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Original Research Article

Histomorphological spectrum of gastrointestinal stromal tumors: an institutional experience

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ABSTRACT

Background: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the abdominal area. They can involve any portion of the gastrointestinal (GI) tract, omentum, mesentery, retroperitoneum, and other sites. They form 1-2% of the histologic types of gastrointestinal tract tumors. Aims and objectives were to analyze and correlate morphological, clinical and histomorphology features of gastrointestinal tumors presenting at different sites.
Methods: This was a retrospective observational study for six years. Medical records of the histopathologically diagnosed GIST cases were reviewed for patient demographics and clinical presentation, and tumor findings were noted.
Results: Of the 28 patients, ages ranged from 28 to 80 years. Symptoms ranged from abdominal pain, epigastric discomfort, mass, upper/lower gastrointestinal bleeding, rectal bleeding, anemia, weight loss, and small bowel obstruction. Sites involved were the small bowel, stomach, mesentery, rectum, duodenum, greater omentum, and retroperitoneum. Of 28 cases of GIST, 25 cases showed both c-KIT and DOG-1 positivity, 1 case showed only c-KIT positivity, 1 case showed only DOG-1 positivity, and 1 case was both c-KIT and DOG-1 negative.
Conclusions: GISTS are unpredictable mesenchymal tumors. Common sites are the stomach and small gut. Mesenteric and omental GIST are rare. Spindle cell morphology was more commonly present.

Keywords: Mitotic count, c-KIT, DOG-1, Immunohistochemical markers

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the abdominal area.[1] The term stromal tumor was initially introduced to describe mesenchymal tumors of the gastrointestinal tract (GI) that does not have features of Schwann cells or smooth muscle cells.[2] They can involve any portion of the GI tract, omentum, mesentery, retroperitoneum, and other sites. About 60% of GISTs occur in the stomach.[3] The tumor is seen to be arising from the interstitial cell of Cajal, the pacemaker cells of the GI muscularis propria.[4]

The American Joint Committee on Cancer (AJCC) cancer staging manual lists the following approximate distributions- stomach (60%), small intestine (30%), rectum (3%), colon (1–2%), oesophagus (<1%), and omentum/mesentery (rare). Infrequently, GIST may arise in the appendix, gallbladder, pancreas, retroperitoneum, and tissues around pelvic organs.[1,5]

For years, they were regarded as leiomyomas and leiomyosarcoma when they had spindle cells and leiomyoblastomas or epithelioid leiomyomas when they depicted epithelioid cells predominantly.[3]

GISTs were found commonly in adult males between ages 28–75 years 40 and 70 years as per published literature and can be benign or malignant. The peak age of

presentation is approx. 60 years with <10% showing presentation <40 years.[2,3]

Presenting complaints depended on the site of the GIST-small gut GIST presented with small gut obstruction and abdominal lump. Gastric GIST presented with epigastric discomfort and upper gastrointestinal bleeding. Rectal GIST presented with rectal bleeding. Mesenteric or omental GIST was reported with abdominal mass and anemia.

Histomorphologically, GISTs can be composed of thin elongated cells classified as spindle cell type or tumors dominated by appearing epithelial cells and are epithelioid type. A mixture of both patterns has been reported as well. Some of the tumors have a neural appearance also. Immunohistochemically majority of GISTs show KIT positivity, with a minority of cases being KIT-negative. Other markers which could be positive include CD34, SMA, and rarely S100 but are primarily negative for desmin.[5]

More than 95% of GISTs are positive for immunohistochemical marker cluster of differentiation (CD) CD117. Still, in 5% of cases, CD117 expression is not found. Although, in these cases, IHC staining with discovered on GIST-1 (DOG1, also known as ANO1) can help confirm the diagnosis of GIST.[6]

This study was taken to analyze and correlate morphological, clinical, and histomorphological features of gastrointestinal tumors presenting at different sites.

METHODS

It was a retrospective observational study conducted at a tertiary care hospital between January 2016 to December 2021 after obtaining ethical clearance from institutional ethics committee.

We included 28 cases with confirmed diagnoses of GIST based on the histopathological findings and immunoreactivity of CD117 and DOG 1 for six (6 years). Clinicopathological data such as age, sex, location, tumor size, stage, clinical manifestations, and surgical treatment were retrospectively retrieved from the records.

For all the 28 cases hematoxylin & eosin (H & E) stained slides were reviewed for histopathological parameters which included cellularity, cell type, and the number of mitosis/50 hpf. Risk stratification was performed using the National Institute of Health (NIH) criteria. IHC markers like CD-117 and DOG-1 were studied for the positivity status.

