

# Gastrointestinal Stromal Tumour at An Unusual Site-Jejunum: A Case Report

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## Abstract

Gastrointestinal stromal tumors (GIST) are mesenchymal tumors of gastrointestinal tract. The incidence of jejunal GIST is extremely rare accounting for 0.1 to 3% of all gastrointestinal tumors. The term GIST should be applied only to neoplasms expressing C-Kit (CD 117) with very rare exceptions. Here we present a rare case of jejunal GIST in a 33-year-old male patient. The patient presented with a mobile lump in abdomen. On USG, diagnosis of Appendicular mass with? peri appendicular abscess was made. Laparotomy was done. A 12 cm segment of jejunum with an ovoid mass measuring 9 x 7 x 5 cm arising from serosa along the antimesenteric border was received. Histopathologically, the tumour was diagnosed as malignant GIST and confirmed immunohistochemically using CD 117 – C-Kit. The patient was given Imatinib mesylate 400 mg once daily as adjuvant chemotherapy. The patient is asymptomatic without any evidence of tumor recurrence after 1 year of postoperative follow up.

**Keywords:** GIST, Jejunum

## INTRODUCTION

GISTs are mesenchymal tumors arising in the gastrointestinal tract and occasionally elsewhere within the abdomen (omentum, peritoneum and retroperitoneum).<sup>1</sup> The incidence of GIST is very low (i.e., 2 in 1,00,000) while jejunal GIST is extremely rare accounting for 0.1-3% of all gastrointestinal tumors.<sup>2</sup> The term GIST should be applied only to neoplasms expressing c-kit (CD 117) with very rare exceptions.<sup>3</sup>

## CASE REPORT

A 33 year old male presented with mobile lump in right lower abdomen with minimal pain since 3 months. H/O intermittent fever. No H/O nausea, vomiting or bowel complaints.

On examination patient was stable. Per abdomen examination revealed a mobile tender lump, 7 cm in diameter in the right lumbar region. Blood investigations

revealed neutrophilic leukocytosis. USG and CT abdomen revealed? lymph node mass with retroperitoneal involvement. Provisional diagnosis of? appendicular lump? LN mass was made. Patient was put on antibiotics and analgesics. Patient responded well and the lump regressed in size clinically. Hence the patient was then discharged. After 3 weeks, patient was readmitted with similar complaints. USG abdomen revealed? Appendicular lump with abscess.

Exploratory laparotomy was performed. A single, mobile tumor of size 9 x 7 x 5 cm was found along antimesenteric border of proximal jejunum, 30 cms away from D-J junction. The specimen of intestine along with the tumor mass was sent to the Department of Pathology, of our institution. Appendicectomy was also performed. No lymph node involvement noted. Liver, spleen and rest of the bowel were normal.

### Gross

A 12 cm segment of intestine with a pedunculated ovoid mass measuring 9 x 7 x 5 cm was received. Externally,

the tumor mass was smooth and at places nodular, soft to firm in consistency. The mass was seen arising from the antimesentric border of the serosa. Cut section of tumor mass revealed a brownish tumor mass with cystic areas containing blood stained fluid. The tumor was not communicating with intestinal lumen. At the base of the tumor mass, a solid greyish white  $2 \times 1.5$  cm area was seen (Figures 1 and 2).

Appendix – unremarkable.

### **Microscopy**

Histopathology revealed

- Partially encapsulated tumor mass (Figure 3)
- With predominant fascicular growth pattern (Figure 4)
- Predominantly spindle cells with eosinophilic to clear cytoplasm
- Minimal nuclear pleomorphism
- Mitotic figures few
- Presence of tumor cell necrosis (Figure 5)



Figure 1: Specimen of segment of Jejunum with tumor mass



Figure 2: Cut section of tumor mass showing areas of cystic change and necrosis

- Absence of mucosal infiltration
- Absence of skenoid fibers.

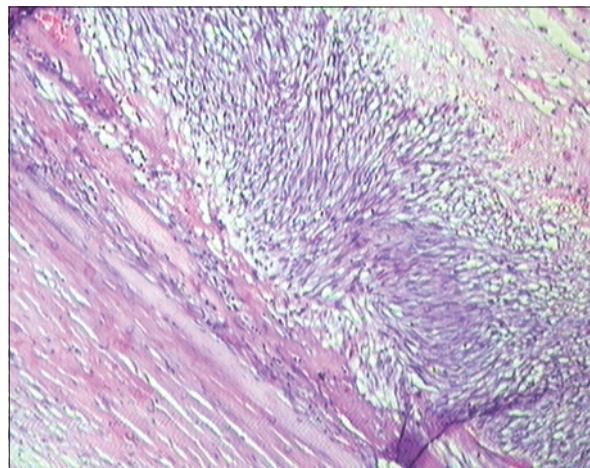


Figure 3: Photomicrograph showing encapsulated tumor mass (H & E 10X)

