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Gastrointestinal Stromal Tumar, Jejunum: Cause of Obscure GI Bleeding

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Abstract

GIST was introduced as a diagnostic term in 1983. GIST are only 0.2% of all GI tumors, the most common sarcoma of the gastrointestinal tract. GIST are thought to arise from the interstitial cells of Cajal (ICC), which are components of the intestinal autonomic nervous system acting as pacemakers regulating intestinal peristalsis. Jejunal GIST is rare and Pre-operative diagnosis is difficult. Diagnosis is confirmed on histopathology and immunohistochemistry.Complete removal with postoperative Imatinib therapy entails optimal treatment. We present a rare case of Jejunal GIST presented with obscure GI bleeding and managed successfully by surgery.

Keywords: GIST- Gastro Intestinal Stomal Tumour; Malaena; Interstitial cells of Cajal.

Introduction

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract and can arise anywhere from the esophagus to the anus.[1,2] 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%).[3] The incidence of GIST is 10–20 million people per year with a malignant potential of 20-30%.[1,2] GIST has been shown to affect men (55%) slightly more than women.[4] 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.[4,5] The majority of GISTs test positive for mutations in the v-kit Hardy-Zuckerman 4 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.[6]

The most common presentation of GIST is bleeding of the gastrointestinal tract, which may be either acute or chronic, and results in anemia.[4] Presentations include abdominal mass (5-50%), obstruction (5%), haemorrhage

Fig 1: X-ray Abdomen Erect Normal

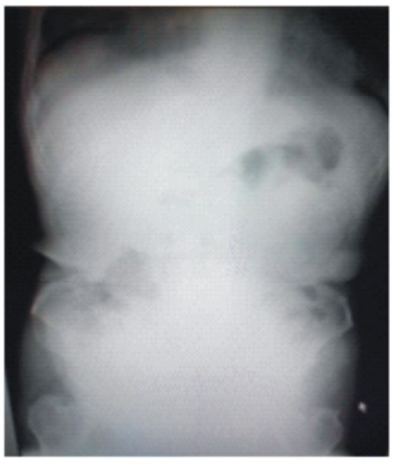
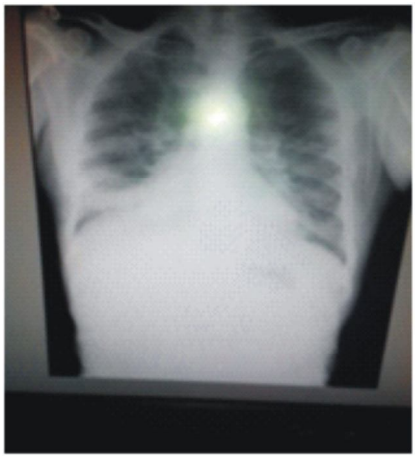


Fig 2: X-ray Chest - Normal



and rarely perforation (0.8%).[1,2] 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.

Case Summary

A 50 year old man presented with a eight days history of vague abdominal pain, dark, "tarry" stools (malena) associated with a one week history of increasing fatigue and dyspnoea on exertion. He denied any history of vomiting, constipation, diarrhea,

