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Adesh University Journal of Medical Sciences & Research

Case Report

Histomorphological spectrum of gastrointestinal stromal tumors – An institutional experience in a series of seven cases

Anshul Gupta[1], Vijay Suri[2], Nikita Goyal[2], Sahil Chhabra[2], Anamika Garg[2], Gajendra Bhati[3], Jasmine Kaur[2]

Departments of [1]Immuno-Hematology and Blood Transfusion, [2]Pathology, [3]Surgery, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India.

***Corresponding author:**
Nikita Goyal,
Department of Pathology,
Adesh Institute of Medical Sciences and Research,
Bathinda, Punjab, India.

nikitagoyal4193@gmail.com

Received : 14 October 2020
Accepted : 10 November 2020
Published : 19 December 2020

DOI
10.25259/AUJMSR_33_2020

Quick Response Code:

ABSTRACT

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the abdominal area. They can involve any portion of GI tract, omentum, mesentery, retroperitoneum, and other sites. The tumor is seen to be arising from interstitial cell of Cajal, the pacemaker cells of the GI muscularis propria. About 60% of GISTs occur in stomach. More than 95% of GISTs are positive for immunohistochemical marker Crohn's disease (CD) CD117. Still in 5% of cases, CD117 expression is not found. Although, in these cases, staining with discovered on GIST-1 (DOG1, also known as ANO1) can be helpful in confirming the diagnosis of GIST histomorphological diagnosis remains the gold standard diagnostic modality with CD 117 positivity leading to more confirmation. Tumor size and mitotic count remain the main factors in the risk categorization of tumors. Furthermore, every spindle cell lesion should undergo CD117 immunohistochemistry markers as an initial workup.

Keywords: Crohn's disease 117, Epithelioid variant, Gastrointestinal stromal tumors, Mitotic count, Spindle cell variant

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the abdominal area.[1] The term stromal tumor was originally introduced to describe mesenchymal tumors of the GI tract that does not have features of Schwann cells or smooth muscle cells.[2] They can involve any portion of GI tract, omentum, mesentery, retroperitoneum, and other sites. About 60% of GISTs occur in stomach.[3] The tumor is seen to be arising from interstitial cell of Cajal, the pacemaker cells of the GI muscularis propria.[4] 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] The peak age of presentation is approx. 60 years with <10% showing presentation <40 years.[4]

Symptoms of GISTs are usually seen due to the mass effect. Mucosal ulceration may lead to blood loss which presents with anemia usually.[4] Small GISTs are typically incidentally detected on the external aspect of stomach or intestines during radiologic studies or surgery for unrelated conditions.[5]

Histomorphologically, GISTs can be composed of thin elongated cells classified as spindle cell type or tumors which are dominated by epithelial appearing cells and are termed as epithelioid type. Mixture of both the patterns has been reported as well. Some of the tumors have neural

appearance also. More than 95% of GISTs are positive for immunohistochemical marker Crohn's disease (CD) CD117. Still in 5% of cases, CD117 expression is not found. Although, in these cases, staining with discovered on GIST-1 (DOG1, also known as ANO1) can be helpful in confirming the diagnosis of GIST.[6] In our study, we analyzed seven cases of GIST with different clinical and histomorphological features presenting at different sites during the time span of 1 year that is from August 2019 to July 2020.

CASE SERIES

Case report 1

A 42-year-old male presented to the hospital with the chief complaints of pain in the left hypochondrium which was radiating to the back. The contrast-enhanced computed tomography (CECT) abdomen of the patient revealed heterogeneously enhancing soft-tissue lesion in the lesser sac measuring 6 × 4 × 2 cm with the loss of the fat planes and possibility of gastric GIST or solid papillary neoplasm of pancreas was extended. We received trucut biopsy which was done endoscopically by gastrosurgeon. Biopsy measured 1 cm in length and it was processed for histopathological examination. Microscopic examination of the biopsy exhibited similar cells arranged in intersecting fascicles. Infrequent mitosis with no nuclear pleomorphism was noted and impression of GIST of spindle cell type was given. Immunohistochemistry (IHC) CD117 was positive in this case which confirmed the diagnosis.

