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Primary Iliocecal Gastrointestinal Stromal Tumor with Co-existent B/L Ovarian neoplasms: A Rare Case Report.

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ABSTRACT

Gastrointestinal stromal tumors(GISTs) are a heterogeneous group of tumors , previously thought to be tumors of smooth muscle differentiation, but now considered to arise from the interstitial cells of Cajal, that act as pace makers for peristalsis. Most frequent site is stomach (95%) followed by small intestine and less frequently involves esophagus, colon, rectum and rarely retro peritoneum respectively. GISTs are rare mesenchymal tumors, slightly more common in males; with peak age of 60 yrs .Majority of the GISTs have oncogenic mutations of the gene encoding tyrosine kinase c-KIT (CD 117). They are classified as tumors of low and high risk of malignancy depending on the size (>5cms) and mitotic count (>5/50 hpf) and associated features like tumor site and metastasis are also significant prognostic parameters. Other macroscopic alterations are tumor necrosis, mucosal ulceration, cystic degeneration, myxoid change and area of hemorrhage and calcification. Histologically, most GISTs are spindle cell tumors (67%) followed by other variants as epithelioid (13%), mixed and myxoid forms respectively and very rarely signet ring cell and extremely rare GANT variant. Other microscopic secondary alterations include cytonuclear pleomorphism, presence of multinucleated giant cells, inflammatory infiltrate and metastasis respectively. Criteria for assessment of degree of malignancy is number of mitoses per 50 hpf as major prognostic factor and tumor size in centimeters. They are further sub classified as tumors having very low degree of malignancy (9%), low degree (21%), intermediate degree and high degree as (47%). IHC study shows CD 117 positivity (97%), CD 34 positivity (63%) and high specificity for two types of antibodies namely SMA specific for smooth muscle tumors (24%) and S-100 for peripheral nerve sheath tumors (13%) respectively, because these tumors are often misdiagnosed as GISTs.

Keywords: GISTs, Mesenchymal, GANT, SMA and IHC etc.

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INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are a diverse set of mesenchymal tumors, arising from a specific category of cells, the interstitial cells of Cajal, in the gastrointestinal tract (GIT). GISTs commonly occur in persons over the age of 50 years with a peak incidence between 60 to 69 years and the mean age is 59 yrs [1]. The youngest patient is 30 yrs and oldest 95 yrs respectively. The overall incidence was seen as little predominance for male. The gross features in terms of tumor size and tumor localization within different segments of GIT were followed, while taking into account, secondary alterations on the cross section surface /or ulceration of mucosal surface. The average tumor size ranges between 5-10 cms or more in different dimensions with a minimum size of 2 cms. Other gross alterations like tumor necrosis, mucosal ulceration, cystic degeneration, myxoid change/or area of hemorrhage and calcifications respectively, were also considered. Most frequently encountered modification was tumor necrosis followed by mucosal ulceration in correlation with tumor size. The consistency is usually nodular, exophytic, polypoid or infiltrative. Most frequently involves organ in sequence is stomach, followed by small intestine (duodenum> jejunum> ileum) and rare site includes esophagus, large intestine and rarest one as retro peritoneum respectively. In our case, the tumor involved another rare location of ileocaecal region and ascending colon.

Histological features of GISTs include tumor localization within wall of GIT. Most of these tumors involve whole wall thickness of GIT and sometime located as smaller tumor involving submucosal layer, muscularis propria, and extremely rare, subserosal location. Histologically, most GISTs are spindle cell tumors (67%), followed by epithelioid elements (13%), mixed tumors (spindle and epithelioid) and myxoid forms respectively, and very rarely, signet ring cell variant and extremely rare, GANT (Gastrointestinal autonomic nerve tumors) variants (i.e, aspect of neural differentiation seen in 16% of GISTs) [3].Another secondary features are cytonuclear pleomorphism, presence of multinucleated giant cells, inflammatory infiltrate and presence of metastasis respectively. Secondary metastasis to liver and lymph nodes were seen along with local metastasis and metastasis within mesentery. Criteria for assessment of degree of malignancy was number of mitoses per 50 Hpf and maximum size of the tumor, expressed in centimeters. The number of mitoses was evaluated as a major prognostic factor. Impressively, 32% of the GISTs analyzed, had a high mitotic activity (i.e >10 atypical mitoses/50 hpf). Statistically, there was no significant correlation between the number of mitoses and tumor size (P=0.2462760-P=0.623958). Based on two major criteria, these tumors are further classified as; GISTs having very low degree of malignancy (9%), low degree of malignancy (21%), intermediate degree of malignancy and high degree (47%) [2,3]. IHC features of GIST include CD 117 positivity (97%), CD 34 (63%) and high specificity for two categories of antibodies and others for differential diagnosis namely SMA, specific for smooth muscle tumors (24%) and S-100 for peripheral nerve sheath tumors (13%) respectively, because these tumors are often misdiagnosed as GISTs.