Fig 3: USS Abdomen Showing Hypoechoic Lesion in Rt Hypochondrium

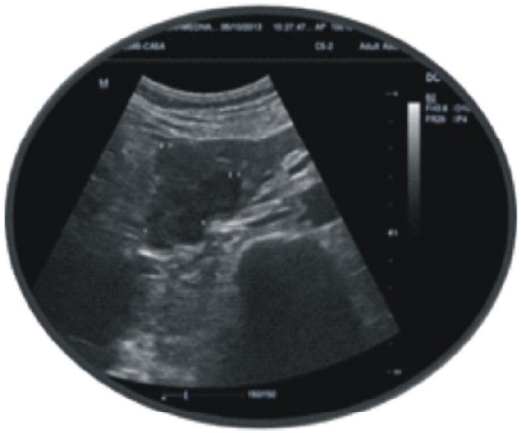
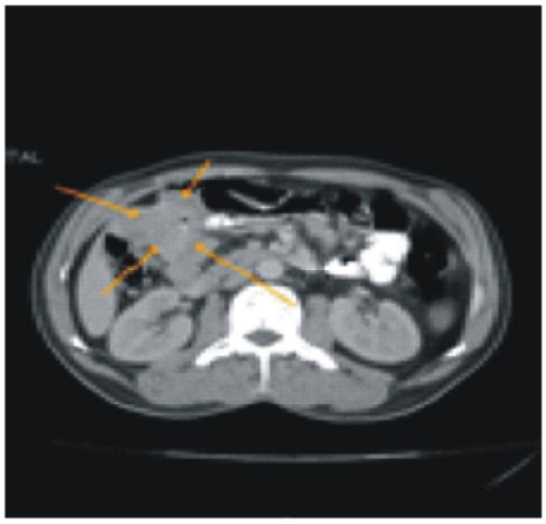


Fig 4: CE CT Scan Abdomen Showing Homogenously Enhancing Solid Mass in Rt Hypochondrium.



haematemesis, bleeding PR or use of non-steroidal anti-inflammatory agents (NSAIDs). His past medical history was positive for hyperlipidemia and recently diagnosed as a case of DM. Social history was negative for alcohol, tobacco, or illicit drug use. His family history was unremarkable. On physical exam, the patient was severely anaemic. His abdomen was soft and nontender, and auscultaion revealed normal bowel sounds. The rest of his exam was unremarkable. Laboratory evaluation was significant for HB being 3.5 gm% with hematocrit of 21.7% (38.4-51.7 gm/dL), mean corpuscular volume (MCV) of 86 (80-97 fl).Patient was given 4 units of PCV to built up his HB upto10 for surgery. He was started on Inj.Human atrapid 10-8-8 units because of BSL Fasting being 180 and Postprandial being 350.

His X ray abdomen Erect and chest was normal (Figure 1 & 2).

USG abdomen and pelvis suggested evidence of heterogeneously hypoechoic lesion at right hypochondrial region on mesentric border at small bowel loop measuring approximately 49*37mm in size (Figure 3). This lesion was showing internal vascularity. No evidence of free fluid or obvious lymphadenopathy. These features were more in favour of growth Jejunum (Figure 3).

Fig 5: Shows Growth Proximal Jejunum

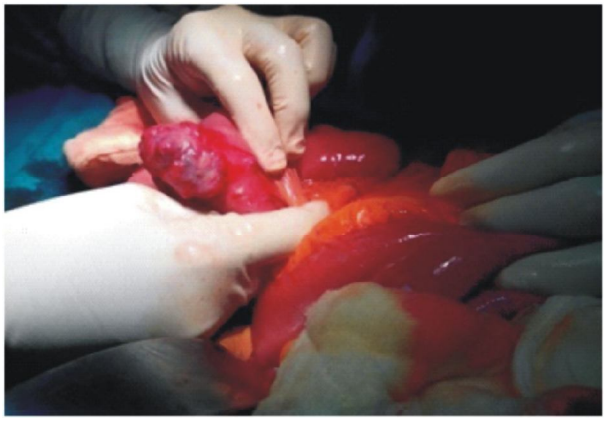
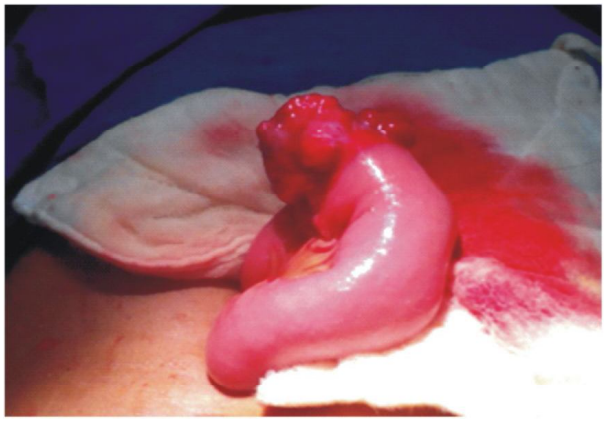
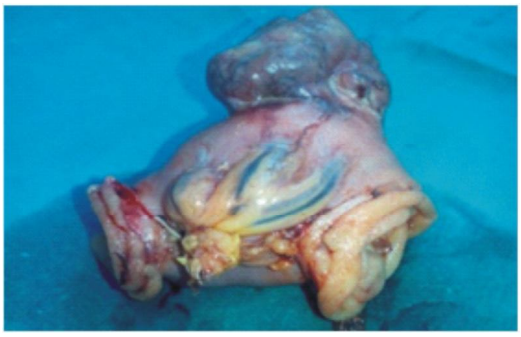


