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Case Report

Multinodular gastro intestinal stromal tumor in small intestine with perforation and Meckel's diverticulitis- An unusual presentation

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ABSTRACT

Background: Gastrointestinal Stromal tumor are rare group of mesenchymal neoplasms originating from the wall of the digestive tract. Outcome strongly dependent on tumor size and mitotic activity.
Case Details: A 60-year male presented with abdominal pain and distention for 3 months. After initial evaluation, emergency laparotomy was done. Intraoperatively found to have multiple small nodules in peritoneum and mesenteric border of small intestine and rupture of a big nodule was observed causing peritonitis. Gross examination-Multiple nodular tumour mass in small intestine along with multiple haemorrhagic nodule of varying size seen in mesentry.
Microscopy: Tumor arising from muscular layer arranged in interlacing fascicles, bundles, whorls and sheets. Tumor cells are elongated having spindle to elongated nucleus with vesicular to dense chromatin and inconspicuous nucleoli. Some of the nodules shows areas of haemorrhage and necrosis. Mitotic figure > 5/50 HPF seen. Histological grade-G2 High grade >5/50 HPF, TNM grade-PT4PNxPMx. Immunohistochemistry-Diffusely Positive for CD117. Focally positive for DOG1, CD34 & SMA.
Discussion: Small intestinal GISTs comprise approximately 30% of all GISTs. Tumor size vary from small nodules to complex masses of around 20 cm.
Conclusion: GIST is more common in patients with age >40 years. CD117 and DOG1 positivity are used to define these tumors. Novelty: Only few cases has been reported in small bowel GIST with perforation and multiple nodules.

1. Introduction

Term "stromal tumor" was first introduced by Mazur and Clark in 1983 to define a group of gastric mesenchymal tumors which cannot be differentiated by immunohistochemistry and ultrastructure and was previously being thought to have smooth muscle origin of the gastrointestinal wall. Later in the year 1998, Kindblom et al and Hirota et al determined these neoplasms to be significantly immunoreactive for CD117 by their independent studies.[1]

Gastrointestinal Stromal tumor (GIST) can be defined as morphologically spindle cell, epithelioid or occasionally pleomorphic, mesenchymal tumours which usually arise from the gastrointestinal tract.13 GIST express the KIT protein and harbour the mutation of gene encoding type III receptor tyrosine kinase.[2]

These tumor cell originate from Cajal cells or their stem cell-like subset and found to occur throughout the gastrointestinal (GI) tract starting from the distal half of the oesophagus till the anorectal area.

The estimated overall incidence vary from 10 to 20 per million population.[3] The median age of presentation is 63 years having male prepondernace.[4] Outcome strongly

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dependent on tumor size and mitotic activity.[4] These tumors are extremely rare in children.[5]

Size of these tumors varies from small nodules to large masses measuring upto 20 cm which extend into the abdomen.[5] GISTs vary from diminutive incidental findings to symptomatic tumors which commonly present as visible GI bleeding or vague abdominal complaints and less commonly by obstruction, perforation, or palpable mass. Bleeding varies from chronic insidious bleeding to anaemia and acute life threatening episodes of melena or hematemesis. Few GISTs may manifest in for of other abdominal emergencies like intestinal obstruction or tumor rupture with hemoperitoneum.[3]

During an evaluation of nonspecifc symptoms, GIST may be detected as an incidental finding. The Common site of occurrence is stomach or small bowel. Symptoms may arise only when tumors becomes large in size or are in a critical anatomic location. Among most of the symptomatic patients, tumors size is larger than 5 cm noted. Patients may present with symptoms like- abdominal pain, abdominal mass, nausea, vomiting, anorexia, and weight loss.[6]

There is no evidence for a preexisting diverticle, so a diverticulum is thought to be a secondary structure formed by the tumor.[5] Meckel's diverticulum is most common congenital abnormality seen in the gastrointestinal tract. Incidence of Meckel's diverticulum in the general population is 1%. Meckel's diverticulum contains ectopic or abnormal tissue in about 30% of cases. Tumors within Meckel's diverticulum are rarely being reported having incidence of 0.5% to 3.2%.[6]

