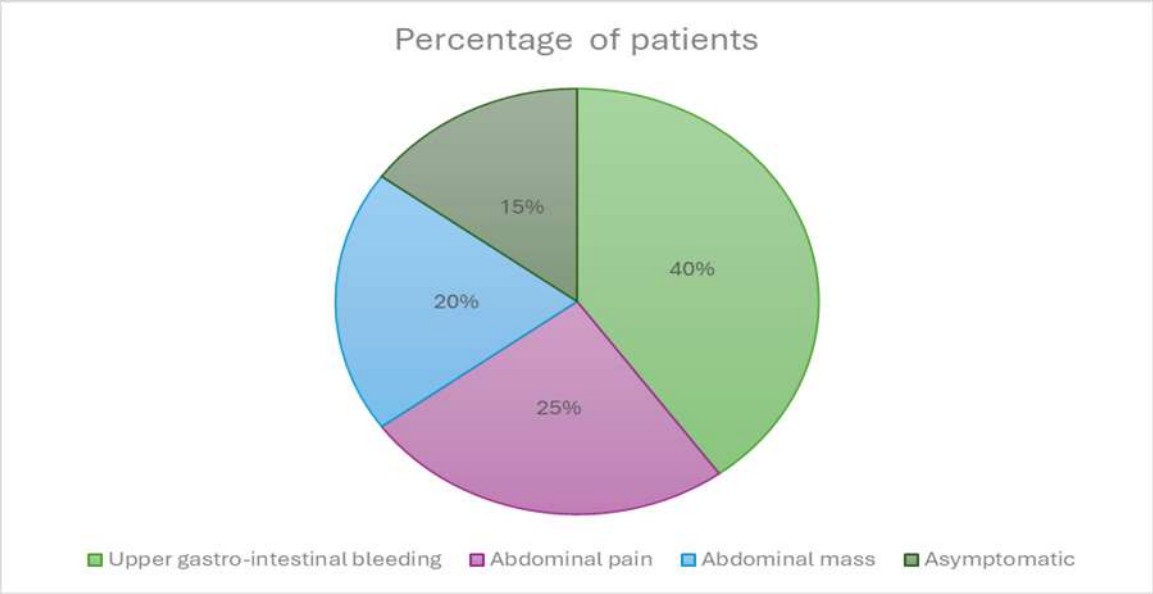
Figure 2: Percentage of patients in each presenting symptom.



Most of the tumours originated in the stomach, while one patient had a tumour located in the small intestine loop, and another presented with a mesenteric mass.

We encountered 3 cases of GISTs with different presentations. The initial case involved chronic abdominal pain, leading to the diagnosis of mesenteric GIST after comprehensive evaluation. Subsequently, surgery was performed electively. In the second case, the patient exhibited symptoms of acute abdomen due to a small bowel GIST causing intraluminal obstruction. In the third case, the patient experienced pain in epigastrium along with recent episodes of hematemesis and melena. Evaluation via upper gastrointestinal endoscopy revealed gastric GIST.

Case 1:

A 40-year-old female arrived at the casualty department presented as acute abdomen, including a history of vomiting and abdominal distension. Upon examination, diffuse abdominal distension with guarding and rigidity was noted, accompanied by the absence of bowel sounds. An abdominal Computed Tomography (CT) scan showed dilated small bowel loops, collapsed large bowel loops, and a mass arising from the small bowel. Emergency laparotomy revealed a mass lesion arising from the jejunum. Clinical impression was Meckel's diverticulum.

We received a specimen of intestinal loop. Grossly, it showed blackish protruding mass of 20 x 5 cm. Cut surface showed irregular, yellowish white, homogenous mass with areas of haemorrhage (Figure 3).

On histopathological examination, it revealed tumour mass composed of sheets of spindle cells with oval elongated nuclei, conspicuous nucleoli, and moderate cytoplasm. There was mild anisonucleosis and pleomorphism. Mitosis was minimal (<5/50 hpf). The features were suggestive of GIST (Figure 4).

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Figure 3: Gross appearance- Protruding mass. Cut surface was homogenous, yellowish white with areas of haemorrhage.

