

Original Research Article

Malignant GIST & EGISTs: A Clinicopathologic and Immunohistochemical Study of 6 Cases

Shere Sunita¹, Gupta Shruti¹, Mulay Vijay², Bindu Rajan³

¹Assistant Professor, ²Associate Professor, ³Professor, GMC Aurangabad,
Dept. of Pathology, GMC Aurangabad, Maharashtra, India

Corresponding Author: Shruti Gupta

Received: 22/11/2015

Revised: 12/12/2015

Accepted: 18/12/2015

ABSTRACT

Gastrointestinal stromal tumors (GIST) and Extra-gastrointestinal stromal tumor (EGIST) are relatively rare mesenchymal tumors. With advent of researches in field of mesenchymal tumors and use of immunohistochemical markers, diagnosis of these stromal tumors has become quite effortless. However, diagnosis of malignant potential of GIST & EGIST takes several factors into consideration. In this study, we discuss 6 cases of GISTs and EGISTs, all labeled malignant, in regard of clinicopathologic correlation, prognostic factors and confirmation of diagnosis by immunohistochemistry using relevant markers.

Keywords: GIST, EGIST, malignant.

INTRODUCTION

Gastrointestinal stromal tumours (GIST) are relatively rare soft tissue mesenchymal tumours occurring in the gastrointestinal tract, originating in the interstitial cells of Cajal involved in the regulation of the digestive system. [1] Extra-gastrointestinal stromal tumor (EGIST) is a special type of gastrointestinal stromal tumor, which has similar biological characteristics to its counterpart, and occurs outside the gastrointestinal tract. It was identified first by Miettinen *et al.*, and named by Reith *et al.* The incidence of EGIST is extremely low, and so far there is no detailed epidemiological figure. [2] In the present study, we analyze the clinicopathologic and immunohistochemical characteristics of 6 cases of malignant stromal tumours including 3 GISTs & 3 EGISTs.

MATERIALS & METHODS

In the present study, all cases diagnosed histopathologically as GISTs with malignant behaviour pattern were included. The demographics, clinical features, lab investigations and radiological findings were obtained. Resected Surgical specimens were collected in fixatives (10% formalin). After fixation, a thorough gross examination was done which includes size, shape, colour, consistency and cut surface. Hematoxylin and eosin stained slides were reviewed in each case. Immunohistochemistry was performed on FFPE (formalin fixed, paraffin embedded) sections with appropriate controls. Two expert histopathologists confirmed the morphologic diagnosis of GIST, identified the pattern and calculated the mitotic index. The main prognostic factors, such as size, mitotic index, metastases were

analyzed and Fletcher's classification was used. Predominant cell type was defined as the pattern present in more than 50% of the tumor. Tumors classified as spindle consisted of spindle or fusiform cells usually associated with a fibrillary collagenous background, whereas epithelioid tumors consisted of relatively round cells. Tumors were classified as mixed when the proportions of the two patterns was roughly equal. Cellularity was considered high when nuclei frequently touched one another, whereas in low cellularity tumors the nuclei were clearly separate from one another. Mitotic activity was determined by counting the number of mitotic figures per 50 HPF in the area of highest cellularity. Metastasis was defined as recurrent tumor at some distance from the original tumor or tumor recurring as multiple lesions. [3] The diagnosis of GIST was confirmed by immunohistochemical staining for CD117 and CD34

OBSERVATIONS

The clinicopathologic features & immunohistochemical characteristics of patients with GISTs and EGISTs are summarized in Table 1 & Table 2 respectively.

Our study comprised of 6 cases of malignant stromal tumours, of which 3 were confined to the gastrointestinal tract while the other 3 were located elsewhere. Amongst the three GISTs, one was located in the Stomach, while other two were found in Sigmoid colon & jejunum. The EGISTs in our study were located in liver & mesentery. All our patients were adults, youngest 25 yrs of age and oldest of 68 years.

GIST arising from stomach and jejunum had spindle morphology while that arising from sigmoid colon showed epithelioid pattern. Few cases of GIST in sigmoid colon are found in literature. Ours was a large Sigmoid mass in a 60 year

male patient with rectal bleeding and abdominal pain.

All had high rates of mitoses (>5/50 hpf) and apart from the morphological diagnosis, immunohistochemical staining of all cases done with CD117 and CD34 showed positive results.

