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JEJUNAL GIST - A Rare Presentation of Obscure GI Bleed

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Abstract: *Gastrointestinal stromal tumours (GIST) are rare gastrointestinal tumours and are one of the causes of obscure gastrointestinal bleeding. Jejunal GISTs are extremely rare. We report a case of gastrointestinal bleeding secondary to bleeding jejunal GIST in a 49 years old gentleman. Endoscopic intervention failed to identify the source of bleeding and CECT showed hypervascular exophytic jejunal mass and patient underwent laparoscopic assisted segmental excision of jejunum and GIST with jejuno jejunal anastomosis. In view of intermediate -risk of histopathological features, Imatinib mesylate 400 mg once daily was given as adjuvant chemotherapy. Patient is asymptomatic without any evidence of tumor recurrence after six months of postoperative follow-up. As per ASCO-2010, and the trial by Nilsson et al. indicates that 1 year of adjuvant treatment with Imatinib 400 mg/day dramatically improves recurrence-free survival and the Food and Drug Administration (FDA) has also approved the use of Imatinib as adjuvant therapy after complete resection of localized, primary GIST.*

Keywords*: GIST- Gastro Intestinal Stomal Tumour, UGI Bleed, Imatinib, Endoscopic Laparatomy Malaena; Interstitial Cells Of Cajal, FDA*

I. Introduction

Gastrointestinal stromal tumors (GISTs), though the most common mesenchymal tumors of the GI tract, are rare accounting approximately 1% to 3% of all gastrointestinal tumors. Mazur and Clarke coined the term GIST in 1983 for a distinct set of mesenchymal tumors of the GI tract having no ultrastructural or immunohistochemical features characteristic of smooth muscles differentiation.[1] Kindblom and associates in 1998 demonstrated that the actual cell of origin of these tumors is a pluripotent mesenchymal stemcell programmed to differentiate into interstitial cells of Cajal, the GI tract "pacemaker cells" - the cells responsible for initiating and co coordinating GI motility.[2] Perhaps, the most critical development that distinguished GIST as a unique clinical entity was the discovery of c- *kit proto*-oncogene gain-of-function mutations in these tumors by Hirota and collegues in 1998.[3] 5% of GI haemorrhage is obscure in nature and GIST has been described as one of the causes.[4]Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract and can arise anywhere from the esophagus to the anus.[5,6] The most common locations of origin for GISTs are the stomach (60%–70%), small intestine (25%–35%), esophagus (2%–3%), and rarely in the colon, rectum or appendix (collectively 5%).[7] GIST has been shown to affect men(55%) slightly more than women.[8] Most patients are diagnosed between the ages of 40 and 80 years with a median age of 60 years, and only 3% of GISTs are diagnosed before the age of 21 years.[8,9] The majority of GISTs test positive for mutations in the v-kit Hardy- Zuckerman4 feline sarcoma viral oncogene homolog (KIT) gene. This leads to the expression of CD34 or the protein marker CD117, which is also known as the mast/stem cell growth factor receptor (SCFR) and c Kit.[10] The most common presentation of GIST is bleeding of the gastrointestinal tract, which may be either acute or chronic, and results in anemia.[8] Presentations include abdominal mass (5-50%), obstruction (5%), haemorrhage and rarely perforation (0.8%).[5,6] Complete surgical resection remains the best treatment option. Unlike carcinomas, GIST does not widely infiltrate at the microscopic level and rarely metastasizes to the lymph nodes; therefore, local excision may be appropriate when technically feasible. This is a report of such an unusual case involving Jejunum and presenting with obscure GI haemorrhage and managed surgically and was a success

II. Case Report

A 49-year-old man presented with a three day history of dark, "tarry" stools associated with a one week history of increasing fatigue and dyspnea on exertion. He denied any abdominal pain, vomiting, or use of non-steroidal antiinflammatory agents (NSAIDs). Social history was negative for alcohol, tobacco, or illicit drug use. His family history was unremarkable. On physical exam, the patient was orthostatic and tachycardiac. His abdomen was soft and nontender, and auscultaion revealed normal bowel sounds. Rectal exam revealed heme-positive, black stool. The rest of his exam was unremarkable with the exception of pale conjunctiva. Laboratory evaluation revealed Hb of 6.1 gm/dl , Blood urea 38 mg/dl and creatinine of 1.0 mg/dl. Chest X-Ray and electrocardiographic (EKG) tracings were normal. Blood sugar LFT, Lipid profile were normal. HBV/HCV/HIV-Neg. Stool for occult blood was repeatedly positive.PBS shows normocytic and normochromic anaemia with polychromasia. Hb electrophoresis was normal.USG abdomen shown normal study . UGI endoscopy revealed reflux oesophagitis and antral gastritis with duodenal ulcer. H. pylori serology was Negative. He was managed with 3 unit of PRBC transfusion along with supportive therapy and patients become stable with Hb of 10 gm/dl. Subsequent UGI endoscopy and colonoscopy were normal however stool for occult blood was still positive He was put on PPI and Sucralfate and discharged from hospital .