CASE SUMMARY

55yrs old female presented with six month history of slowly increasing firm mass occupying hypogastrium and right iliac fossa . C T scan abdomen showed 20×18cm mass (figure 1) involving iliocecal and ascending colon along with bilateral ovarian mass. Resected specimen was sent for Histological examination.

DISCUSSION

Recently, IHC and molecular biological methods of study established important diagnostic, prognostic and treatment criteria for GITS [6] with high sensitivity and specificity [5,7]. Genetic studies described that majority of GISTS have frequent oncogenic mutations of gene encoding tyrosine kinase c-KIT (CD117). Data analysis shows that, tumors appear predominantly after 50 yrs with a peak around 60 yrs showing little predilection for male. GISTs can appear in any segment of the GIT involving stomach, small intestine and large intestine respectively in the decreasing order of frequency and rarely retro peritoneum. Most frequent site is jejunum followed by ileum and duodenum [7] respectively. In our case, the site was ileocaecal and ascending colon. Grossly, most of GISTs are nodular whitish tumors. Majority has secondary non-specific alterations cross sectionally with most frequent being tumor necrosis [9], when size of tumor is > 5 cms. Some rare cases with cystic and myxoid degeneration were seen and a few exceptional cases showed hemorrhage and calcification. GISTs of GIT also showed mucosal ulceration with tumor size > 5 cms.

Microscopically, larger tumors mostly involves entire wall thickness. Smaller tumors tend to involve muscularis propria first, followed by sub mucosa. Most frequent cytological aspect was spindle cell variant as in our case, followed by epithelioid tumors. Other variants appeared less frequently or exceptionally like GANT. General secondary microscopic features like cytonuclear pleomorphism and multinucleated giant cells were uncommon [7]. Presence of chronic inflammatory infiltrate was seen in over 50% of the cases with co-existing tumor size > 5 cms. Metastasis in GISTs was very rare and usually seen in liver and lymph nodes [8] .The criteria for malignancy includes, tumor size >5cm and presence of high mitotic activity. Larger tumors usually have high mitotic activity, but some smaller tumors may also show high mitotic activity. Analytically, number of mitoses and degree of malignancy revealed that highly malignant GISTS may have minimum number of mitoses as 2/50 hpf or vice versa. So series of correlations between degree of malignancy and other parameters has been established to ascertain, the value of potential secondary prognostic factors. Additional prognostic factors in correlation with malignity are young age, female gender, small or large intestinal GISTs, necrosis and invasion of mucosa' respectively. Conclusively, retroperitoneal GISTs are very aggressive tumors in terms of degree of mucosal invasion. Similar results were obtained regarding degree of malignancy v/s tumor necrosis, when grading GISTs [9]. Microscopic view in the case revealed a high risk giant GIST involving whole thickness of intestine (figure-2(10x) and Figure-3(40x) with metastatic deposits in omentum and locoregional lymph nodes. There was coexisting mature cystic teratoma (left ovary) and serous cyst adenoma (right ovary) with seedings on serosal surface. IHC features showed CD 117 as a highly specific marker (figure-4) for the diagnosis and confirmation of these tumors. Since, CD 34 positivity is lower, so this antibody can be used as an additional, but less specific marker [10]. As far as SMA and S 100 are concerned, they are less useful in the diagnosis of GISTs, but are highly valuable in differentiating these tumors from macro/microscopically similar smooth muscle tumors and peripheral nerve sheath tumors [8,9].