Exclusion criteria

Patients treated with Imatinib before surgery are excluded from the study.

Statistical analysis

Data were entered into a Microsoft excel data sheet and analyzed using statistical package for the social sciences (SPSS) 22 version software. Categorical data was represented in the form of frequencies and proportions. Continuous data were represented as mean and standard deviation.

RESULTS

We included 28 subjects with confirmed diagnoses of GIST, out of which 19 (67.85%) were male and 9 (32.15%) were female. The study subject's ages ranged from 28-80 years with a mean age of 54.25 years and median age of 61 years (Table 1).

Clinical presentation

Abdominal mass was the most common presentation in 35.7% of the subjects. Followed by abdominal pain was present in 28.5% of the subjects. Gastrointestinal bleeding was present in 17.8% of the subjects. In 7.1% of cases, it was an incidental finding. Nausea and vomiting were present in 7.1% of the subjects. Anemic symptoms were present in 3.6% of the subjects (Table 1).

Table 1: Demographical and clinical manifestations.

Variables	N (%)
Age, mean (range) (years)	54.25 (28-80)
Sex n (%)	
Male	19 (67.85)
Female	9 (32.15)
Clinical manifestations n (%)	
Abdominal mass	10 (35.7)
Abdominal pain	8 (28.5)
Gastrointestinal bleeding	5 (17.8)
Nausea and vomiting	2 (7.1)
Incidental finding	2 (7.1)
Anemic symptoms	1 (3.6)

The majority of the subjects, 53.5%, had a tumor in the small intestine, followed by the stomach, about 21.4%. Rectum was the site in 10.7%, duodenum was the site in 7.2 %, and extra gastric site was present in 7.2% of the subjects (Figure 1).

In the majority of the subjects 57.1% had tumor size >10 cm, followed by 5-10 cm in about 28.6% of the subjects, and 14.3% of the subjects had tumor sizes between 2-5 cm. The minimum size of the tumor was 2.5 cm, and the maximum was 22 cm (Table 2). Grossly most of the cases were well circumscribed and in few cases it showed areas of necrosis and haemorrhage (Figures 2 and 3).

On histopathology, spindle cells were present in 71.4% of the tumor, mixed type was present in 21.4% of the tumor,

and epitheliod form with vacuolated cytoplasm was present only in 2 subjects which are 7.1% (Figures 4-6).

Table 2: Tumour size.

Tumor size (cm)	n (%)
2-5	4 (14.3)
5-10	8 (28.6)
>10	16 (57.1)

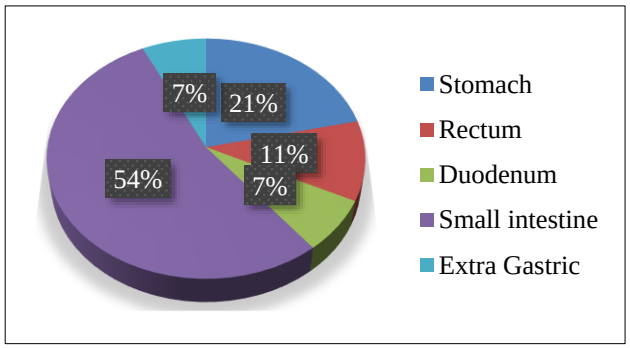

Figure 1: Distribution of tumors according to site.

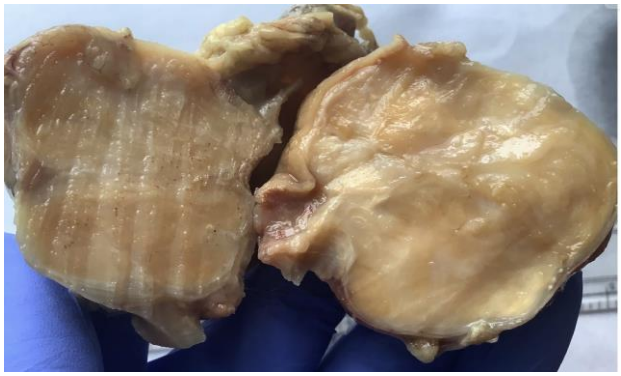

Figure 2: Gross showing well circumscribed GIST.

Figure 3: Gross showing mesenteric GIST with variegated appearance.