We had two EGISTs arising from liver, few cases with liver as primary have been described in literature. Both had epithelioid morphology and positive immunohistochemical staining with CD117 & CD34. 45 year male who presented with pain in right hypochondrium and jaundice and a large liver mass of 20x15x10 cm also showed a large mass of 7x4x4 cm attached to the colon, which was found to be metastatic deposits of GIST, hence reported as malignant EGIST. (Fig. 1(a) and 1(b)). Another was a 47 year male with a 10x 8 x 6 cm mass arising from left lobe of liver, histologically showed epithelioid pattern and positive staining with CD117 and CD34. (Fig.2) The EGIST arising from mesentery was in a 56 year male presenting with a huge mass of 30x 25x10 cm filling the abdominal cavity with a grey white necro-haemorrhagic cut surface.

Prognosis was assessed in regard to 2002 NIH consensus guidelines of GIST [4] and all our cases were found to be high risk category and thus malignant.

DISCUSSION

Gastrointestinal stromal tumor (GIST) is a nonepithelial, mesenchymal tumor first described by Mazur and Clark in 1983. [5] Gastrointestinal Stromal Tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract, it actively express CD-117. Predilection sites of GIST are stomach (60~70%), small intestine (25~35%), large intestine and appendix (5%), esophagus (2~3%) and extra-gastrointestinal (<5%). The mesenchymal tumor in extra-gastrointestinal always occurs at a lower frequency in extra-gastrointestinal regions

such as omentum, mesentery, retroperitoneum and undefined abdominal sites. This tumor is called

Extragastrintestinal Stromal Tumor (EGIST).^[6]

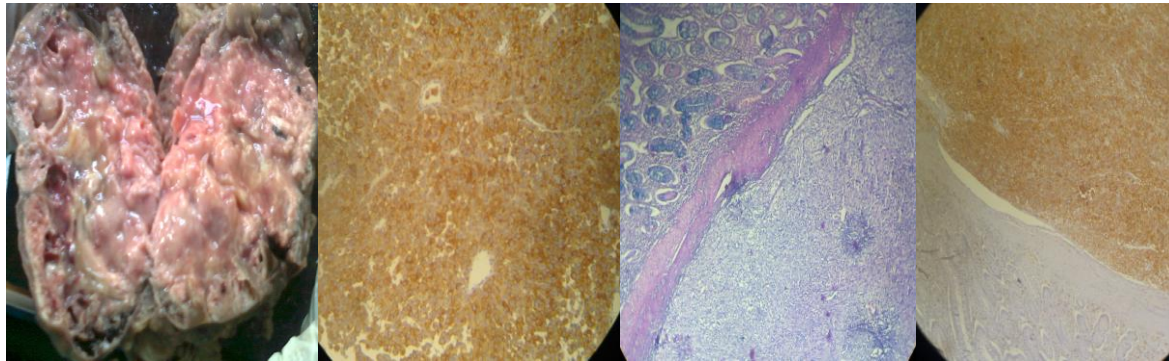


Fig. 1: Intra-operative gross photograph of the hepatic mass and microphotograph showing immunohistochemical staining by CD117. Microphotograph of sections from colonic mass showing tumor mass composed of epitheloid cells compressing surrounding colonic tissue. (H& E,100X) followed by immunohistochemical staining by CD117 showing positivity.

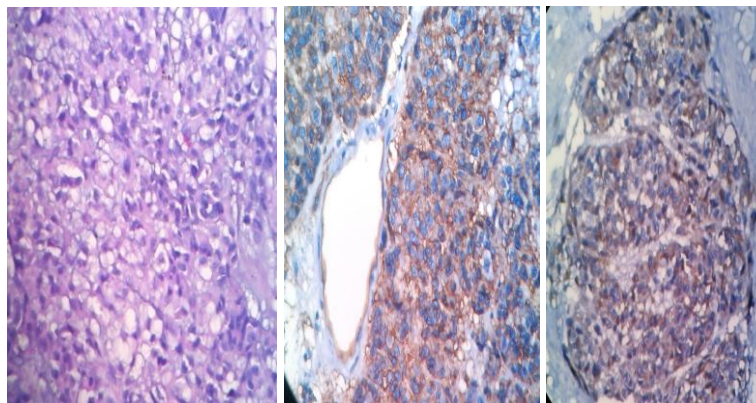


Fig. 2: Microphotograph from liver mass showing epitheloid pattern of cells(H & E, 400X) and positive immunohistochemical staining with CD34 and CD117.

