

Original Research Article

Histopathological spectrum of spindle cell tumours of gastro-intestinal tract

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ABSTRACT

Background: Spindle cell lesions of gastro-intestinal tract (GIT) are relatively uncommon tumours compared to epithelial tumours. The anatomic location of spindle cell tumour is important, whether the tumour is located in mucosa, submucosa or muscularis propria.

Methods: Authors endeavoured to study the histopathological spectrum of spindle cell lesions for a period of one year from January 2018 to December 2018 in our hospital.

Results: This was a prospective study of 1 year starting from January 2018 to December 2018. A total of 30 cases of spindle cell lesions of gastrointestinal tract were seen. Out of 30 cases 23 were gastrointestinal stromal tumours (GIST), 2 cases were schwannomas, 2 cases were of leiomyomas, 1 case was fibromatosis, 1 case was inflammatory fibroid polyp, and one case was inflammatory myofibroblast tumour.

Conclusion: GISTs are the commonest spindle cell tumours of GIT. Besides GIST, there are other spindle cell tumours which range from benign to malignant, and need to be differentiated from GIST for proper management.

Keywords: Fibromatosis, Gastrointestinal stromal tumour, Gastrointestinal tract, Inflammatory fibroid polyp, Inflammatory myofibroblast, Schwannoma, Tumour Spindle cell lesions

INTRODUCTION

Spindle cell lesions of gastrointestinal tract are relatively uncommon tumours compared to epithelial tumours. These lesions are mesenchymal in nature and can be derived from fibroblasts, smooth muscles, neural tissue, endothelial cells.¹ The anatomic location of spindle cell tumour is important, whether the tumour is located in mucosa, submucosa or muscularis propria.² Lesions common in mucosa are benign epithelioid nerve sheath tumour, sporadic ganglioneuroma, Schwann cell hamartoma, psammomatous melanotic schwannoma, benign fibroblastic polyp, peri-neuroma, leiomyoma and Kaposi sarcoma.² Submucosal lesions include inflammatory fibroid polyps and lipomas. Lesions present

in muscularis propria are gastrointestinal stromal tumour (GIST), leiomyoma, leiomyosarcoma, inflammatory myofibroblastic tumour, fibromatosis, schwannoma, GI clear cell sarcoma and plexiform fibromyxoma.² Mesenteric lesions are found in the small bowel mesentery. These include mesenteric fibromatosis, inflammatory myofibroblastic tumour, sclerosing mesenteritis and calcifying fibroblastic pseudotumour.² GISTs should always be considered in the differential diagnosis of spindle cell tumours of the GIT as GISTs constitute the largest subset of mesenchymal tumours of the GIT. GIST cell morphology is usually spindle-shaped (70%), although certain GISTs consist of epithelioid cells (20%) or a mixture of cells.^{3,4}

METHODS

Authors endeavoured to study the histopathological spectrum of spindle cell lesions in our hospital. This was a prospective and observational study. This study was conducted for a period of one year from January 2018 to December 2018 in our hospital. A total number of 30 cases were included in our study. Patients with spindle cell tumours and its different histopathological subtypes were included in this study. Patients with adenocarcinomas, carcinoids and undifferentiated tumours were excluded from this study. The study was conducted on the surgical specimens which were received in our department of pathology. The specimens which were included in our study were total gastrectomy specimens, partial gastrectomy specimens, partial colectomy specimens, total colectomy specimens or resected tumour specimens. All the specimens transported from the surgical operation theatres were fixed in 10% formalin for 48-72 hours. After fixing the specimens, they were subjected to grossing. Macroscopic features like size, external surface, consistency, cut-section and colour of the tumour were noted in each case. The grossed specimens were then processed routinely in the department. The sections received were subjected to routine haematoxylin and eosin (H and E) staining. Authors also used special stains wherever necessary. Special stains used in this study were Masson's trichrome, Periodic Acid Schiff (PAS) and reticulin. Immunohistochemistry was done in all the cases for confirmation. The IHC markers used were CD117, CD34, DOG1, SMA, vimentin, desmin, beta-catenin ALK and S-100.

Statistical analysis

The data was analysed using statistical software's SPSS v 20 and STATA v 11. Categorical variables were described in terms of percentage.

RESULTS

This was a prospective study of 1 year starting from January 2018 to December 2018. A total of 30 cases of spindle cell lesions of gastrointestinal tract were seen. Out of 30 cases 23 were gastrointestinal stromal tumour (GIST), 2 cases were schwannoma, 2 cases were leiomyoma, 1 case was fibromatosis, 1 case was inflammatory fibroid polyp, and single case was inflammatory myofibroblastic tumour.