After 3 months he again reported to our hospital with similar complaint and again Hb has dropped down to 6.0 gm/dl with haematocrit of 18.3 % , MCV of 81 fl, Plt count 1-4 lac/cmm, Stool for occult blood was again positive and he was again managed with 2 unit of PRBC transfusion and Hb risen to 8.7 gm /dl. UGI Endoscopy again done revealed similar reflux eosophagitis and erosive gastritis with duodenitis, He was also empirically treated with H Pylori treatment and discharged on PPI and Sucralfate.

He was again reviewed after 3 months and this time he was asymptomatic and stable with Hb of 13.4 g/dl, H Pylori serology was negative , Stool for occult blood was again positive. USG abdomen revealed – normal study. UGI Endoscopy done this time from other centre showed Duodenitis with duodenum diverticulum but serum ferritin was low with value of 11.43 ng/ml (30-350), he was discharged on same treatment with PPI , Sucralfate and Iron supplement .

After 3 months he again reported with complain of malena and easy fatigability. This time Hb come down to 9.2 gm/dl , Stool for occult blood was again repeatedly positive . UGIE again showed same nonspecific finding of reflux eosophagitis and erosive gastritis. Colonoscopy done again was Normal. In view of non correction of anaemia and resource limited setting we referred the case to higher centre for further evaluation and management as a case of obscure GI bleed.

At higher centre he was re-evaluated there and evaluation revealed Hb of 8.6 gm/dl, PCV -27% ,Stool for occult blood was positive ,UGI endoscopy and colonoscopy done there were normal. USG Abdomen there revealed hypervascular mesenteric tumor in close relation to bowel likely mesenteric tumor. On further evaluation CECT Abdomen revealed hypervascular exophytic mass arising from the jejunum likely GIST(Fig-1 & 1A-Axial Section (cross marked) at the level of lesion and Fig-2& 2A Coronal Section (cross marked) at the level of lesion), mesenteric lymphadenoathy was also there. patient underwent laparoscopic assisted segmental excision of jejunum and GIST with jejuno jejunal anastomosis .Tumor size was 6 x 3.5 cm. Histopathological examination of excised mass shows benign gastrointestinal stromal tumor .IHC revealed CD117 strongly positive and CD 34 Negative, Mitotic count -2 /50 hf, chromogranin –Neg. Opinion of Oncologist taken and started on TKI - Imatinib 400 mg OD . In view of intermediate risk as per risk stratification treatment been planned for 2 yr of adjuvant chemotherapy with Imatinib . Post operative follow up after six month patient is asymptomatic and doing well with Hb of 14 gm/dl ,Normal haemogram and biochemistry with normal scan abdomen.

FIGURES

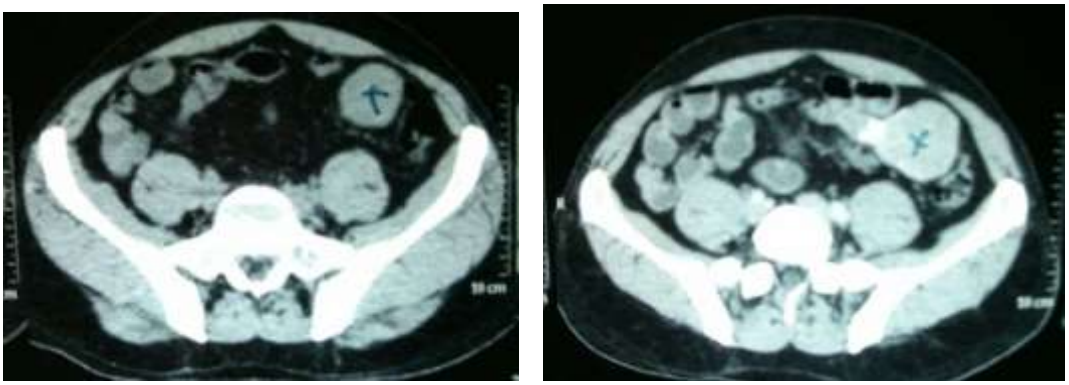
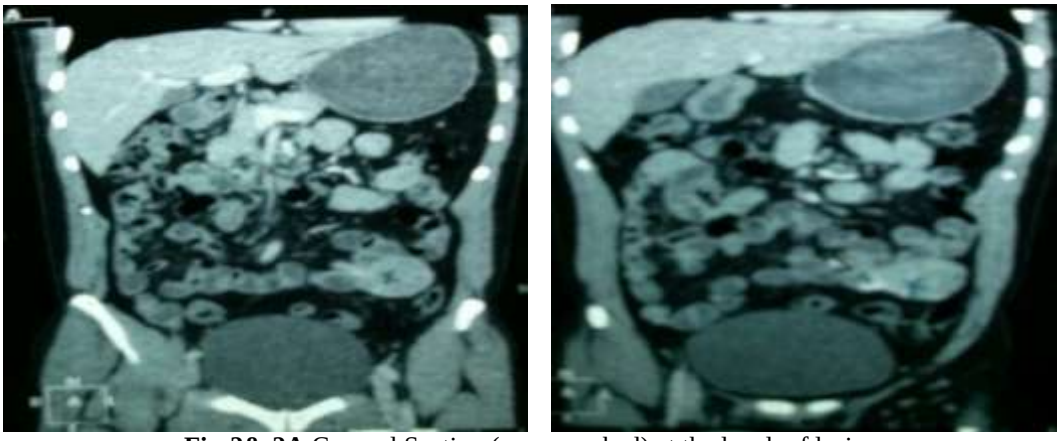


