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GUT MESENCHYMAL TUMORS: AN INSTITUTIONAL PERSPECTIVE

General Surgery

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ABSTRACT

IntroductionTumors arising from the mesenchymal layer of the gastrointestinal tract are classified as gastrointestinal stromal tumors or neuroendocrine tumors based on the immunohistochemical markers they express and the hormones they produce. They are often diagnosed postoperatively on histopathology. This study aimed to examine the clinical presentation, diagnosis, and management of mesenchymal gut tumors in a tertiary care center in a low-income country. **Patients and methods** We conducted a retrospective study of histopathological reports of gut resection specimens (excluding nonspecific appendicitis) collected from patients diagnosed with gastrointestinal stromal tumors and neuroendocrine tumors treated at our facility from 2017 to 2021. We evaluated clinical presentation, diagnosis, and management. **Results**Of 38 gastrointestinal resection specimens, we found seven patients with gut mesenchymal tumors (two in the foregut, five in the midgut). There were no hindgut mesenchymal tumors. Five were gastrointestinal stromal tumors, and two were neuroendocrine tumors (one in the foregut and one in the midgut). All tumors were resected entirely. Two patients underwent postoperative adjuvant chemotherapy. All patients were disease-free at follow-up (range, eight months to four years). **Conclusion** Gut mesenchymal tumors clinically presented with nearly the same features as those of more common pathologies like intestinal tuberculosis. The gut mesenchymal tumors had good prognosis after adequate surgical resection irrespective of histological type and grade of the tumor. Adjuvant chemotherapy seemed to provide no additional benefit, and in primary completely resectable tumors, it is probably redundant and not economically viable.

KEYWORDS

Gut mesenchymal tumors, gastrointestinal stromal tumors, neuroendocrine tumors, histology, surgical resection.

Introduction

Tumors of the gastrointestinal tract are of varied etiology and present in myriad ways depending on the site of origin. Some are easily diagnosed when they are small, and some are not diagnosed until they are in advanced stages. Adenomas, adenocarcinomas, and adenosquamous carcinoma arising from epithelial layers are the most common [1]. Tumors that arise from the mesenchyme, such as gastrointestinal stromal tumors (GIST; from the interstitial cells of Cajal), leiomyoma, leiomyosarcoma, and gastrointestinal neuroendocrine tumors (GI NETs; from enterochromaffin cells), comprise 6% to 16% of all gastrointestinal (GI) tumors [2,3].

NETs are the only known tumors to produce quantifiable tumor markers such as serotonin, 5-hydroxy tryptamine, and 5-hydroxy indole acetic acid, and they express somatostatin receptors on their cell surfaces, which is part of carcinoid syndrome [4]. However, hormones secreted by the tumor cells do not aid in the early detection of the tumor because hormone secretion is only found in 1.7% of total GI NETS [5]. Most jejunoileal carcinoids are detected after bowel resection to relieve intestinal obstruction [6].

We conducted this study to examine the clinical presentation, diagnosis, and management of mesenchymal gut tumors in a low-income tertiary care center with strict financial and infrastructure resources limits.

Patients and Methods

Study design

We isolated gut resection specimens from our institute's histopathological register to identify patients with mesenchymal tumors, including GISTs, GIST-like tumors, and neuroendocrine tumors. We reviewed the associated inpatient records and collected clinical presentation, diagnostic workup, and management data. We used patient contact information provided for follow-up to obtain written informed consent for inclusion. The data were tabulated and compared with other pathologies detected in the gut resection specimens.

Inclusion criteria

Patients were included if they had a histopathological report mentioning diagnoses including leiomyoma, leiomyosarcoma, GISTs, GIST-like tumors, autonomic nerve tumors, lipoma, neuroendocrine tumors, and neuroendocrine carcinoma. The specimen was part of the GI tract from stomach to rectum. Patients were excluded if the specimen was from an inflamed appendix or small biopsies. We excluded aspiration pathology cytology reports, gangrenous bowel specimens, and patients who could not be contacted after discharge from the hospital. The institutional review board approval was not required given the study's retrospective nature.