Small intestinal GIST are having higher malignant potential than gastric GISTs because of 2 reasons: 1) Small intestinal GISTs are larger in size and more advanced at the time of diagnosis; and 2) With similar size and mitosis taken into study, small intestinal GISTs are has a more aggressive behavior than gastric GISTs.[5] Neoplasms of the gastrointestinal stromal tract is associated with high rates of malignant transformation.[6] Among all GISTs cases, 10% to 30% of cases may progress to malignancy. GISTs which occur outside the stomach are associated with a higher malignant potential.[6] The proliferative activity of the cells is measured by size of primary tumor and the mitotic index.[6]

The Common gross patterns of GIST are dumbbell-shaped lesions with internal and external components, solid outward bulging nodules and large external cystic masses. These tumor may fistulate into lumen and thus creates a diverticular appearance.[5]

Immunohistochemical positivity of KIT receptor tyrosine kinase protein may appears as pan-cytoplasmic although KIT is a transmembrane protein. Expression of KIT in GIST is a important feature of the tumor.[5] In the recent literature, only stromal tumors which shows CD117 positivity by immunohistochemistry can be defined as true GISTs.[7]

Incidence of gastrointestinal perforation at the site of the GIST is rare, but has been reported.6 Tumor rupture belongs to the high-risk category according to Johnsue's classification.[6]

2. Case Details

A 60 year male presented to general surgery OPD with abdominal pain and distention for 3 months. CECT abdomen reported gastrointestinal stromal tumour with multiple peritoneal metastasis.

After initial evaluation, emergency laparotomy was done. Intraoperatively found to have multiple small nodules in peritoneum and mesenteric border of small intestine with rupture of a big nodule causing peritonitis which eventually sealed off by the omentum and coils of intestine. The unusual presence of Meckel's diverticulitis with gangrenous tip was seen just 14 cm away from the ruptured bigger nodule.

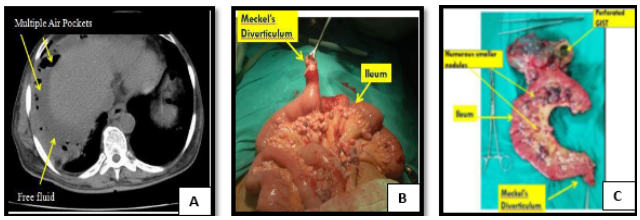

Fig. 1: A- Preoperative CT SCAN showing GIST with sign of perforation; **B**- Intra-operative finding of Meckel's Diverticulitis; **C**- Intraoperative finding of perforation in larger nodule causing peritonitis.

2.1. Gross examination

There were multiple grey white to hemorrhagic nodular tumor mass in ileum of small intestine, largest hemorrhagic and necrotic nodule measures 11x8x6 cm and the smallest nodule measuring size of 0.3x0.3 cm along with diffuse mesenteric peritoneal seedings. Meckel's diverticulitis with gangrenous tip was seen. Cut section of largest nodule-shows greenish black discolouration with necrosis and cystic changes.

2.2. Microscopy

Multiple sections studied show wall of small intestine infiltrated by tumor arranged in interlacing fascicles, bundles, whorls and sheets. Tumor cells are elongated having spindled to elongated nuclei with vesicular to dense chromatin and inconspicuous nucleoli. Some of the tumor nodules shows areas of haemorrhage and necrosis. Mitotic figure > 5/50 HPF seen. Also seen are congestion

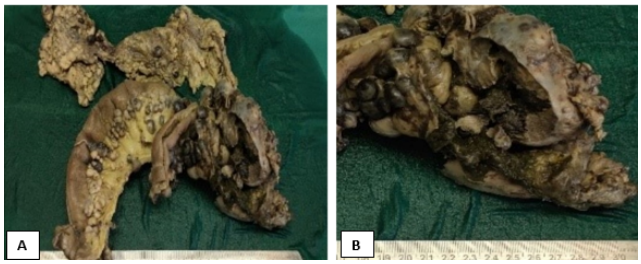

Fig. 2: A: Gross pathology showing multiple nodular mass in small intestine; **B:** Ruptured larger nodule.

and inflammatory infiltrates around Meckel's diverticulum. Labelled as Gastrointestinal Stromal Tumor, Spindle cell type. Histological grade- G2, High grade >5/50 HPF, TNM Grade- PT4NxMx.