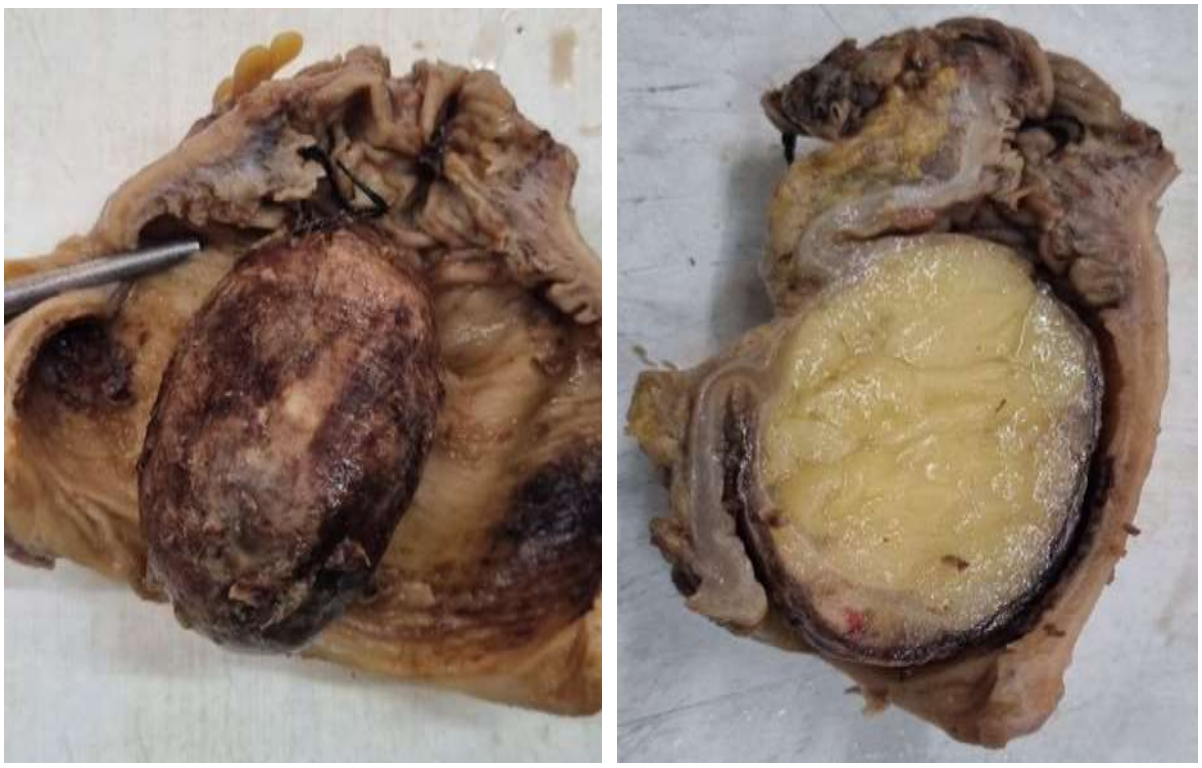
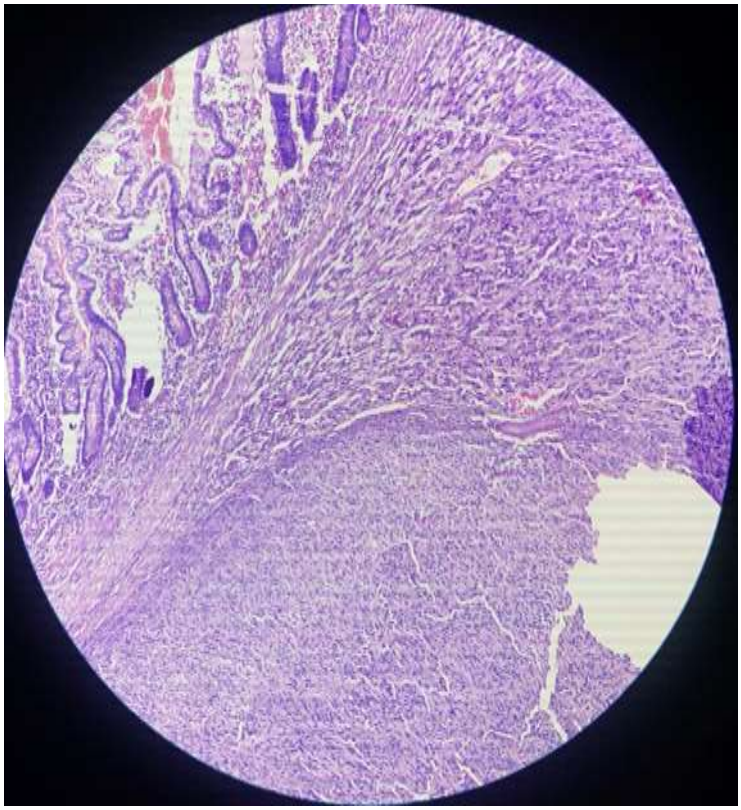