Fig 6: Shows Proximal Jejunal Growth (Close View)



CECT abdomen and pelvis reported homogenously enhancing solid mass lesion in (rt) subhepatic space along the mesenteric border of proximal jejunal loops about 4.9*3.9cm with possibilities were LYMPHOMA or GIST (Figure 4). CT guided biopsy showed Proliferative spindle shaped cells having spindle shaped nucleii arranged in interlacing bundles. Focally cellular areas with plump vesicular nucleii seen with sparse inflammatory infiltration. Impression came as stromal tumour. Exploratory laparotomy was performed with Midline incision extending infraumbilically. On exploration, Exophytic mass about 7cm*5cm over proximal jejunum on antimesentric border 15 cm away from Duodeno jejunal flexure was seen with Regional mesenteric lymphadenopathy. Liver, other small intestine, Large intestine was Normal. There was no ascites. The abdominal

Fig 7: Shows GIST with Segment of Jejunum after Resection

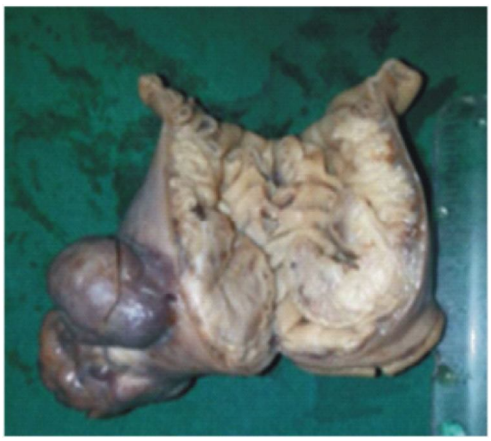


cavity was free of metastatic lesions by gross inspection. Local resection of jejunum 5 cms from margin and segment of mesentery along with LNs & end to end anastomosis of jejunum was done. Lymph node was sent for biopsy. (Figure 5 & 6 before excision and Figure 7 & 8 after excision)

After Excision

Post operative course was uneventful. Oral feedings started on 3rd day. Sutures were removed on 10th day and patient discharged .Histopathology of the resected specimen showed, a submucosal nodular tumour composed of interlacing fascicles of spindle shaped cells with elongated, plump nuclei. There was mild nuclear pleomorphism and more than five mitotic figures per fifty high power fields. No tumour necrosis found. Pathologically it was jejunal GIST of

Fig 8: Shows Growth along with Opened Segment of Resected Jejunum



intermediate risk. Surgical lines of resection were free. Immuno-histochemistry study revealed diffuse immunoreactivity for CD-117, focal CD-34 positivity,negative for desmin, S-100 and SMA; Ki 67 less than 5%. The patient is on six months follow-up receiving oral Imatinib 300 mg twice a day & is doing well till now.

Discussion

GIST was first described by Mazor and Clark (1983).[3] It originates from the interstitial cells of Cajal (ICC) ,located in the muscularis propria (myenteric plexus) responsible for triggering smooth muscle contraction.[3,7] Basic pathology is an activating mutation (gain in function) of chromosome 4 which codes for c-Kit resulting in uncontrolled proliferation of stem cells that differentiate towards ICC. GIST is sporadic.[3] Familial forms with autosomal dominant inheritance have also been documented 6. 90% of GIST occurs in adults more than 40 years of age (median age 63 years). There is slight male preponderance.[4] Our patient was a 50 yrs old male. No documented elements indicating any association with geographic location, ethnicity, race or occupation has been elucidated.