Fig-1 &1 A-Axial Section (cross marked) at the level of lesion



eFig-2& 2A Coronal Section (cross marked) at the level of lesion

III. Discussion

The incidence of GIST is very low, that is 2 in 1,00,000 while jejunal GISTs are extremely rare, [11] accounting for 0.1–3% of all gastrointestinal (GI) tumors [12]. GI bleeding (acute or chronic) is the most common clinical presentation of GISTs while nonspecific symptoms, such as obstruction, invagination, perforation or anemia occur in approximately 20% of cases [13] .Up to one fourth of gastric GISTs and half of all small intestinal GISTs are clinically malignant with metastases commonly occurring intra-abdominally, i.e. preferentially in the liver; rarely in soft tissues, bones or skin; and even less frequent in lymph nodes and lungs. Metastases may develop a long time (> 15 years) after primary surgery and long-term follow-up is, therefore, encouraged[14]. Reaching the diagnostic of small intestine haemorrhage is difficult, and in as many as 5% of patients with obscure GI bleeding, a source cannot be identified despite extensive examination [15]. In many occasions, lesions cannot be identified after upper endoscopy and colonoscopy, and more specific studies must be performed to explore the small intestine such as enteroclysis, sonde enteroscopy, wireless capsule endoscopy or even intraoperative enteroscopy [16].Morphological features such as tumor size and mitotic activity (Ki-67 staining) have gained greatest acceptance for predicting outcome and distinguishing benign from malignant GISTs[17]. Histological features are site dependent with a majority being spindle cell tumors (70%) and a minority presenting with an epithelioid (20%) or mixed spindle, epithelioid, or a nested paraganglioma-like or carcinoid-like growth pattern or,rarely, a cytological pleomorphism (2%-3%)[17]. Usually, the primary therapy of localized GISTs is surgical. Nevertheless, about 50% of patients treated by resection relapse within 5 years. In cases of very low and low/intermediate grade GISTs, surgical resection has a good prognosis[18,19]. In patients with intermediate/high-risk GISTs increased recurrence and decreased survival rates occur despite complete surgical resection [20]. GIST is considered to be an extensively chemotherapy-resistant soft-tissue sarcoma subtype [21]. The standard systemic treatment for soft-tissue sarcomas is a Doxorubicin-based chemotherapy, which achieves a 2-year survival rate of only 20% in patients with GIST [22]. For these patients, the development of Imatinib, a tyrosine kinase inhibitor targeting both c-kit and platelet derived growth factor alpha (PDGFRA), has considerably improved the outcome. Imatinib mesylate was first approved by the FDA in 2001. Imatinib mesylate is the first and only effective drug for the treatment of gastrointestinal stromal tumor at present. Mutated exon 11 of the KIT receptor is essential for the pathogenesis and response to imatinib mesylate of gastrointestinal stromal tumor. The efficacy rate (complete response + partial response) of imatinib mesylate is 53.8%, and the disease-control rate (complete response + partial response + stable disease) is 84% [23]. As per ASCO-2010, and the trial by Nilsson et al. indicates that 1 year of adjuvant treatment with Imatinib 400 mg/day dramatically improves recurrence-free survival [24]. Imatinib as such is recommended in metastatic, residual, or recurrent cases of GISTs or which are surgically not removable; however, recent recommendations suggests the use of Imatinib mesylate after radical surgery in high-risk cases, because it has shown 14% absolute decrease in the recurrence rate , 97% of the patients receiving Imatinib were free of recurrence (PFS) compared to 83% in the placebo group) [25]. There are established guidelines for the follow-up of a patient, such as ours, after resection with curative intent. According to the GIST Consensus Conference for low- or very low risk GIST, i.e. tumors < 5 cm and with a mitotic index < 5/50 high power fields, a systematic follow-up with CT scan every 6 month for 5 years would be reasonable. [26].

IV. Conclusion

The small intestine is an uncommon site for GISTs. When present, symptoms are usually non-specific and can include fatigue from occult anaemia or abdominal pain. Asymptomatic jejunal GISTs also occur, preoperative radiological diagnosis is imperative. Surgery remains the mainstay of treatment in resectable

tumours but absolute requirement is complete surgical resection. The development of Imatinib heralds the era of targeted cancer therapy. Preoperative Imatinib mesylate can be considered in unresectable or borderline resectable cases. GI-bleeding is a typical presentation of GIST. In these cases Multile Detector CT is a useful tool for (initial) diagnosis and quick localization of submucosal GI tumors, since endoscopic diagnostic tools such as video capsule endoscopy (VCE) and Double balloon endoscopy (DBE) may miss these lesions. In cases of very low and low/intermediate grade GISTs surgical resection has a good prognosis. However, novel therapeutic targets have been identified which may lead to potential new treatment options in the case of GIST.

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