Our patients were in age range of 38-75 years and predominant age group was >50 years. 21 patients were males and 9 patients were females. The most common symptom was pain in abdomen in all the 30 patients, however, in oesophageal lesions dysphagia was the common complaint.

The gastric lesions presented with epigastric pain, fullness along with vomiting. Intestinal lesions presented

with pain in abdomen and intestinal obstruction. Most common site of tumour was stomach in 16 patients (Table 1).

Table 1: Location of spindle cell tumours.

Site	No. of patients (n) (%)
Oesophagus	2 (6.7)
Stomach	16 (53.3)
Small Intestine	6 (20.0)
Large Intestine	6 (20.0)
Total	30 (100)

Table 2: Histopathological diagnosis of spindle cell tumours.

Histopathological Diagnosis	No. of patients (n) (%)
GIST	23 (76.7)
Leiomyoma	2 (6.7)
Fibromatosis	1(3.3)
Inflammatory fibroid polyp	1 (3.3)
Inflammatory myofibroblastic tumour	1(3.3)
Schwannoma	2 (6.7)
Total	30(100)

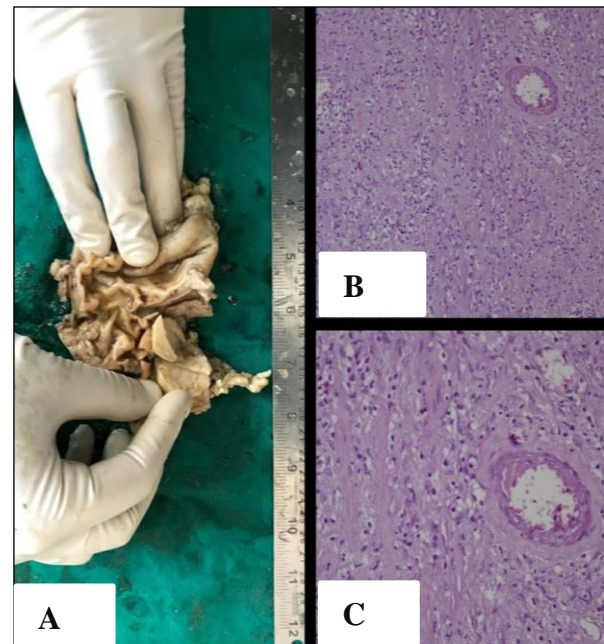


Figure 1: (A): Gross photograph of colon showing a pedunculated mass lesion measuring 3x3cm. External surface is regular and cut section is grey white firm. (B): Scanner (4x) view photomicrograph of the same lesion revealing spindle cells arranged in fascicles with mixed inflammatory cells and prominent vasculature. Cells have pink cytoplasm with ovoid to spindle nuclei. Features are suggestive of inflammatory fibroid polyp. (C): Low(10x) power view of the same lesion.

On histopathology 1 patient had inflammatory fibroid polyp (Figure 1), GIST (Figure 2) was the commonest spindle cell tumour diagnosed in our study in 23 patients (Table 2). Out of 16 patients of gastric lesions histopathology revealed schwannoma in 2 patients (Figure 3), inflammatory myofibroblastic tumour in 1 patient and rest 13 patients had GIST. Out of 13 patients, 2 had epithelioid GISTS, 9 patients had GIST with low malignant potential, 4 has GIST with high malignant potential. 2 Patients with oesophageal tumour had leiomyoma. 6 Small intestinal lesions proved out to be GIST on histopathology and were CD117 positive on IHC. In patients with colonic lesions 4 had GIST, 1 had fibromatosis (Figure 4).