Presentation is erratic. Seventy percent are symptomatic at presentation, 20% are asymptomatic and 10% are detected at autopsy.[5,6] Common presentations include abdominal pain, palpable mass, gastro intestinal bleeding, fever, anorexia, weight loss and anaemia.[8] Our patient presented with obscure anaemia due to hidden malena. Isolated jejunal GIST associated with perforation and peritonitis is a rare and unique.

Clinical diagnosis of GIST is based on index of suspicion.[8] Specific diagnostic signs and symptoms are absent. Chronicity is a rule.[8] Preoperative imaging modalities like contrast enhanced abdominal computerized tomography (CT) aids in diagnosis.[9] The extent of the tumor, metastases and involvement of other organs can be assessed. A dedicated magnetic resonance imaging (MRI) provides better information than CT in the preoperative staging workup.[9] We had clue of GIST/lymphoma in CECT abdomen and pelvis. Endoscopic ultrasound with guided fine-needle aspiration is diagnostic for primary lesions in 89% of the cases.[9,10] We had no opportunity for the same.

The decisive diagnosis rests on the pathological and immunohistological tests.[3,5] In our patient, CT guided biopsy report showed Proliferative spindle shaped cells having spindle shaped nucleii arranged in interlacing bundles. Focally cellular areas with plump vesicular nucleii seen with sparse inflammatory infiltration.

Optimal surgical treatment of GIST entails complete removal of the tumor with clear surgical margins including the adjacent involved organs.[5-10] Complete surgical resection entails 48-65% five-year survival.[7] In our case, Exophytic mass about 7cm*5cm over proximal jejunum on antimesentric border 15 cm away from Duodenojejunal flexure was seen with Regional mesenteric lymphadenopathy. Local and regional lymph node involvement is infrequent in GIST. GIST response to conventional chemotherapy is very poor (<10%), while radiotherapy is only used in cases of intraperitoneal hemorrhage, when the precise location of the tumor is known, or for analgesic purposes.[7,8] In our case, the abdominal cavity was free of metastatic lesions by gross inspection. Local resection 5cms from margin and end to end anastomosis was done.Lymph node was sent for biopsy. STI571 (imatinib), acts as a powerful selective inhibitor of tyrosine-kinase, PDGFR (platelet derived growth factor receptor) and c-kit receptor.[10] Oral imatinib at doses >300 mg per day achieves curative results.The selection criteria underpinning the decision for possible use of imatinib in these settings include a risk assessment based on pathological factors such as tumor size, mitotic rate, and location can be used to predict the risk of recurrence in GIST patients. Tumors <2 cm with a mitotic rate of <5/50 HPF have been shown to have

lower risk of recurrence than larger or more aggressive tumors. If resistance to imatinib is encountered, the multiple tyrosine kinase inhibitor sunitinib (marketed as Sutent) can be considered. Regorafenib (Stivarga) received FDA approval for locally advanced, unresectable GISTs that no longer respond to imatinib or sunitinib. Our patient is on six months follow-up receiving oral imatinib 300 mg twice a day & is doing well till now.

Histopathologically GISTs are composed of spindle (70%), epithelioid and round cell or an admixture.[9] Similarities with histological picture of gastrointestinal leiomyosarcoma, leiomyoblastoma and poorly differentiated carcinomas may cause diagnostic dielemma, Immuno-histochemical assays for CD117 antigen (KIT) is the mainstay for diagnosis.[9,10] In our patient, . Immuno-histochemistry study revealed diffuse immunoreactivity for CD117, focal CD-34 positivity, negative for desmin, S-100 and SMA;Ki 67 less than 5%. The 5-year survival rate is 35%. It increases to 54% after complete surgical excision.[1-10] However 40% will recur within 18 – 24 months. Once recurrence has occurred median survival is 9–16 months.[3,5,7,8,10] Our patient is doing well for last 6 months of followup.

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 jejuna 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.

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