Case report 2

A 67-year-old female presented to the surgery outpatient department (OPD) with the symptoms of pain in abdomen for 15 years which was exaggerated for the past 2 weeks. CECT abdomen revealed that possibility of mesenteric GIST/small bowel GIST/mesenteric cyst was given. No metastatic nodules or lymph nodes were seen. Tumor was excised and sent for histopathological analysis. We received a large mesenteric mass measuring 19 × 12 × 10 cm with attached intestinal segment measuring 15 cm. Cut section of the mass was solid and firm with necrotic and hemorrhagic areas. Microscopic examination of the sections from various representative areas of the mass showed spindle cells arranged in fascicles, sheets, and focal storiform pattern. Individual spindle cells were slender to plump having moderate pleomorphism with pointed ends and wavy nuclei. Mitotic activity of 5/50 hpf was noted along with extensive areas of necrosis [Figure 1]. Impression of mesenteric GIST with neural differentiation and high risk of progression was given. The patient was administered adjuvant chemotherapy for 2 years after the diagnosis.

Case report 3

A 40-year-old male presented to the department of surgery with the complaints of pain left lumbar region for 20 days with associated history of multiple episodes of vomiting. Intraoperative findings of large growth in the lumen of stomach were noted. For the histopathology examination of the tumor, we received already opened up partial gastrectomy specimen with irregular nodular growth measuring 9 × 7 × 6 cm which was protruding outside the serosal surface as exophytic well-circumscribed nodular growth [Figure 2]. Multiple sections studied from the tumor show spindle to ovoid to elongated cells with blunt ended nuclei and fibrillary eosinophilic cytoplasm. Large areas of necrosis hemorrhage and dense mixed inflammatory infiltrate were noted. Mitotic activity was low <2/50 hpf. Diagnosis of spindle cell GIST was given [Figure 3]. IHC marker report of CD 117 was negative.

Case report 4

A 50-year-old female with the symptoms of pain in abdomen and constipation for 20 days presented to surgery OPD. Intraoperative findings revealed jejunojejunal intussusception with the presence of distal jejunal mass. We received an intestinal segment with pedunculated gray-brown mass measuring 5 × 3.5 cm arising from wall into the lumen [Figure 4]. Cut section of the mass was gray-white and homogeneous. Microscopy of the tumor sections revealed cells arranged in sheets, fascicles with focal whorling. Individual tumor cell was round to ovoid with enlarged vesicular nuclei and abundant clear eosinophilic fibrillary cytoplasm. Mitotic activity of around <2/50 hpf was noted. Histopathological impression of GIST – epithelioid variant was given. IHC markers revealed CD 117 positivity in tumor cells.

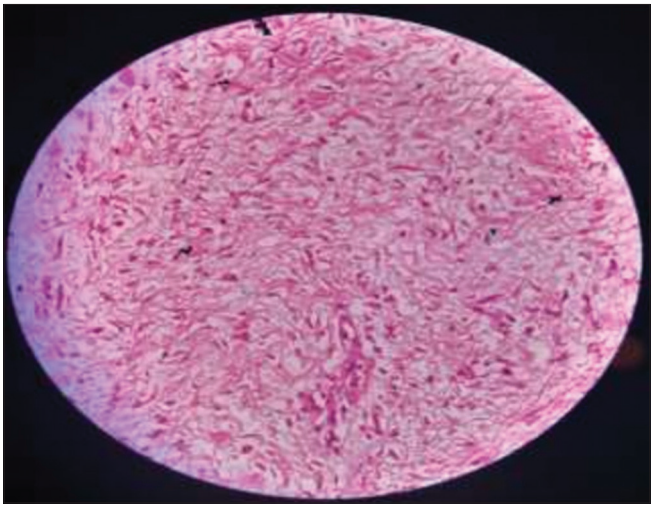

Figure 1: Microscopic study showing spindle to plump cells with pointed and wavy nuclei arranged in fascicles. Impression of GIST with neural differentiation was given in this case (case report 2).