Statistical analysis was done by calculating p value using software medistica And p value of ≤ 0.05 was considered significant.[7]

Results

There were seven patients with gut mesenchymal tumors; two in the stomach, four in the small bowel (two in the jejunum and two in the ileum), and one in the caecum. Five tumors were GIST or GIST-like tumors, one was a NET, and one was a neuroendocrine carcinoma. For comparison, we classified them as foregut and midgut tumors.
We found 10 patients with foregut lesions, five with adenocarcinoma in the stomach, five with periampullary adenocarcinoma, and two with pyloric stricture (Table 1). We found 21 midgut lesions, 11 hyperplastic and strictural tuberculous lesions, three nonspecific inflammatory strictures, three with Crohn's disease, two with adenocarcinoma of the cecum, and ascending colon, and two with Meckel's diverticulitis.

Mesenchymal tumors were more common in the midgut than the foregut. There were three emergency admissions and four elective admissions. Compared to other causes with similar presentations, there was no statistically significant difference (Table 2).

Of the two mesenchymal tumors arising from the stomach, one was intraluminal (NET) (figure 1), and the other was on the outer wall adherent to the spleen (GIST) (figure 2). The patients presented with upper GI bleed in both cases: one in the emergency department with syncopal attack and one electively with chronic anemia (Table 3).

Of the five midgut tumors, four were GIST or GIST-like tumors, and one was a neuroendocrine carcinoma. Of the four GISTs, two were intraluminal (both presenting with acute intestinal obstruction) (figure 3), and two were serosal(figure 4). One of those two was detected incidentally during a routine abdominal ultrasound and confirmed on magnetic resonance imaging (MRI) (figure 5); the other was discovered during an investigation for hematochezia and melena. The lone patient with neuroendocrine carcinoma presented with repeated colicky abdominal pain and vomiting episodes. Of the seven patients only three were diagnosed preoperatively with the help of definitive radiological investigation like abdominal computed tomography (CT) scanning or MRI. Postoperative immunohistology was conducted in four patients. Of the four diagnosed via postoperative immunohistology, one was negative, and three were positively correlated with the histological diagnosis (two GIST and one neuroendocrine carcinoma).

All patients had a definitive surgical intervention, and two underwent postoperative adjuvant chemotherapy (Table 3). All patients were disease-free at data collection (with follow-up ranging from eight months to four years).

Table 1. Site of pathology in mesenchymal tumors vs other causes

	Foregut lesions		Midgut lesions	
Admission type	Mesenchymal tumors	Other lesions	Mesenchymal tumors	Other lesions
Elective, n	1	6	3	7
Emergency, n	1	4	2	14
Total, n	2	10	5	21

Table 2. Summary of patients' course in the hospital

Case no.	Presenting Concern	Diagnosis	Definitive Radiological Test (Yes/No)	Diagnose Preoperatively (Yes/No)	IHC (Yes/No)	If Yes, Confirmatory or Not
1	Hematemesis and syncopal attack	Gastric NET	No	No	No	
2	Hematemesis and melena	Gastric GIST	Yes (CT scan)	Yes	Yes, CD 117	confirmatory
3	Pain abdomen	Jejunal GIST	Yes (MRI)	Yes	Yes, CD 117 and SMA	Not confirmatory
4	Hematochezia and melena	Jejunal GIST	YES (CT scan)	Yes	Yes CD 117 and DOG 1	Confirmatory
5	Acute Intestinal obstruction	Ileal GIST	No	No	No	
6	SAIO	Ileal Neuroendocrine carcinom	Yes (CT Abdomen)	No	Yes Chromogranin A	Confirmatory
7	Acute Intestinal obstruction	Caecal GIST	No	No	No	

Table 3. Managemnet summary

Case no.	Final Diagnosis	Surgical Procedure	Adjuvant Chemotherapy	Follow-up Monitoring
1	Gastric NET	Wide excision	No	8 months
2	Gastric GIST	Distal partial gastrectomy with splenectomy	Yes Imatinib	42 months
3	Jejunal GIST	Wedge resection	No	33 months
4	Jejunal GIST	Jejunal segmental resection	Yes Imatinib	28 months
5	Ileal GIST	Ileal segmental resection	No	48 months
6	Ileal neuroendocrine carcinoma	Right Hemicolectomy	No	19 months
7	Caecal GIST	Right Hemicolectomy	No	17 months

Abbreviations: GIST, gastrointestinal stromal tumor; NET, neuroendocrine tumor.