NIH-Flechter criteria were used for predicting the risk of metastasis in 28 cases of GISTs. There were 21 cases (75%) in the high-risk category, 5 cases (17.9%) in the intermediate-risk category, and 2 cases (7.1%) in low risk. There were no cases in the very low-risk categories (Table 3).

Table 3: Histopathological parameters.

Parameters	N (%)
Histopathology	
Spindle cells	20 (71.4)
Mixed	6 (21.4)
Epithelial form	2 (7.1)
Mitosis	
<5/50 hpf	10 (35.7)
>5/10 hpf	18 (64.3)
Risk level	
Low	11 (39.2)
Intermediary	10 (35.7)
High	7 (25)

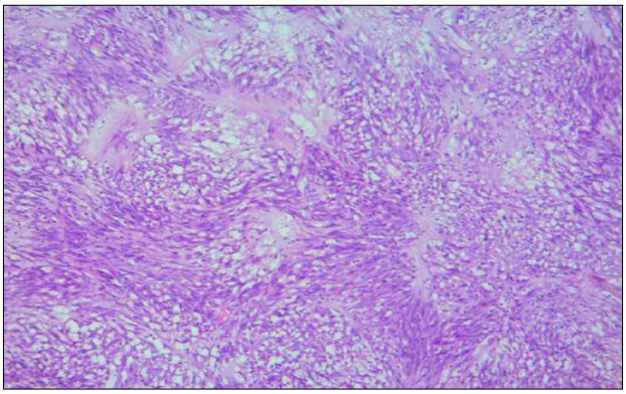

Figure 4: Spindle cell morphology of GIST H&E (100X).

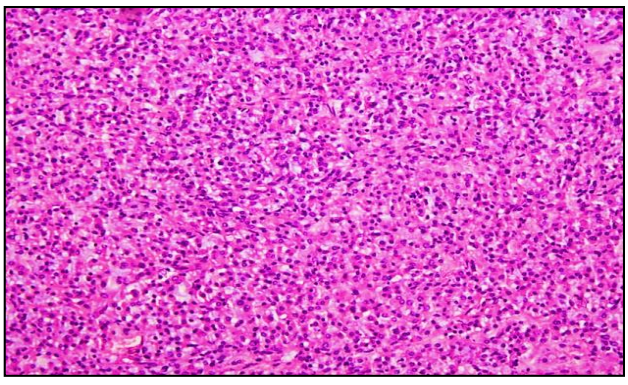

Figure 5: Epithelioid morphology of GIST H&E (100X).

On IHC in our study found that 92.85% of the cases were positive for C-KIT, and DOG1 was also positive in 92.85% of cases (Figures 7 and 8). Of 28 cases of GIST, 25 cases showed both KIT and DOG 1 positivity (89.28%), 1 case showed only KIT positivity (3.57%), 1 case showed only DOG 1 positivity (3.57%), and 1 case was both c-KIT and DOG 1-negative (3.57%) (Table 4).

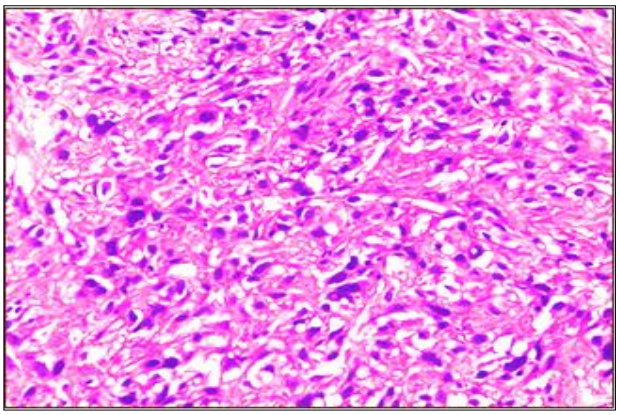

Figure 6: GIST showing mixed and epithelioid morphology H&E (400X).

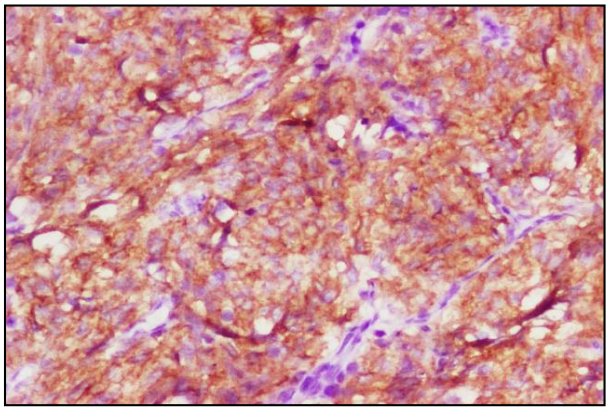

Figure 7: IHC C-KIT showing strong diffuse cytoplasmic and membranous (400X).