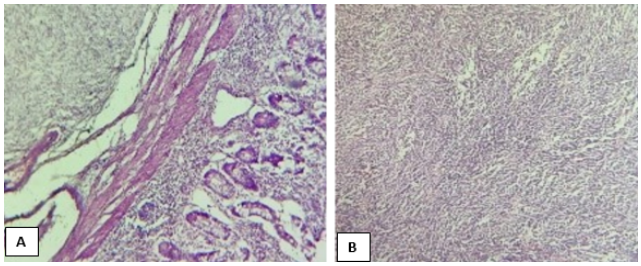

Fig. 3: A: Tumor arising from muscularis propria; H&E 100X; **B**: Microscopy shows tumor cells are arranged in interlacing fascicles, bundles and whorls; H&E- 100X.

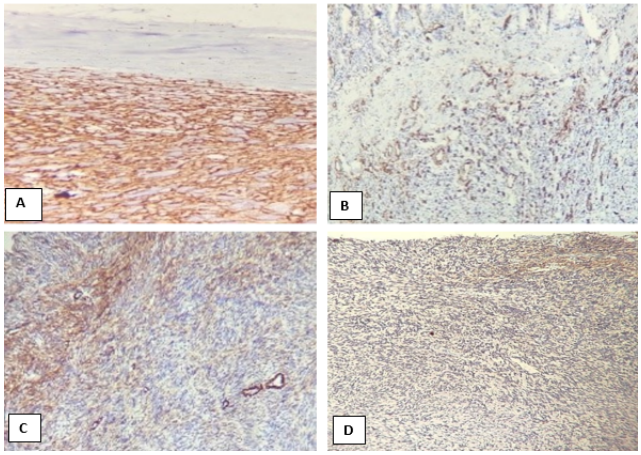

Fig. 4: A: CD117: Diffuse positivity (40X); **B:** SMA: Focally Positive (100X); **C:** CD34: Focally Positive (100X); **D:** DOG1: Focally Positive (100X).

2.3. Immunohistochemistry

Diffuse cytoplasmic positivity for CD117. Focally membraneous positivity for DOG1 and CD34. Focally cytoplasmic positivity for Smooth Muscle Actin (SMA).

3. Discussion

Small intestinal GISTs comprises of approximately 30% of all GISTs. GISTs size ranges from a few millimetres to 35 cm, with a median size of between 5 cm and 8 cm.

In a population-based epidemiological study done by Mucciarini et al on 124 patients, 53.2% were men and 46.8% were women. Median age of presentation was 69 years. Most frequent symptoms seen among them were abdominal pain (36%), gastrointestinal bleeding (25% followed by worsening of general condition.[2,8]

Meckel's diverticulum can cause perforation of the small intestine which is even more rarely reported entity. Perforation can caused by spontaneous perforation due to ulceration of the gastric mucosa present in the diverticulum or may due to foreign objects like fish bone. A perforation caused by a tumor is a very rare incidence.[9] Spontaneous perforation in Gastro Intestinal diverticulum is rarely being reported.[10]

Till now, only 45 cases have been reported in literature with the incidence of perforation associated with a GIST.[9]

Size of the tumor correlates with mitotic count. So large sized tumors usually have higher mitotic counts and are frequently unresectable. Hence, GISTs with size > 10 cm show poorer survival rates.[1]

GISTs which arises from jejunum and ileum comprises around 30%. In large tumors, Cystic degeneration and intratumoral hemorrhage are commonly seen. In case of large sized GISTs, Cystic degeneration or central necrosis can also be seen.[2] GISTs arising from small intestine almost always composed of spindle cells which are arranged in sheets, short fascicles, or in vague storiform pattern. These spindle cells have fibrillary, pale eosinophilic or basophilic cytoplasm with bland, ovoid to elongated nuclei having fine chromatin and inconspicuous nucleoli. Nuclear palisading can also be seen in. In the small intestine, epithelioid cytomorphology is associated with high mitotic rate and malignant behaviour.[11] On microscopy, morphology of GIST is predominantly seen as spindle-shaped (70%) and few shows rounded cells (epithelioid type 20%) or a mixture, but it can be pleomorphic also.[2] In present case, multiple grey white to hemorrhagic and necrotic nodular tumor mass was seen in ileum of small intestine.