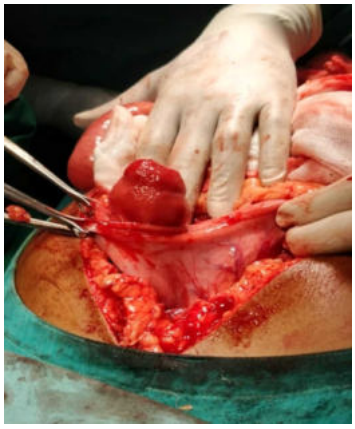


Figure:1-Intra operative image showing intraluminal gastric NET arising from anterolateral wall of stomach.

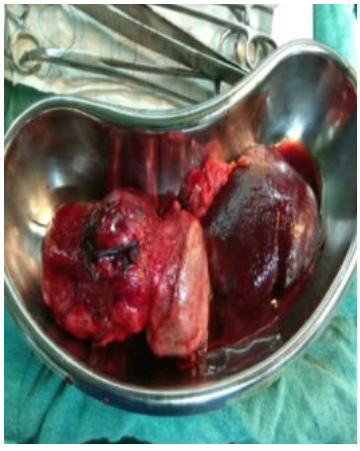
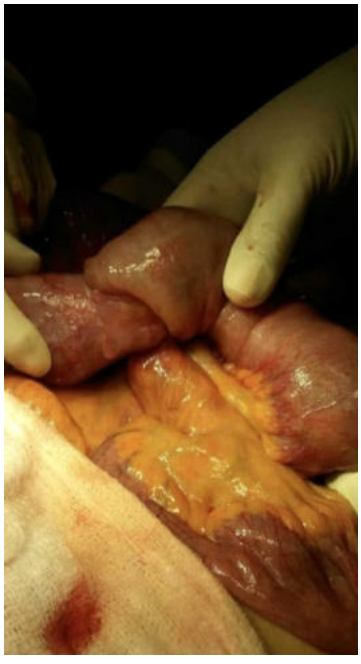


Figure 2:Post operative specimen post partial gastrectomy with splenectomy for stomach GIST.



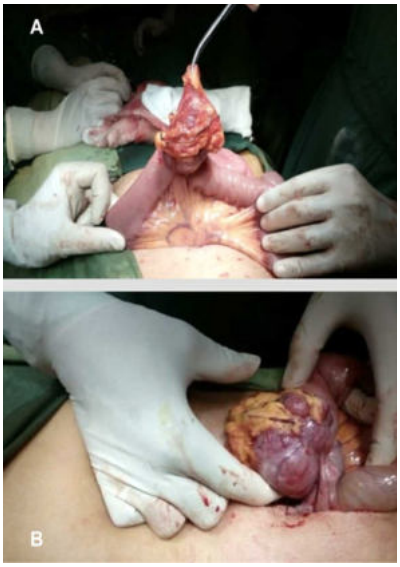


Figure 4:-Jejunal GIST-Serosal Extraluminal Growth

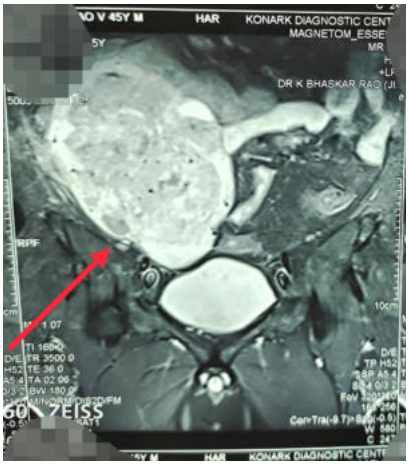


Figure 5:MRI Showing Large Space Occupying Lesion Arising From Small Bowel

DISCUSSION

GISTs, as the name implies, can arise from anywhere in the GI tract but are reportedly most common in the stomach (60%) and the small intestine (30%) [8]. This is in stark contrast with our study where small bowel (midgut) GISTs constituted the majority (80%) of tumor locations, with only 20% found in the stomach (20%). While some authors claim a majority of GIST are submucosal and detected on endoscopy [9], others report that large pedunculated masses arising from the outer aspect of the gut wall are most common [10]. We have found three externally pedunculated tumors and two tumors projecting intraluminally.