TABLE 1 Gist: Clinicopathologic & Immunohistochemical Features

| CASE No. | AGE/SEX | C/P | LOCATION | HISTOPATHOLOGY | | | IHC | |
|----------|---------|----------------------------|---------------|----------------|------------|-----------|-------|------|
| | | | | SIZE(cms) | PATTERN | MITOSES | CD117 | CD34 |
| 1 | 68/F | Pain Abdo, Epigastric lump | STOMACH | 9X8X6 | SPINDLE | >5/50 HPF | +VE | +VE |
| 2 | 25/F | Pain abdo | JEJUNUM | 9X5X4 | SPINDLE | >5/50 HPF | +VE | +VE |
| 3 | 60/M | Pain abdo, PR bleeding | SIGMOID COLON | 15X12X10 | EPITHELOID | >5/50 HPF | +VE | +VE |

C/P- Clinical presentation, M- male, F- female, IHC- immunohistochemistry, Abdo- abdomen, PR- per rectal, HPF- high power field, +VE- positive.

TABLE 2 Egist: Clinicopathologic & Immunohistochemical Features

| Case No. | AGE/SEX | C/P | LOCATION | HISTOPATHOLOGY | | | IHC | |
|----------|---------|--------------------------------|-----------|----------------|------------|-----------|-------|------|
| | | | | SIZE(cms) | PATTERN | MITOSES | CD117 | CD34 |
| 1 | 45/M | Pain in Rt. hypo, h/o jaundice | LIVER | 20X15X10 | EPITHELOID | >5/50 HPF | +VE | +VE |
| 2 | 56/M | Pain Abdo Abdo distention | MESENTERY | 30X25X10 | SPINDLE | >5/50 HPF | +VE | +VE |
| 3 | 47/M | Pain Abdo | LIVER | 10X8X6 | EPITHELOID | >5/50 HPF | +VE | +VE |

Rt.- Right, hypo- hypochondrium, h/o- history of, abdo- abdomen

TABLE 3 2002 Nih Consensus Guidelines of Gist Risk Assessment Bases of tumour size and Mitotic Frequency [4]

| RISK CATEGORY | TUMOUR SIZE (cms) | MITOSIS/50 HPF |
|-------------------|-------------------|----------------|
| Very Low Risk | <2 | <5 |
| Low Risk | 2-5 | <5 |
| Intermediate Risk | <5 | 6-10 |
| | 5-10 | <5 |
| High Risk | >5 | >5 |
| | >10 | Any |
| | Any size | >10 |

Malignant GISTs (previously termed “leiomyosarcomas” or “epithelioid leiomyosarcomas”) are known to show wide variability in their malignancy. Several factors, such as a large tumor size, a high mitotic rate, and the presence of severe nuclear atypia, high cellularity, and tumor necrosis, have been correlated with a poor prognosis. [7]

GISTs normally present a wide clinical-pathological spectrum, from a small incidental nodule to large pedunculated mass. They are usually described as a tan to white, well circumscribed lesions within the walls of the stomach. GISTs demonstrate either of the 3 main histologic cell types: spindle cell type (most common), epithelioid cell type, and the mixed spindle-epithelioid type. [5] GISTs are consistently positive for expression of the c-KIT receptor tyrosine kinase (detected as CD 117 antigen), and about 60% to 70% GISTs show immunopositivity for CD34, 30% to 40% show immunopositivity for smooth muscle actin (SMA), and about 5% show immunopositivity for S-100 protein. [8] We received three cases of GIST, localised to the stomach, jejunum and sigmoid colon. All the three cases presented with large abdominal masses with grey white cut surface. GIST originating from stomach and jejunum were of Spindle cell type while that arising from sigmoid colon was of Epithelioid cell type. All of them were highly cellular and mitotic activity > 5/50 hpf was observed and cases were labeled malignant and follow up was advised.