Figure 4: 40X: Sheets of spindle cells with oval elongated nuclei, and moderate cytoplasm showing mild anisonucleosis and pleomorphism



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Case 2:

A 32-year male with a background of chronic abdominal pain underwent basic and radiological investigations. An abdominal ultrasound revealed a solid-cystic growth in the mesenteric region, leading to a clinical diagnosis of mesenteric cyst.

We received a specimen labelled as mesenteric cyst. Grossly, it was encapsulated, irregular, bosselated solid cystic mass measuring 15 x 11 x 8 cm. Cut surface showed irregular, solid, and cystic areas with haemorrhage (Figure 5).

On histopathological examination, it revealed tumour mass composed of cells with spindle and epithelioid morphology. There was mild anisonucleosis and pleomorphism. Mitosis is minimal (<5/50 hpf). Areas of haemorrhage and karyopyknotic debris were also seen, the features were suggestive of GIST- Mixed type (Spindle and Epithelioid) (Figure 6).

Figure 5: Gross appearance- Solid cystic tumour mass with areas of haemorrhage.

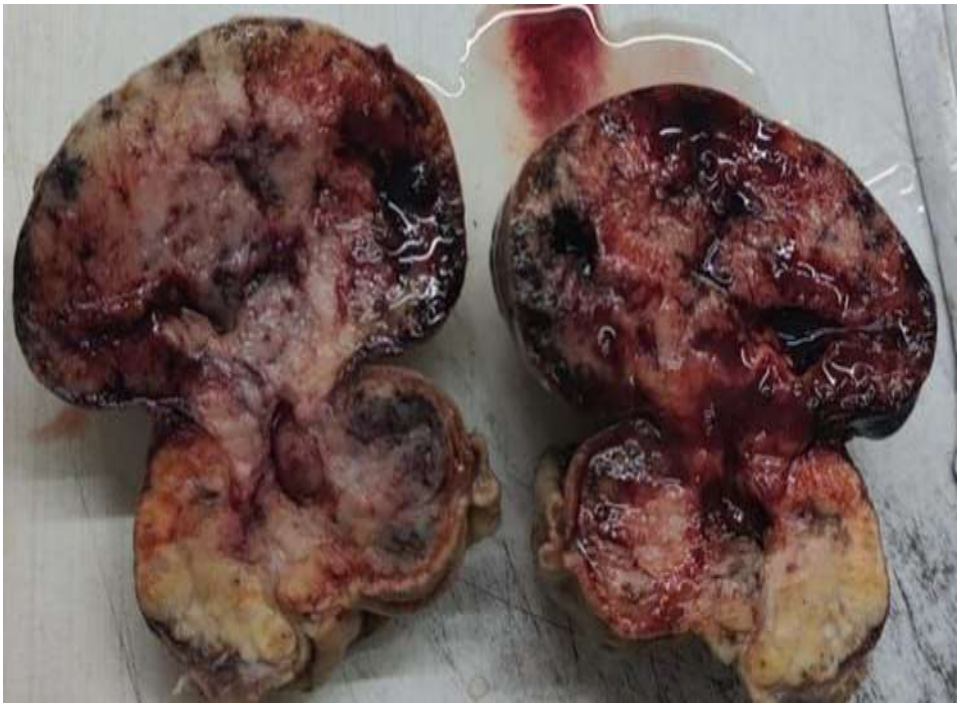

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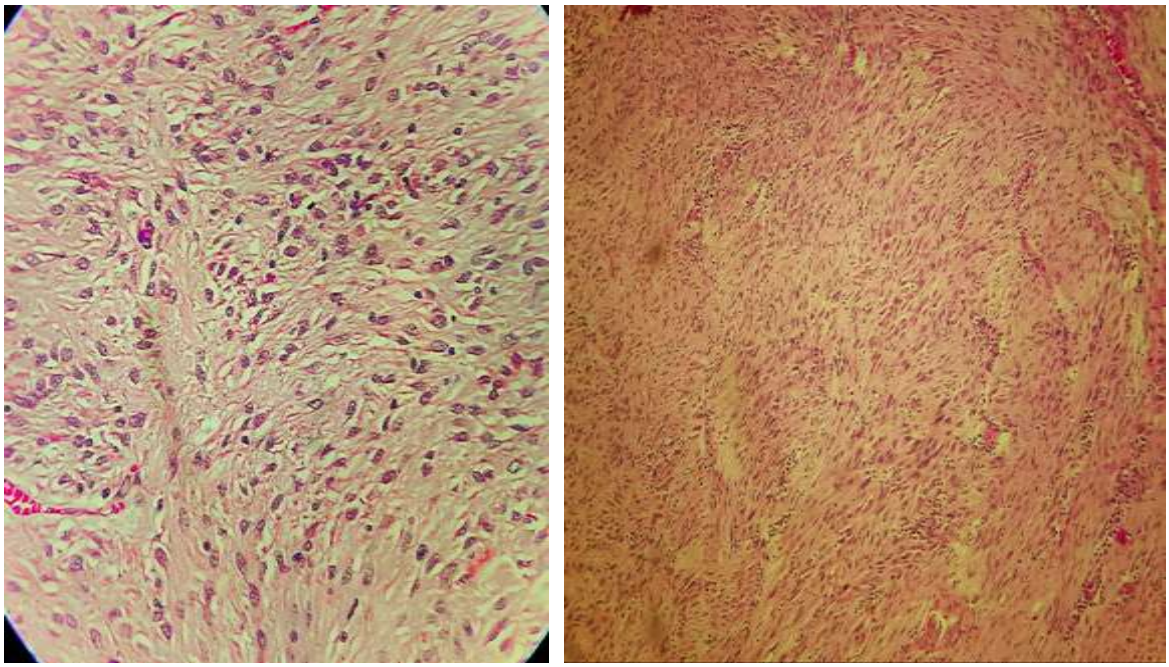
Figure 6 (a,b): 40X: Cells with spindle and epithelioid morphology with mild anisonucleosis. Mitosis is minimal.



Case 3:

A 28-year female presented with epigastric pain, hematemesis, and melena, but examination revealed no positive findings. She underwent upper gastrointestinal endoscopy, revealing large sub mucosal, solid-cystic mass measuring 11 x 8 cm arising from greater curvature of the stomach.

We received a specimen of mass with greater curvature of stomach with sleeve of anterior wall of stomach. Grossly, it was large, irregular, solid-cystic mass measuring 19 x 16 x 8 cm. Cut surface showed irregular, solid-cystic, brownish mass with cystic spaces contain haemorrhagic material (Figure 7).

On histopathological examination, sections from solid areas revealed tumour mass composed of sheets of spindle cells with oval or elongated nuclei with fine chromatin and moderate eosinophilic or vacuolated cytoplasm. There was mild to moderate anisonucleosis and pleomorphism. Mitosis (>5/50 hpf) were seen. Intervening fibrous tissue septum showed dense chronic inflammatory infiltrate. Areas of necrosis and haemorrhage were also seen. The features were suggestive of GIST, High grade- prognostic category 6b (Figure 8). Immunohistochemical analysis was performed for this case, revealing positive expression of DOG1, as well as vimentin, CD117, and CD34.