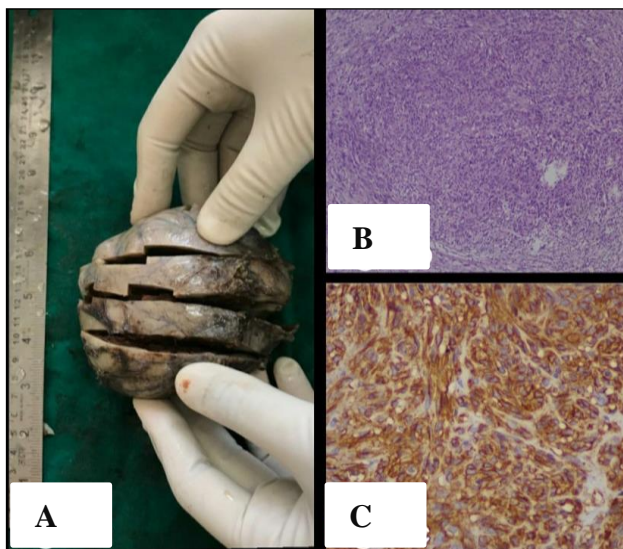


Figure 2: (A): Gross photograph showing a globular mass lesion measuring 4x4 cm. external surface is encapsulated and cut section is grey white, firm. **(B):** Low(10x) power view photomicrograph showing spindle cells arranged in fascicles and whorls with eosinophilic cytoplasm and spindle nuclei. There nuclear palisading with minimal nuclear pleomorphism. Features are suggestive of gastrointestinal stromal tumour (GIST). **(C):** Photomicrograph showing the strong diffuse positivity for CD117 thus favouring the diagnosis of GIST.

Cont'd

Axial contrast-enhanced CT images of upper abdomen of the same patient showing a heterogeneously enhancing soft tissue attenuation rounded lesion (2d) measuring 3.8 x 3.1 cm (2e) arising from 2nd part of duodenum and extending anteriorly.

DISCUSSION

Gastrointestinal malignancy is a global oncological problem.⁵ Kashmir is a high-risk area for Gastrointestinal tract cancers, which comprise more than half the frequency of all the cancers.⁶ However it is important to categorise the tumours into spindle cell tumours and

differentiate them from epithelial tumours. The most common spindle cell tumour in our study was GIST in 23 patients and the most common location was stomach (in 13 patients).

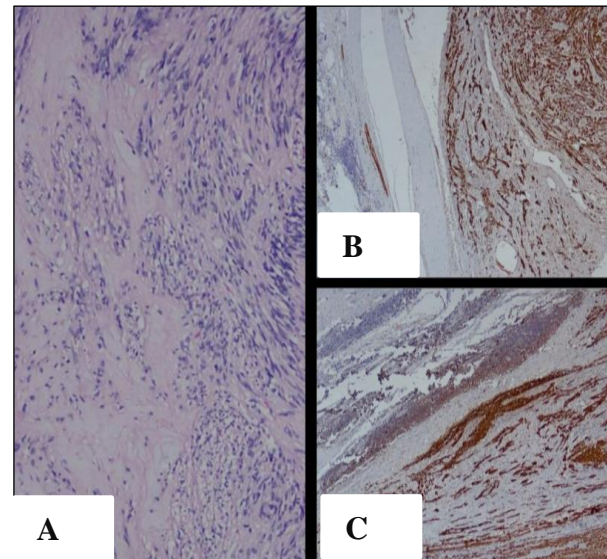


Figure 3: (A): Low(10x) power view photomicrograph showing bland spindle cells arranged in fascicles with hypercellular and hypocellular areas and eosinophilic cytoplasm. Areas of vacuolation are also seen. Features are suggestive of schwannoma. **(B):** and **(C):** Photomicrograph showing diffuse and strong positivity for S-100 however the capsule shows lymphocytic cuff which is negative.

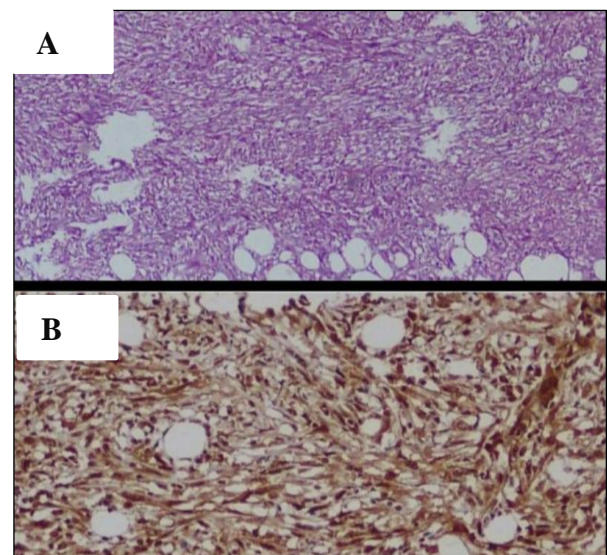


Figure 4: (A): Low(10x) power photomicrograph showing spindle cells with uniform appearing nuclei arranged in fascicles with pale pink cytoplasm in collagenous stroma. Nuclei are bland. **(B):** Photomicrograph showing cells with diffuse and strong positivity for beta catenin. Above histological features along with the IHC favour diagnosis of fibromatosis.