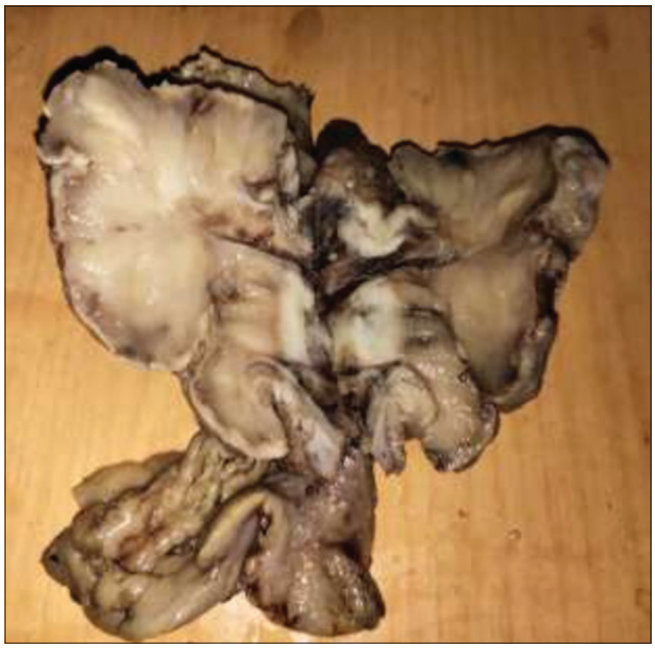

Figure 2: Irregular nodular growth measuring 9 × 7 cm which was protruding as a exophytic nodular growth in a partial gastrectomy specimen (case report 3).

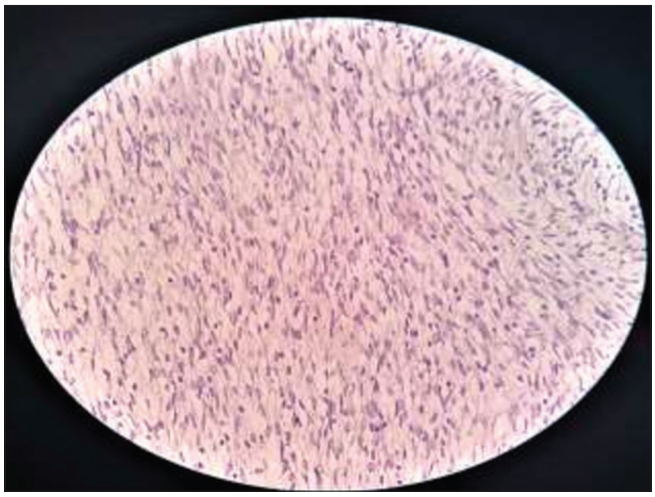

Figure 3: Microscopy examination exhibiting spindle to ovoid cells arranged in interlacing bundles. Impression of this case was GIST – spindle cell type (case report 3).

Case report 5

Another 36-year-old female with a history of upper GI bleed presented to the surgery department. CECT abdomen revealed 14.2 × 13.6 × 10.5 cm cystic lesion in left hypochondrium inseparable from posterior wall of stomach along greater curvature and gave first possibility of neoplastic tumor – atypical GIST. No evidence of metastatic nodules was noted. Cyst wall excision and sleeve gastrectomy including ulcer bearing greater curvature resection was done

Figure 4: Gross appearance of pedunculated gray-brown mass measuring 5 × 3.5 cm. Note the gray-white homogeneous cut section of the growth (case report 4).

and the resected specimen was sent to histopathology section in four different containers. Multiple random sections studied from the cyst wall depicted cells arranged in sheets, nests, and diffusely scattered. Individual cells were round to ovoid with abundant vacuolated to clear to eosinophilic cytoplasm having round to ovoid vesicular nuclei, finely dispersed chromatin and inconspicuous to small nucleoli. Areas of hemorrhage, necrosis, and cystic degeneration were seen. Tumor was seen breaching the muscularis propria of stomach in areas and reaching into the mucosa causing ulceration. Mitotic activity of around 2/50 hpf was noted. Histomorphology was suggestive of GIST – epithelioid variant [Figure 5]. In view of large size, invasion of mucosa, and high nuclear pleomorphism, high risk of progression was to be considered. IHC markers for the tumor were CD117 positive. The patient was administered adjuvant chemotherapy for 2 years after the diagnosis.