GISTs are differentiated from other gut mesenchymal tumors by expressing kit receptors (CD117) and their cell membranes in 90% to 95% of cases [9-11]. Most GIST-like tumors test positive for vimentin [11]. In our study, three were positive for CD117 expression, one was negative, and one did not undergo immunohistochemical evaluation.
NETs arise from neuroendocrine cells, which are distributed mainly in the mucosa and submucosa of the GI tract. NETs express serotonin and have somatostatin receptors, depending on their differentiation and the tumor site. However, chromogranin A and synaptophysin are the most common markers used to confirm the endocrine nature of neoplastic cells [12]. In our series, only two patients had NETs, one of which had a terminal ileal tumor showing a strong immunohistochemical reaction for chromogranin A. None showed carcinoid syndrome symptoms, which was expected because serotonin produced by the small bowel tumors is broken down in the liver from portal circulation [4]. Patients in whom biochemical and clinical evidence of serotonin is noted are usually in advanced stages of the disease with liver and distant metastases [13].

All the tumors in our study were detected because they produced symptoms such as GI bleeding or intestinal obstruction. Three were diagnosed preoperatively on the radiological investigation (two via CT and one via MRI). Upper GI endoscopy detected a submucosal lesion whose biopsy was inconclusive, but resection revealed a neuroendocrine tumor. This contrasts with a study advising aggressive use of endoscopic ultrasound (EUS) and EUS-guided fine-needle aspiration for early diagnosis and management of subepithelial lesions [14]. The other four patients were diagnosed because they presented with features of intestinal obstruction and had to undergo surgical intervention. This was in line with studies advising early explorative laparotomy and a high index of suspicion in diagnosing small bowel tumors [3,15]. The point of diversion comes in other causes of intestinal obstruction—in our study, the most common cause was intestinal tuberculosis. All the patients with intestinal obstruction received laparotomy for suspected tuberculous lesions. There is no definitive test for confirming abdominal tuberculosis other than histopathology of the specimen—either of the lymph node or resected bowel [16]. Hence, a retrospective study of intestinal obstruction done in a low-income country like Chile without a single case of intestinal tuberculosis [15] comes as a mild surprise to the authors.

In our series, all patients who underwent surgical operation irrespective of final diagnosis (GIST or NET) are doing well without any recurrence during the follow-up time ranging from eight months to four years. This includes two large GISTs—one adherent to the peritoneum and bowel and the other to the spleen—and one neuroendocrine carcinoma. Only two patients (both GIST) took adjuvant chemotherapy. This outcome aligns with contemporary literature showing surgical resection as the gold standard option in GIST management and complete resection as the main predictor of patient survival [17]. Neoadjuvant and adjuvant therapy used in scenarios similar to adenocarcinomas (i.e., large, unresectable tumors) can downsize the tumors and decrease the chances of rupture while maintaining bowel function [18]. Similarly, surgery is the best choice for the neuroendocrine tumors of the gut, even for metastatic disease [19].

The small number of patients with gut mesenchymal tumors limited the study, which precluded a proper statistical analysis and comparison with other epithelial tumors. The small number was, in turn, due to the unique nature of health care system in a country like India, where patients get treated in any number of small hospitals that lack robust documentation and reporting systems, which confounds the actual incidence rates. The small numbers are also due to patient nonadherence to treatment and follow-up investigations after being discharged from the treating hospital.

CONCLUSIONS

Gut mesenchymal tumors arise most frequently from the midgut either as intraluminal projections of subepithelial lesions or as pedunculated masses on the outer wall of the gut. They can escape detection until they are revealed in postoperative histopathology of the resected specimen. The role of immunohistochemistry is limited to confirmation of histological findings with negative results in no way changing the course of management. Clinical presentation of these tumors often mimics other more common conditions, and management is similar to the other conditions. There is little use in devising separate management protocols for gut mesenchymal tumors. Adjuvant chemotherapy has been shown to provide no additional benefit, and in primary completely resectable tumors, it is probably redundant and economically not viable.

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