In the study conducted by Voltaggio L et al, it is mentioned that the most common site of GIST is stomach and is located in muscularis propria. GISTs are occasionally diagnosed on mucosal biopsy if the lesion is too aggressive to have invaded mucosa.² GISTs are most common in adults of 50–60 years and about 25% of GISTs are malignant, representing almost 1% of all GI malignancies.⁷ According to the location, oesophageal GISTs are rare, 50-70% are seen in the stomach; 25-40% involve the small intestine and <10% are colorectal.⁷ In our study stomach was the commonest site followed by small intestine. IHC was done for the confirmation of diagnosis of GIST, only 3 tumours (epithelioid GISTs) were negative for CD117, these however, were positive for DOG1. Rest all the tumours were positive for CD117. However, an important pitfall is that nearly a third of gastric adenocarcinomas express DOG1 which makes the diagnostic issue with epithelioid GIST, but strong diffuse keratin expression is observed in carcinomas.⁸ Another pitfall is that epithelioid GISTs sometimes label with melan-A which is positive in malignant melanoma.⁹

Inflammatory fibroid polyp was seen in 64-year-old female and was located in right colon. Microscopy revealed spindle cells arranged in fascicles with mixed inflammatory cells and prominent vasculature. The spindle cells show amphophilic cytoplasm and pale nuclei which are ovoid to spindle shape, with variable collagen deposition and infrequent mitosis. IHC was done which was CD 34 positive, smooth muscle actin (SMA) negative, beta catenin negative and thus favoured the diagnosis. Inflammatory fibroid polyp was described in a case series in 1949, although there were prior case reports. Most patients are in the age group of 60 and 80 years.^{2,10} Clinical presentation is based on the site of the tumour thus the small intestinal examples can lead to intussusception or obstruction, and gastric examples are found in patients with pain, nausea, and vomiting.¹¹ Inflammatory fibroid polyps were reported in a family in which three generations of women had these 'Devon polyposis' lesions.^{12,13} These polyps were believed to be reactive in the past, but they are now known to have mutations in the platelet-derived growth factor receptor alpha (PDGFRA) gene, a feature that they share with a subset of GISTs.¹⁴ However, in contrast to GISTs, inflammatory fibroid polyps are always benign.²

Two cases of schwannoma were seen. These patients presented with pain epigastrium and vomiting. Mostly schwannomas show female preponderance and are located in the stomach, the layer of origin being muscularis propria.¹⁵ Likewise in our study both the tumours were situated in stomach and both the patients were females who were above 50 years of age. As the schwannomas arise from muscularis propria, they are nearly always assumed to be GISTs preoperatively and intra-operatively.¹⁶ Grossly schwannomas have fibrotic, rubbery, white-yellow cut surface, and well-circumscribed outline typically without a capsule. The

tumour is surrounded by a lymphoid cuff in >90% of the cases.¹⁶ On biopsy or fine needle aspiration, the material is obtained from this lymphoid cuff rather than the mesenchymal lesion, potentially misleading the observer to a diagnosis of lymphoma.¹⁶

One patient with fibromatosis was a 40-year old female with a lesion in hepatic flexure. Authors received a small colonoscopic biopsy of the patient and the biopsy revealed spindle cells arranged in fascicles, low mitotic activity and bland nucleus, fine collagen stroma with evenly spaced blood vessels. Features were suggestive of fibromatosis. Patient was operated and a huge mesenteric fibromatosis infiltrating the right sided colon was noticed. Mesenteric fibromatosis is commonest among the intrabdominal fibromatosis and besides involving the mesentery, they often infiltrate into the muscularis propria but never into the submucosa or mucosa.² Grossly, the tumour is firm with coarse white trabeculation resembling a scar and cuts with a gritty sensation. IHC was negative for CD 117, S100, CD34, however SMA was positive, beta catenin showed nuclear positivity, hence confirming fibromatosis.

Another 60-year old patient came with complaint of recurrent pain epigastrium, endoscopy revealed a mass, patient was operated, and histopathology revealed bland spindle cells with abundant amphophilic cytoplasm and prominent nucleoli with lymphoplasmacytic inflammatory infiltrate in the background. IHC was done and SMA, desmin, ALK were positive, however CD117, S100 and CD34 were negative. Thus, the diagnosis of inflammatory myofibroblastic tumour (IMFT) was made. Inflammatory myofibroblastic tumour (IMFT), is a type of submucosal spindle cell tumour, and was first described in 1939. It commonly occurs in the lung and the orbit however, an IMFT can basically be found throughout the body.¹⁷

There were 2 cases of leiomyoma involving oesophagus. One patient was 62-year old male with complaint of dysphagia for 1 month with endoscopy revealing mass lesion in lower oesophagus. Tumour excision was done, and diagnosis of leiomyoma was made. Other patient was a 50-year old male with similar complaints. On histopathological examination, the oesophageal leiomyomas appear as circumscribed lesions composed of intersecting fascicles of bland spindle cells with abundant cytoplasm. The spindle cell bundles are demarcated by adjacent tissue or a definite connective tissue capsule. The tumour cells have blunt elongated nuclei and display minimal atypia and very few mitotic figures. On IHC, these are positive for desmin and alpha-smooth muscle actin while staining negative for the CD34, CD117 and S100.