EGISTs are very rare tumors, and a large study by Agaimy and Wunsh reports

that they account for 1.5% of total GISTs. These tumors may appear in different sites of the abdomen such as in the pancreas, spleen, retroperitoneum, mesocolon, mesentery of the small intestine, mediastinum and in the pelvis as vulvovaginal/rectovaginal septal masses. EGISTs usually behave more aggressively. The risk of malignant behavior of these tumors ranges from very low to high based on mitotic rate and size (tumors larger than 5 cm with more than 5 mitoses per 50 HPFs are considered to be high-risk) and also on location (small bowel GISTs and EGISTs have a higher tendency for malignant behavior compared to those in the stomach). [9] Over the past few years, it has become increasingly apparent that these tumors need to be studied on a site specific basis because of differences in behavior and that malignancy is best described in terms of risk factors. [3]

We received three cases of EGIST, two of which were present in liver as large solid grey white masses while the third over the Mesentery filled the entire abdominal cavity. All the cases presented with large masses with extensive mitotic activity > 5/50 hpf and one case even had metastatic deposits over colon. EGISTs which are more likely to metastasize have high cellularity, mitotic figures more than 2 per 50 high power fields and any amount of coagulative necrosis. [10] In EGISTs the immunohistochemical findings are similar to that of GISTs. All cases showed positive staining for CD117 and CD34. The colonic deposits of the Hepatic GISTs also showed positivity for CD117 and CD34. All the cases were labeled as malignant and strict radiological follow up was advised after resection.

Goh et al in their study suggested that most, if not all, cases of EGISTs are likely to represent mural GIST with extensive intramural growth with eventual loss of contact with the muscle layer of the gut. [10] Based on this, further studies on EGIST are mandatory.

CONCLUSION

GISTs and EGISTs, although relatively rare have a wide variety of presentation in regard to tumor size, location etc and can variably range from being low risk to very high risk and even metastasize as in case of Malignant GIST. Thus, accurate assessment of prognostic factors is essential to effectively categorize these tumors to prolong disease free survival.

REFERENCES

1. Starczewska Amelio et al.: Prevalence of gastrointestinal stromal tumour (GIST) in the United Kingdom at different therapeutic lines: an epidemiologic model. *BMC Cancer* 2014 14:364.
2. Zhou-Yu Li, Qi-Lian Liang, Guo-Qiang Chen, Yuan Zhou, Qiu-Long Liu. Extra-gastrointestinal stromal tumor of the liver diagnosed by ultrasound-guided fine needle aspiration cytology: a case report and review of the literature. *Arch Med Sci* 2012; 8, 2: 392-397.
3. John D. Reith, John R. Goldblum, Robert H. Lyles, Sharon W. Weiss. Extra gastrointestinal (Soft Tissue) Stromal Tumors: An Analysis of 48 Cases with Emphasis on Histologic Predictors of Outcome. *Mod Pathol* 2000;13(5):577-585.
4. Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Hum Pathol* 2002;33(5): 459-65.
5. Christopher B. Tan, Wanqing Zhi, Ghulamullah Shahzad, Paul Mustacchia. Gastrointestinal Stromal Tumors: A Review of Case Reports, Diagnosis, Treatment, and Future Directions. *ISRN Gastroenterology*, Volume 2012, Article ID 595968, 16 pages.
6. Reshalaiti Abuduwayite, Aidibai Muhemaiti, Hadeti Biekemituofu, Patamu Mohemaiti. Malignant Retroperitoneal Extra- Gastrointestinal Stromal Tumor: A Case Report. *British Journal of Medicine & Medical Research*, 2(2): 142-149, 2012.
7. Yoshiya Fujimoto, Yukihiko Nakanishi, Kimio Yoshimura, and Tadakazu Shimoda. Clinicopathologic study of primary malignant gastrointestinal stromal tumor of the stomach, with special reference to prognostic factors: analysis of results in 140 surgically resected patients. *Gastric Cancer* (2003) 6: 39-48.
8. Patnayak R, Jena A, Parthasarathy S, Prasad PD, Reddy MK, Chowhan AK, et al. Primary extra gastrointestinal stromal tumors: A clinic pathological and immunohistochemical study-A tertiary care center experience. *Indian J Cancer* 2013;50:41-5.
9. Petros Antonopoulos et al. Gastrointestinal and Extra gastrointestinal Stromal Tumors: Report of Two Cases and Review of the Literature. *Case Rep Gastroenterol* 2014;8:61-66.
10. Goh BK et al. A single institution experience with eight CD117 positive primary Extra-gastrointestinal stromal tumours: critical appraisal and comparison with their gastrointestinal counterparts. *J Gastro intest Surg*. 2009 Jun;13(6): 1094-8.

How to cite this article: Sunita S, Shruti G, Vijay M et. al. Malignant GIST & EGISTs: A Clinicopathologic and Immunohistochemical study of 6 cases. *Int J Health Sci Res*. 2016; 6(1):133-137.