Case report 6

A 65-year-old female presented in surgery OPD with complaints of constipation and pain abdomen with melena for 7 days. We received an intestinal segment with presence of diverticulae along with elongated globular growth measuring 5 × 3 × 2.5 cm. Cut section of the growth showed homogeneous gray-white appearance. Multiple sections from the tumor studied showed benign tumor arising from submucosa comprising of round to ovoid to slightly spindly cells arranged in fascicles, whorls, and scattered diffusely. Individual cells had round to plump, slightly elongate nuclei with abundant clear to eosinophilic cytoplasm. Mitotic

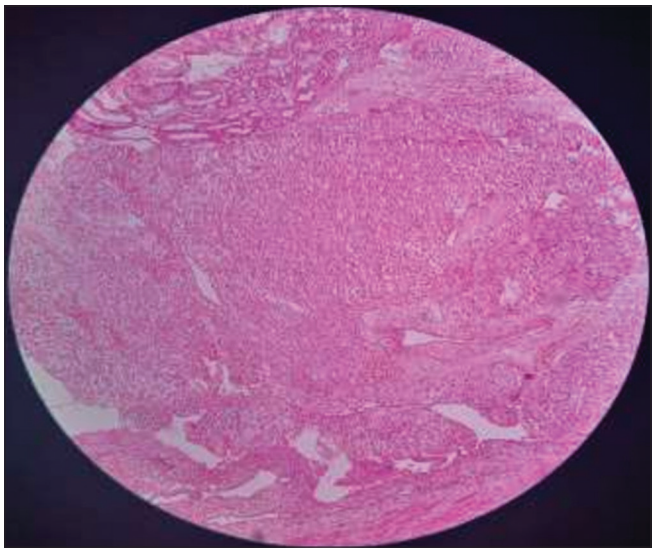

Figure 5: Tumor invading the muscularis propria and reaching the mucosa seen (case report 5).

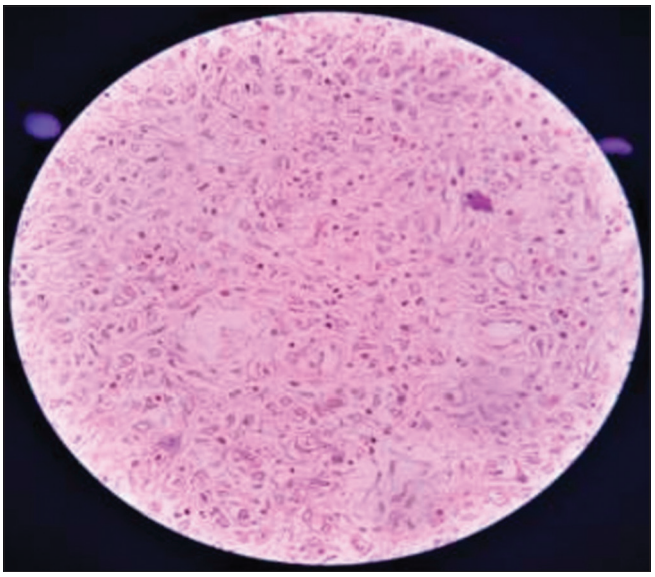

Figure 6: Microscopy of epithelioid variant of GIST showing round to avoid cells with vesicular nuclei and clear cytoplasm arranged in sheets and fascicles (case report 6).

activity was not increased. Microscopic impression of excised jejunal segment with GIST – epithelioid type [Figure 6] was extended. IHC of this case shows CD117 positivity.

Case report 7

A 50-year-old male who was diagnosed with cholelithiasis and soft-tissue lesion at duodenal region underwent cholecystectomy with excision of part of duodenum. Histopathology section received gallbladder with small intestinal segment having gray-white tumor measuring 1.8 × 1.2 cm near one of its end. Microscopic examination of the sections from the tumor showed well-circumscribed tumor with cells arranged in interlacing fascicles and sheets. Individual tumor cells were elongated, spindle to round nuclei, and moderate eosinophilic cytoplasm. Histomorphological diagnosis of GIST – spindle cell type was given. IHC was not done for this case as patient refused for the same.