About 40% of small intestinal GISTs are clinically malignant, much higher than the rate for gastric GISTs. Liver and peritoneum are the atypical sites of metastasis. Prediction of aggressive behaviour in GISTs calculated by a combination of anatomic site, tumor size, and mitotic rate. Rarely GISTs may recur locally at anastomotic sites.[11] Small intestinal GISTs are more malignant than gastric GISTs and mortality is being higher in tumors of size >5 cm or with mitotic rate >5/50 HPFs. Rupture of tumor into

the abdominal cavity can occur either before surgery or during the surgery and it carries a very high risk of tumour recurrence.[2]

In our present case, tumor size was >10 cm in greatest dimension and mitotic count was 5/50 HPF and hence reported as malignant GIST.

The pathological diagnosis of GIST is based on identification of mesenchymal neoplasm having spindle cell or epithelioid histology which shows positivity for KIT. Immunohistochemically about 97% of GISTs are positive for KIT and CD34. Among 70% of GISTs show immunopositivty for CD34 and are nearly consistently detected in cases of gastric spindle cell GISTs.[3] CD34 is expressed in around 70% of GISTs. Immunoreactivity of CD34 varies which ranges from 47% in small intestinal GISTs to 96% to 100% in rectal and esophageal tumors. Mature interstitial cell of cajal (ICCs) seen in benign GISTs which shows absence of CD34 expression while, dedifferentiated ICCs seen in malignant GISTs express CD34.

About 95% of GISTs show immunopositivity for the KIT protein which is the CD117 antigen, an epitope of the KIT tyrosine kinase. KIT protein (CD117 Antigen) can show a diffuse, focal or mixed staining pattern. Expression of KIT and other immune-histochemical stainings are judged together along with tumour morphology which is used in distinguishing GISTs from the other mesenchymal neoplasms which are not expressing KIT.[2] GISTs may be seen in multiple number and carries better prognosis.[2]

As compared to gastric GISTs, small intestinal GISTs are show more positivity for KIT with a strong and diffuse cytoplasmic staining pattern. In small intestinal GISTs, KIT and DOG1 shows similar sensitivity and specificity. Among mesenchymal tumors of the GI tract, KIT and DOG1 shows highly specificity for GIST. CD34 and smooth muscle actin (SMA) shows about 50% immunoreactivity in small intestinal GISTs.[11]

Smooth muscle and neural markers shows variably positive in GISTs. Smooth muscle actin is commonly expressed in small intestinal GISTs (47%) and rarely expressed in rectal and esophageal GISTs. Actin is generally expressed as focal which indicates that smooth muscle differentiation is incomplete. Small sized GIST may show 30-40% smooth muscle actin positivity.[2,8,12,13]

Most of the GISTs carries an uncertain malignant potential. Most common scheme which is used to assess the risk of recurrence is consensus approach which is based on the diameter of primary tumour and mitotic count.[2] KIT immunostaining is used as important diagnostic of GIST which differ it from leiomyoma, leiomyosarcoma and schwannomas which do not exhibit KIT positivity.[1]

Immunohistochemically GISTs are consistently with CD117 positivity and found to be CD34 positive in most cases. They rarely express smooth muscle actin.[4]

4. Conclusion

GIST is more common in patients with age > 40 years. CD117 and DOG1 positivity are used to define these tumors. The clinical outcome becomes worst when gastrointestinal stromal tumor presents with perforative peritonitis. In present case, we came across the multinodular GIST with Meckel's Diverticulitis and perforation peritonitis which is extremely rare presentation.

5. Source of Funding

None.

6. Conflicts of Interest

There is no conflict of interest.

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