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Figure 7: Gross appearance- Large, irregular, solid-cystic tumour mass.

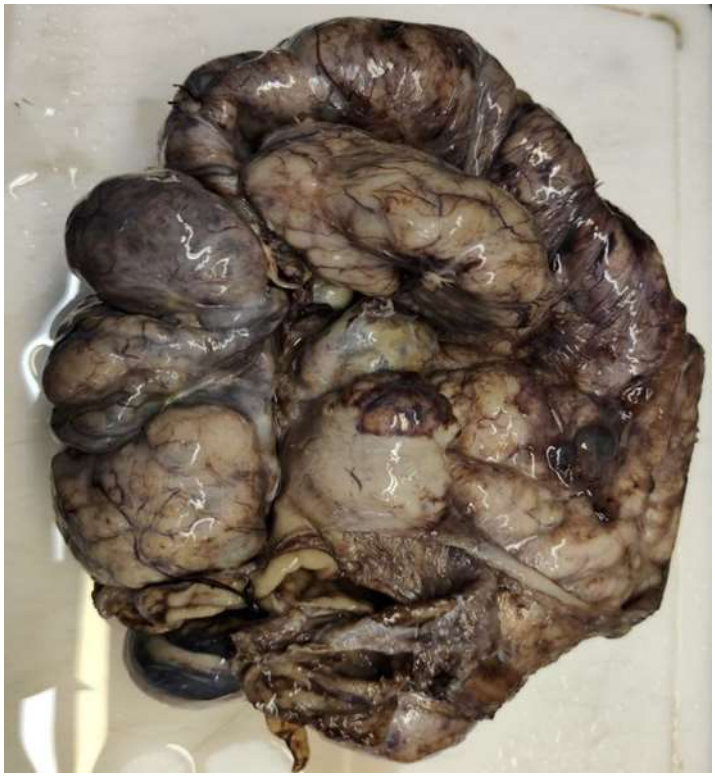
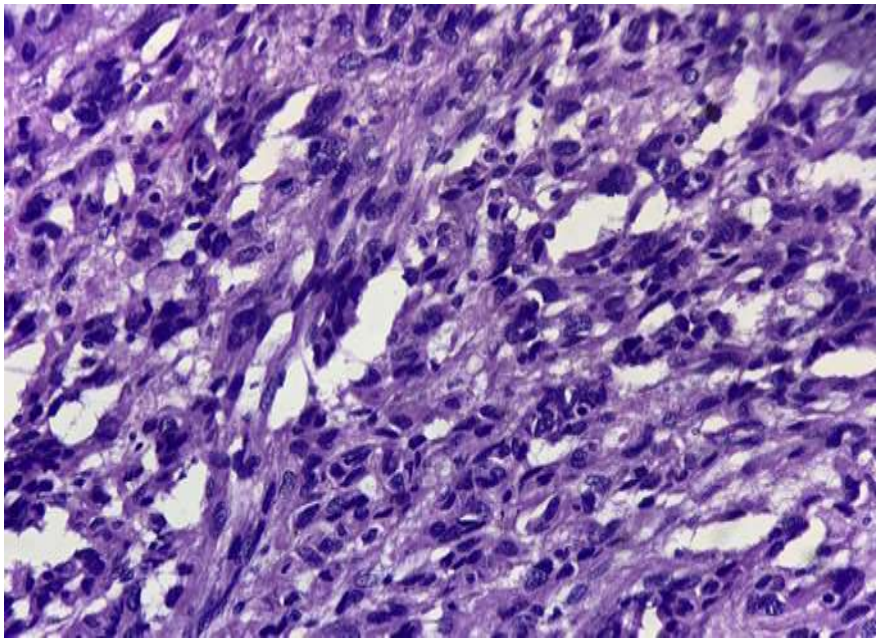


Figure 8: 40X: Sheets of spindle cells with oval or elongated nuclei with fine chromatin. Many mitotic figures seen.