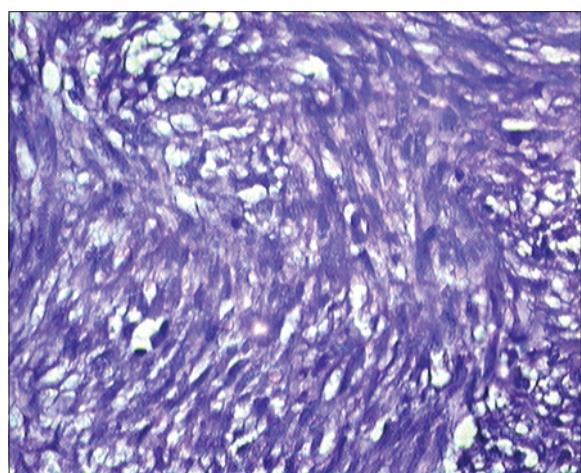


Figure 4: Photomicrograph showing fascicles of spindle cells (H & E 10X)

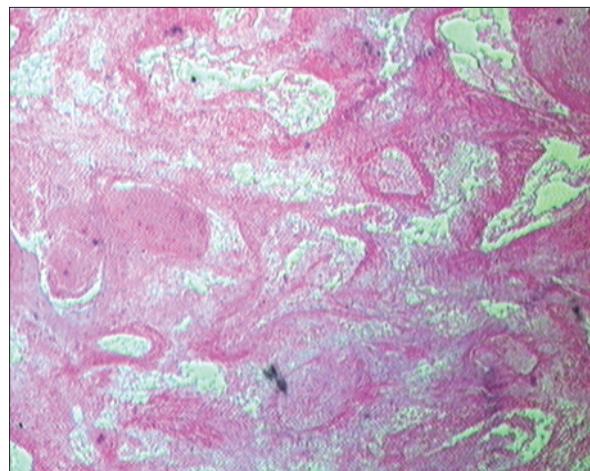


Figure 5: Photomicrograph showing large areas of necrosis (H & E 10X)

In view of

- Large tumor size ( $> 5$  cm in diameter)
- High mitotic count ( $>5/50$  hpf)

The diagnosis of Malignant GIST with areas of haemorrhagic necrosis and cystic degeneration was suggested. Immunohistochemistry revealed c-kit (CD 117) positivity, which further confirmed the diagnosis of GIST.

The patient was put on Imatinib mesylate 400 mg OD for 1 year and discharged. Patient is still on follow up and is doing well.

## DISCUSSION

Gastrointestinal stromal tumors were classified in earlier literature as smooth muscle or nerve sheath tumors. But evidence of such differentiation was difficult to find even in the benign tumors and Mazur and Clark introduced the term stromal tumor in 1983 for such lesions. GIST constitutes a distinct group of rare gastrointestinal tract tumors that originate from or differentiate towards the interstitial cells of Cajal which are involved in regulation of gastrointestinal motility by pacemaker activity and also have a role in muscle relaxation.<sup>1</sup>

GISTs are most common in adults, 50-60 years of age.<sup>1</sup> However Dhull et al reported a case of jejunal GIST in a 38 year male patient.<sup>2</sup> Both men and women are equally affected.<sup>4</sup> The vast majority of GISTs (up to 70%) arise in the stomach with 20-30% originating in small intestine and remaining 10 % occurring in esophagus, colon and rectum.<sup>5</sup> The most common clinical manifestation for symptomatic GIST is occult gastrointestinal bleeding from mucosal ulceration and pain in abdomen.<sup>2</sup> The tumor may present clinically as a

- Mass<sup>1</sup>
- Acute abdomen caused by tumor rupture
- GI obstruction
- Appendicitis like pain
- Other clinical symptoms include: fatigue, dysphagia and satiety
- Smaller lesions may be incidental findings.<sup>4</sup>

In our case, the patient was a 35 year old male patient, who presented with a mobile painful lump in the abdomen. Pain and fever are due to secondary changes of necrosis and inflammation.

Grossly, GIST usually produces a mass that may involve all layers of the gut, may grow extramurally and may extend intraluminally to cause mucosal ulceration. Most GISTs are circumscribed, solitary, rounded or ovoid masses. On cross section, GISTs are not whorled or bulging rather;

they have a relatively nondescript pinkish white appearance, often with areas of hemorrhage, necrosis, myxoid change or cavitary degeneration. Both benign and malignant GISTs have similar macroscopic appearances, thus preventing the categorization of biologic behaviour based on gross configuration.<sup>3</sup>

In our case the tumor presented as a extramural tumor and had the characteristic appearance of GIST as described.

Histologically, most cases fall into one of the following three categories

- Spindle cell type-70%
- Epithelioid type- 20%
- Mixed type-10%

Histologically, the tumor was of the spindle cell type, in our case.

The best predictor of biologic behaviour is size and mitotic count.