DISCUSSION

GISTs show presence in variables site of GI tract and the presentation of the patient to the hospital may vary according to the site from where it arises. In upper GI tract, GIST may present with features of upper GI bleed, whereas in lower GI, GIST may present with acute abdomen features. Extra GISTs may be silent or present with vague clinical features and are usually an incidental finding during radiological examination for some other disease. Same was observed in our series also where most common complaint was predominantly pain in abdomen, followed by constipation, upper GI bleed, and vomiting. Management of GIST varies depending on the site and presenting features apart from its malignant potential and other prognostic factors. GISTs occur throughout the GI tract most commonly arise from stomach small intestine, colon and rectum, mesentery or omentum, and esophagus in order. In our series, we studied seven cases of GIST in which age of the patients varied from 30 years to 70 years with the youngest patient being 36 years and oldest being 67 years. The various sites of lesion in our study were stomach, mesentery, ileum, jejunum, and duodenum.

Diagnosis is mainly based on CECT of abdomen and pelvis along with excision and histopathological examination of the tumor. Markers such as CD117 which are confirmatory test for the diagnosis of GIST cannot be considered gold standard as studies done have revealed as much as 6% of cases with CD117-negative GIST.[7] Prognosis mainly depends on tumor size, mitotic index, and site of origin, especially small bowel GISTs have bad prognosis.[8]

Grossly, these tumors vary in size and can reach up to 30 cm in diameter. The tumors are normally solitary and well circumscribed and may be covered with ulcerated and intact mucosa. Furthermore, these tumors can project outward toward serosa or toward the lumen. Cut surface of the tumor generally shows whorling. Size of the tumor in our cases was of the range 1.8 cm–20 cm. Out of seven cases reported, one was trucut biopsy and the cut section of the rest of the tumors was mostly gray-white homogenous with areas of necrosis and hemorrhage in few of them.

The microscopic type of tumor in three out of seven cases studied was spindle cell predominant, three were epithelioid cell predominant, and one was having neural differentiation. IHC, which was done for five out of seven cases, revealed

CD117 positivity in four of them and CD117 negativity in one. According to Fletcher criteria,[9] four out of seven cases were low risk, two were high risk and one was very low risk [Tables 1 and 2]. Five out of seven cases were reported to be benign with low risk of progression and two larger lesions were reported to have risk of progression in view of large size and histopathological features. They were put on adjuvant chemotherapy. All the patients are on follow-up and no history of metastatic process has been reported in any of the case as of now.

CONCLUSION

Thus, GISTs are the tumors which can be seen at many different sites with varied clinical presentation. Laparotomy and surgical resection remains the mainstay of treatment in which complete microscopic and macroscopic clearance of tumor should be achieved and thorough search for local and distant metastasis to be done.[2] Histomorphological diagnosis remains the gold standard diagnostic modality with CD117 positivity leading to more confirmation. Tumor size and mitotic count remain the main factors in the risk categorization of tumors. Furthermore, every spindle cell lesion should undergo CD117 IHC markers as an initial workup.

Table 1: Risk categorization of GISTs according to NIH-Fletcher criteria.

S. No.	Size (largest dimension)	Mitosis (/hpf)	Location	Risk category
1.	6 cm	<1/50	Stomach	Low risk
2.	20 cm	5/50	Mesentery	High risk
3.	9 cm	<2/50	Stomach	Low risk
4.	5 cm	<2/50	Ileum	Low risk
5.	14 cm	<2/50	Stomach	High risk
6.	5 cm	<1/50	Jejunum	Low risk
7.	1.8 cm	<1/50	Duodenum	Very low risk

Table 2: NIH-Fletcher criteria for GIST risk assessment.[9]

Risk category	Primary tumor (cm)	Mitotic count (/50 hp1)
Very low risk	<2	<5
Low risk	2-5	<5
Intermediate risk	<5	6–10
	5–10	<5
High risk	>5	>5
	>10	Any mitotic rate
	Any size	>10

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Gupta A, Suri V, Goyal N, Chhabra S, Garg A, Bhati G, *et al.* Histomorphological spectrum of gastrointestinal stromal tumors – An institutional experience in a series of seven cases. Adesh Univ J Med Sci Res 2020;2(2):112-6.