Discussion

In 1983, Mazur & Clark were the first to attribute the term GIST to tumors originating in the gastrointestinal tract, which displayed characteristics of both smooth muscle and nerve cell-like organelles under electron microscopy.[7] Although GIST can occur across various age groups, multiple studies have indicated a predominant occurrence in older individuals, typically aged over 50 years. Furthermore, advanced age has been identified as a significant etiological risk factor

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for GIST. [8,9] As the study mentioned, our research also found a notably lower incidence of GIST among individuals under the age of 40. Typically, GIST manifests equally in both males and females. However, a recent study examining the impact of age and gender on GIST prognosis found that younger age (under 50 years) and female gender were significantly linked to better tumor-related outcomes in terms of disease-specific survival.[10] Gastrointestinal stromal tumors (GISTs) can originate throughout the gastrointestinal tract, most frequently found in the stomach, small intestine, colon, rectum, mesentery or omentum, and esophagus, in descending order of frequency. In rare cases, they may also develop within the abdominal cavity independent of any direct gastrointestinal tract connection, termed as extra-gastrointestinal GISTs.[11]

The clinical manifestations of GISTs correlate with both the tumor's size and its location. Larger tumors tend to exacerbate symptoms related to mass effects, such as discomfort in abdomen, pain in abdomen and feeling of abdominal fullness. Conversely, patients having smaller tumors typically remain asymptomatic. Asymptomatic tumors are often discovered incidentally during procedures like upper endoscopy or through other imaging techniques. However, symptomatic GISTs are usually identified either during imaging studies for the initial symptoms or during urgent surgical procedures in specific instances.[12] In emergency situations, the small bowel was the most frequently affected site, with gastrointestinal hemorrhage emerging as the predominant symptom in GIST cases. In consistent with various literature sources [13,14], the authors' research revealed that gastrointestinal bleeding was the primary symptom initially presented by gastric GISTs is followed by abdominal pain. Our study shows the same result most of the patients presented with upper gastrointestinal bleeding (40%) followed by abdominal discomfort (25%) then abdominal mass (20%) and very few were asymptomatic (15%). The tumor's location was observed to correlate with various symptoms. Gastric GISTs were more often associated with gastrointestinal bleeding and abdominal pain, while ileal & Jejunal GISTs often presented as acute abdominal symptoms.[13]

Under microscopic examination, most cases in our study exhibited a common feature of spindle cell morphology, with elevated mitotic activity, and mild to moderate cytonuclear atypia. Only one case displayed a mixed morphology of spindle and epithelioid cells. Multinuclearity was infrequent. We use Armed Force Institute of Pathology (AFIP) criteria for risk stratification and prognostic indicator. According to these criteria, we mostly got category 3b type i.e. size of the tumor >10 cm & mitotic figures of ≤5/50-HPFs & one case of category 6b i.e. tumor size >10 cm & mitotic figures of >5/50-HPFs.[15] Because of their spindle cell morphology, differential diagnoses such as leiomyoma, schwannoma, or solitary fibrous tumor should be considered. DOG1 should be the preferred IHC marker, while additional markers such as CD117 and CD34 are particularly valuable for differentiation purposes.

Conclusion

While GIST is a rare condition, it can impact individuals of all genders and ages. Clinical presentation of GIST can range from showing no symptoms to requiring urgent medical attention. Predominantly located in the stomach, most cases of gastric GIST manifest with gastrointestinal bleeding. Gastric GIST, often characterized by smaller tumour sizes, generally has a more favourable prognosis compared to intestinal GIST. Therefore, timely diagnosis and appropriate treatment are crucial for saving lives and enhancing prognostic outcomes, particularly for patients with small tumours and GIST-related emergencies. Surgical removal remains the mainstay treatment for GIST, although chemotherapy also has importance in managing high-risk cases. The most compelling CD117 (KIT) positivity pattern involves both a cell membrane and cytoplasmic component. Mesenchymal tumours, unlike GIST, that stain for CD117 typically exhibit only cytoplasmic staining with a coarse granular pattern. DOG1, a recently identified immunohistochemical marker for GIST, demonstrates high sensitivity and specificity for this tumour.[16]

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