1. Probably benign

Intestinal tumors: maximum diameter less than or equal to 2 cm and no more than 5 mitosis per 50 hpf

2. Probably malignant

Intestinal tumors: maximum diameter greater than or more than 5 cm and more than 5 mitosis per 50 hpf

3. Uncertain or low malignant potential

Intestinal tumors: maximum diameter greater than 2 cm but no more than 5 cm and no more than 5 mitosis per 50 hpf.

In small intestine, most GISTs are malignant.<sup>3</sup> With the help of the above criteria we classified the tumor in the present case as malignant GIST.

Brainard, Jennifer A et al studied 39 cases of stromal tumors of jejunum and ileum and concluded that the features associated with adverse outcome included tumor size  $>5$  cm, and mitotic counts  $>5$  mitotic figures per 50 hpf.<sup>6</sup>

### Immunohistochemistry

CD 117 positivity (diffuse cytoplasmic staining with membranous accentuation) is seen nearly in all GISTs with spindle cell or epithelioid morphology, though less intensely in the latter. A small number of otherwise typical GISTs are CD 117 negative and immunoreactivity for CD 117 is sometimes lost in metastasis. Other tumor markers include CD 34, h- caldesmon and calponin. Cytokeratin are usually absent but occasionally seen in epithelioid GIST. A few GISTs have presumed neuronal differentiation with positivity for S-100 (especially in small bowel tumors, in 10-15%, PGP9.5 and NSE and some of these additionally express smooth muscle actin, implying both neurogenic and myoid differentiation.<sup>1</sup>

IHC was carried out in our case which revealed c-kit (CD 117) positivity.

### Genetics

The c-kit protooncogene, located on chromosome 4q 11-21 encodes a type III receptor tyrosine kinase protein CD 117. Over 95% of GISTs have mutations in one of the 2 genes kit (CD117) and PDGFRA. Recent gene expression profiling has shown that a novel gene DOG1 is expressed ubiquitously in GIST irrespective of kit or PDGFRA mutation status, which might be useful for diagnosis or guidance of therapy in kit negative cases.<sup>1</sup>

### Prognosis

Small intestinal tumors have a worse prognosis than gastric GISTs. The overall 10 year survival is around 17% in small intestinal tumors.<sup>1</sup> Pfetin appears to be a novel clinically applicable prognostic factor, which may be useful for deciding whether to administer imatinib mesylate or not.<sup>7</sup>

### TREATMENT

Surgery is the primary treatment of choice. Local recurrence and or metastatic spread after surgery has been seen in 40-90% of cases treated surgically.

Over 95% of GISTs have mutations in one of the 2 genes kit (CD117) and PDGFRA. The drug Imatinib mesylate targets both of these mutated genes and blocks cellular communication that result in tumor growth. Imatinib mesylate was the first approved by FDA in 2001. It is the first and only effective drug for treatment of GIST at present. As per latest ASCO guidelines, recurrence free survival is increased in patients who take one year of imatinib 400 mg/day. Imatinib is recommended in metastatic, residual, or recurrent cases of GISTs or which are surgically not removable; however, recent recommendations suggests that use of imatinib mesylate as adjuvant therapy after radical surgery in high risk cases, because it has shown significant decrease in recurrence rate.<sup>2</sup>

The patient, in our case, received imatinib as per ASCO guidelines so as to decrease chances of recurrence.

Most malignant GISTs run a slow course with recurrence and metastases developing over years sometimes 10-15 years. These features indicate that long term follow up is essential.<sup>3</sup> In our case, the patient is on regular follow up and is doing well.

### CONCLUSION

The differential diagnosis of GIST include a wide range of tumors with spindle cell and epithelioid morphology. They include smooth muscle cell tumors inflammatory myofibroblastic tumor, Schwannomas, inflammatory fibrous, polyp, glomus tumor, fibromatosis solitary fibrous tumour, spindle cell carcinoma, follicular dendritic cell sarcoma, PEComas, mesothelioma and dedifferentiated liposarcoma. Almost all GISTs show strong diffuse positivity for CD 117, which is a defining feature of this tumor. An estimate of risk (malignant potential) can be made from tumor diameter and mitotic index. Tumors arising in oesophagus, small intestine or colon behave more aggressively than those in the stomach. Specific targeted therapy with a selective inhibitor of receptor tyrosine kinase such as imatinib, can produce a significant therapeutic response in GISTs. Most malignant GISTs run a slow course with recurrence and metastasis developing over years, sometimes 10-15 years. These features indicate that long term follow up is essential. In our case, the patient is on regular follow up and is doing well.

### ACKNOWLEDGEMENTS

Authors want to give special thanks to Dr. Sandesh Gawde (Lecturer, Surgery) for providing the clinical details of the patient and informing about the follow up of the case. They would also like to thank Mrs. Maitreyee Marathe for helping them with the preparation of this manuscript.

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**How to cite this article:** Jaison J, Joshi SR, Pathak S, Tekwani D, Nagare M. Gastrointestinal Stromal Tumour at An Unusual Site-Jejunum: A Case Report. Int J Sci Stud 2014;2(4):80-83.

**Source of Support:** Nil, **Conflict of Interest:** None declared.