CONCLUSION

GISTs are the commonest spindle cell tumours of GIT. Besides GIST, there are other spindle cell tumours which

range from benign to malignant and need to be differentiated from GIST for proper management. Thus, diagnosis of spindle cell tumour is a challenge to a pathologist who should properly examine the histopathology slides and support his diagnosis by IHC.

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Conflict of interest: None declared

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

REFERENCES

1. Virani N, Pang J, Lew M. Cytologic and immunohistochemical evaluation of low-grade spindle cell lesions of the gastrointestinal tract. Arch Pathol Lab Med.. 2016 Oct;140(10):1038-44.
2. Voltaggio L, Montgomery EA. Gastrointestinal tract spindle cell lesions- just like real estate, it is all about location. Modern Pathol. 2015;28(S1):47-66.
3. Miettinen M, Sarlomo-Rikala M, Sobin LH. Mesenchymal tumours of muscularis mucosae of colon and rectum are benign leiomyomas that should be separated from gastrointestinal stromal tumours - A clinicopathologic and immunohistochemical study of eighty-eight cases. Mod Pathol. 2001;14(10):950-6.
4. Rosai J. Gastrointestinal stromal tumour and its mimics. Int J Surg Pathol. 2010;18: S79-87.
5. Sahid J, Nadira M, Mushtaq S, Luqman M. Analysis of gastrointestinal malignancies at the armed forces institute of pathology, Rawalpindi, Pakistan. Asian Pac J of cancer prev. 2005;6(4):497-500.
6. Pandith A, Siddiqi M. Burden of cancers in the valley of Kashmir.5-year epidemiological study reveals a different scenario. Tumour Biol. 2012 Oct; 33(5):1629-37.
7. Emory TS, Sobin LH, Lukes L, Lee DH, O'Leary TJ. Prognosis of gastrointestinal smooth-muscle (stromal) tumors: dependence on anatomic site. The Am J surgical pathol. 1999 Jan 1;23(1):82-7.
8. Miettinen M, Wang ZF, Lasota J. DOG1 antibody in the differential diagnosis of gastrointestinal stromal tumours: a study of 1840 cases. Am J SurgPathol. 2009;33(9):1401-8.
9. Guler ML, Daniels JA, Abraham SC, Montgomery EA. Expression of melanoma antigens in epithelioid gastrointestinal stromal tumours: a potential diagnostic pitfall. Arch Pathol Lab Med.2008;132(8):1302-6.
10. Vanek J. Gastric submucosal granuloma with eosinophilic infiltration. Am J Pathol.1949;25:397-411.
11. Liu TC, Lin MT, Montgomery EA, Singhi AD. Inflammatory fibroid polyps of the gastrointestinal tract: spectrum of clinical, morphologic, and immunohistochemistry features. Am J SurgPathol. 2013;37(4):586-92.
12. Allibone RO, Nanson JK, Anthony PP. Multiple and recurrent inflammatory fibroid polyps in a Devon family ('Devon polyposis syndrome'): an update. Gut.1992;33(7):1004-5.
13. Anthony PP, Morris DS, Vowles KD. Multiple and recurrent inflammatory fibroid polyps in three generations of a Devon family: a new syndrome. Gut.1984;25(8):854-62.
14. Schildhaus HU, Cavlar T, Binot E, Büttner R, Wardelmann E, Merkelbach-Bruse S. Inflammatory fibroid polyps harbour mutations in the platelet-derived growth factor receptor alpha (PDGFRA) gene. J Pathol: A Journal of the Pathological Society of Great Britain and Ireland. 2008 Oct;216(2):176-82.
15. Voltaggio L, Murray R, Lasota J, Miettinen M. Gastric schwannoma: a clinicopathologic study of 51 cases and critical review of the literature. Human pathol. 2012 May 1;43(5):650-9.
16. Rodriguez E, Telschow S, Steinberg DM, Montgomery E. Cytologic findings of gastric schwannoma: a case report. Diagn Cytopathol.2014;42(2):177-80.
17. Narla LD, Newman B, Spottswood SS, Narla S, Kolli R. Inflammatory pseudotumor. Radiographi. 2003 May;23(3):719-29.

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