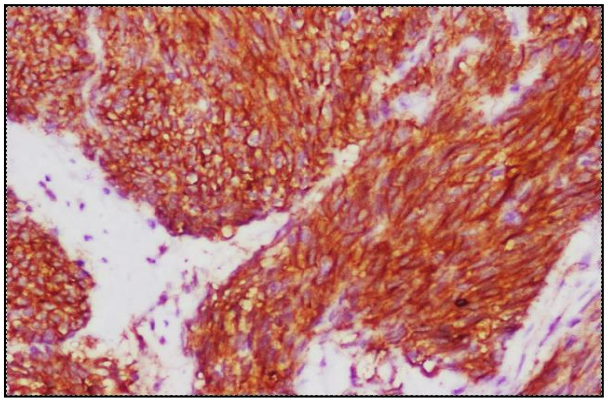

Figure 8: IHC DOG-1 showing strong diffuse cytoplasmic and membranous (400X).

Table 4: Expression of C-KIT and DOG1 in gastro intestinal stromal tumors.

IHC marker	N (%)
c-KIT and DOG-1 both positive	25 (89.28)
c-KIT and DOG-1 both negative	1 (3.57)
c-KIT positive and DOG-1 negative	1 (3.57)
c-KIT negative and DOG-1 positive	1 (3.57)

DISCUSSION

Gastrointestinal stromal tumors can occur anywhere in the gastrointestinal tract. They are usually submucosal local and are endophytic growing. Rarely can grow exophytically. In our study, subjects age ranged from 28-80 years with a mean age of 54.25 years and median age of 61 years. In a study done by Varsha et al, mean age of presentation was 52.8 years.[7] Our finding was comparable with studies by Patnayak et al, Ravikumar et al, and Lakshmaiah et al.[8-10] Global data had a higher median age of presentation of around 60 years.[3]

In our study, male predominance was observed with a male-to-female ratio of 2:1, which was similar to the study done by Varsha et al, which had male to female ratio of 1.5:1.[7] Our finding was also comparable with other Indian studies by Patnayak et al and Rajappa et al.[8,11] Global data showed equal distribution between males and females.[3]

Gastrointestinal stromal tumors have varied clinical presentations like pain abdomen, mass per abdomen, and gastrointestinal bleeding. In our study, the majority had abdominal mass present in 35.7% of the subjects, followed by abdominal pain in 28.5% of the subjects. In a study by Varsha et al, pain abdomen was the joint presentation followed by mass per abdomen.[7] Intestinal obstruction is a common symptom in both Indian and global studies.

In our study, the small intestine, followed by the stomach, was the most common site, whereas in a study done by Varsha et al.[7] Stomach was the most common site of involvement, followed by the small intestine. The most common site was not similar to other Indian and global studies.[3,8,11]

In our study, tumor size varied from 2.5 to 22 cm. Most GISTs had a size of more than 10 cm (57.1%), similar to the study done by Varsha et al and similar to data obtained from both Indian studies and global epidemiological data.[3,7-9,11]

Histologically maximum gastrointestinal stromal tumors commonly show spindle cell morphology. Spindle cell pattern was the most common histological pattern observed in this study and was present in 20 cases (71.4%) which was in concordance with studies by Varsha et al, Vij et al, Kim et al, and Lakshmi et al.[7,12-14]

The epithelioid pattern was observed in 2 cases (7.1%), and mixed epithelioid and spindle cell pattern was observed in 6 cases (21.4%) which, in comparison to other studies, showed more cases of epithelioid morphology than mixed morphology.[12-14]

Secondary changes like hyalinization, calcification, and necrosis were also noted in a few cases.

Every GIST has been thought to have malignant potential in recent study years. Hence risk stratification using NIH criteria is essential to predict the risk of metastasis. NIH criteria use tumor size and mitotic rate per 50 hpf as prognostic determinates of GIST. Based on this, four risk groups were formed very low risk, low risk, intermediate risk, and high-risk category.[7]

In this study, the majority were seen in the intermediate category, followed by low and high risk.