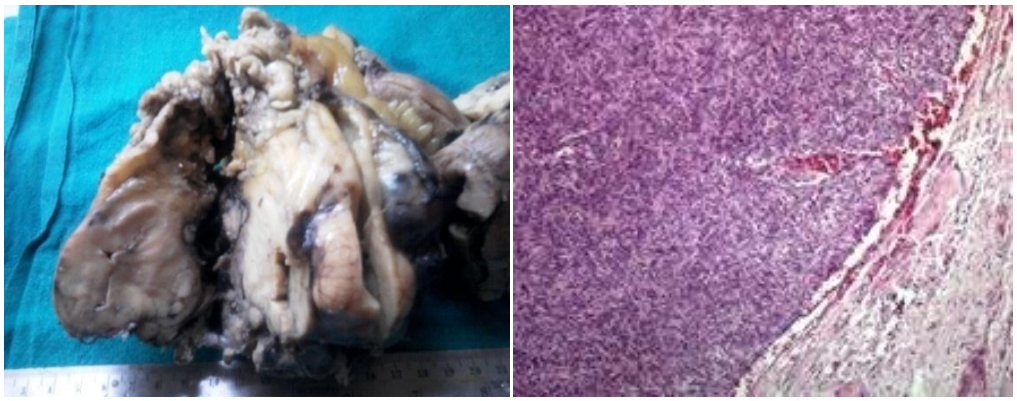

Figure 1: Gross view showing Giant GIST (Iliocaecal &Ascending colon). Figure-2 Microscopic view (100X) Sub mucosal GIST.

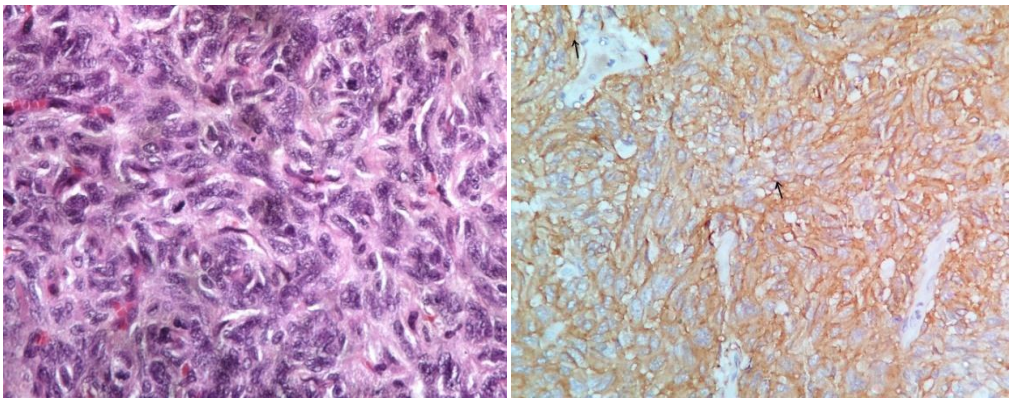

Figure 3: Microscopic view (400X) showing malignant spindle cells, cytological pleomorphism and mitotic figures (H&E Stain).Figure-4 M/E IHC (400X) showing strong CD 117 positivity (Arrows).

CONCLUSION

Gastrointestinal stromal tumors are rare tumors. However, they represent an important category of tumors arising from mesenchymal component and usually localized in gastrointestinal tract. Correct histopathological diagnosis is important because of direct implications on prognosis and treatment. Microscopically, they commonly appear as spindle cell entity followed by other cellular variants. Our case presents another rare site of ileocaecal localization and coexisting ovarian neoplasms. The degree of malignancy or malignant transformation depends on size (> 5 cms), site, nuclear pleomorphism, and number of atypical mitoses respectively, as part of major criteria. The minor criteria, includes tumor invasion of mucosa and presence of tumor necrosis. The final diagnosis of GIST is based on the immune expression of CD117, CD34, SMA and S-100 respectively. Specific markers for smooth muscle tumors and peripheral nerve sheath tumors may have similar microscopic appearances in GIST. These tumors must be differentiated from peripheral nerve sheath tumors to conclude the final diagnosis of GISTs, its degree of cytological behavior and treatment.

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