Immunohistochemistry is a compassionate tool which plays a critical role in diagnosis of GIST and helps in differentiating from other mesenchymal tumors. c-KIT and, recently, DOG-1 have been primarily used as diagnostic markers of GIST. C-KIT positivity varies from focal to diffuse, weak to strong cytoplasmic and membranous positivity. In this study, c-KIT and DOG-1 showed 92.8% sensitivity. C-KIT and, recently, DOG-1 have primarily emerged as diagnostic markers of GIST. KIT positivity on IHC varied from focal–to-diffuse and weak to-strong cytoplasmic and membranous positivity.

In a study by Varsha p et al, c-KIT was positive in 91.9% of cases, and DOG-1 was also positive in 91.9% of cases.[7] Both KIT and DOG-1 positivity (82%), only KIT positivity (8%), Only DOG-1 positivity (8%), and both KIT and DOG1-negative (3%) which was in comparison to our study. C-KIT-positive cases were put on targeted treatment with imatinib, and all the patients were on follow up with no history of recurrence or metastasis was reported.

CONCLUSION

Gastrointestinal stromal tumors are uncertain and the most common mesenchymal tumors out of all mesenchymal tumors. Histopathological diagnosis remains the gold standard diagnostic modality, and IHC marker like C-KIT and DOG-1 helps in confirmatory diagnosis. Tumor size and mitotic rate help in risk stratification, which further helps the treatment plan.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Graadt van Roggen JF, van Velthuysen ML, Hogendoorn PC. The histopathological differential diagnosis of gastrointestinal stromal tumours. J Clin Pathol. 2001;54(2):96-102.
2. Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM. Gastrointestinal pacemaker cell tumor (GIPACT): Gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. Am J Pathol. 1998;152(5):1259-69.
3. Søreide K, Sandvik OM, Søreide JA, Giljaca V, Jureckova A, Bulusu VR, et al. Global epidemiology of gastrointestinal stromal tumours (GIST): A systematic review of population-based cohort studies. Cancer Epidemiol. 2016;40:39-46.
4. Miettinen M, Lasota J. Gastrointestinal stromal tumors: Pathology and prognosis at different sites. Semin Diagn Pathol. 2006;23(2):70-83.
5. Lasota J, Miettinen M. KIT and PDGFRA mutations in gastrointestinal stromal tumors (GISTs). Semin Diagn Pathol. 2006;23(2):91-102.
6. Miettinen M, Wang ZF, Sarlomo-Rikala M, Osuch C, Rutkowski P, Lasota J, et al. Succinate dehydrogenase-deficient GISTs: a clinicopathologic, immunohistochemical, and molecular genetic study of 66 gastric GISTs with predilections to young age. Am J Surg Pathol. 2011;35(11):1712-21.
7. Varsha P, Champaka G, Kumar RV, Krishnamurthy S. Pathological Spectrum of Gastrointestinal Stromal Tumors-A 1.5-year Experience at Kidwai Cancer Institute. Int J Sci Stud. 2018;6(6):38-45.
8. Patnayak R, Jena A, Prasad PD, Rukhamangadha N, Chowhan AK, Parthasarathy S, et al. Evaluation of mesenchymal tumors of the gastrointestinal tract with special reference to gastrointestinal stromal tumors - A tertiary care center experience. Onco Gastroenterol Hepatol Rep. 2013;2:52-7.
9. Ravikumar G, Kalegowda IY, Ananthamurthy A. Clinicopathologic spectrum of gastrointestinal stromal tumors - experience at a tertiary care center. Indian J Cancer. 2011;48:466-70.
10. Lakshmaiah KC, Suresh TM, Babu G, Purohit S, Guruprasad B, Jacob L, et al. Gastrointestinal stromal tumors: A single institute experience from South India. Clin Cancer Invest J. 2014;3:62-5.
11. Rajappa S, Muppavarapu KM, Uppin S, Digumarti R. Gastrointestinal stromal tumors: A single institution experience of 50 cases. Indian J Gastroenterol. 2007;26:225-9.
12. Vij M, Agrawal V, Kumar A, Pandey R. Gastrointestinal stromal tumors: A clinicopathological and immunohistochemical study of 121 cases. Indian J Gastroenterol. 2010;29:231-6.
13. Kim KM, Kang DW, Moon WS, Park JB, Park CK, Sohn JH, et al. Gastrointestinal stromal tumors in Koreans: Its incidence and the clinical, pathologic and immunohistochemical findings. J Korean Med Sci. 2005;20:977-84.
14. Lakshmi VA, Chacko RT, Kurian S. Gastrointestinal stromal tumors: A 7-year experience from a tertiary care hospital. Indian J Pathol Microbiol. 2010;53:628-33.

15. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67(2):93-9.

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