

Case Report: A Rare Presentation of Large Abdomino-Pelvic Malignant GIST (Gastrointestinal Stromal Tumor)

Navin Kasliwal¹, Siddhant Jayaghosh Kaddu²

¹Assistant Professor, Department of General Surgery, Mahatma Gandhi Mission's Hospital and Medical College, Aurangabad, Maharashtra, India

²Resident in Department of General Surgery, Mahatma Gandhi Mission's Hospital and Medical College, Aurangabad, Maharashtra, India

Abstract: *Gastrointestinal stromal tumors (GISTs) are the most common sarcomatous tumors of the gastrointestinal tract and are commonly seen in Stomach (60 % -40%), Small Intestines (30 %) and Colon (15%)^[1], they may occur anywhere in the entire length of Gastrointestinal tract from the esophagus to anus, even in mesentery and omentum adjacent to but separate from stomach and intestines^[2] which is rare. Pathologically Spindle cell form is the most common (70%) subtype of GISTs, less common are Epithelioid (20%) and rare are mixed type (10%)^[1]. Small tumors <2 cm of benign variety make up most of the presentations of GISTs and are usually seen in the age group of 40 – 60 years. Here we present to you a rare presentation of the less common Epithelioid variety of a large hemorrhagic fluid filled malignant GIST measuring 27cm x 15cm occupying the whole of abdomen and pelvis in a 88 year old man.*

Keywords: Gastrointestinal Stromal Tumor, Sarcomatous Tumors, Epithelioid Tumors

1. Introduction

Gastrointestinal stromal tumor is a distinct tumor derived from the interstitial cells of Cajal, an intestinal pacemaker cell.¹ They are the most common mesenchymal tumors of the gastrointestinal tract.^[2] The interstitial cells of Cajal and GIST cells express the hematopoietic progenitor cell marker CD34 and the growth factor receptor c-Kit. Expression of the c-Kit gene protein product, CD117, has emerged as an important defining feature of GISTs^[3]. Other possible markers include DOG-1, desmin, and vimentin.⁴ They can appear anywhere within the GI tract but most commonly found in the stomach (40% to 60%), small intestine (30%), and colon (15%). GISTs may present with myriad of features, ranging from small benign tumors to massive lesions with necrosis, hemorrhage, and wide metastases.^[1] Surgical resection is the mainstay of treatment for tumors >2cm and resection is warranted for tumors <2cm if high risk features like irregular borders, ulceration and heterogeneity are present^[1]. Important risk factors for malignancy include tumor size > 10 cm and more than 5 mitoses per 50 HPF. Intestinal GIST mostly arise from muscularis propria and generally grow extramurally.^[1] GISTs tend to displace rather than invade adjacent structures. Larger GISTs (>10cm) can exhibit heterogeneity on CT which usually signifies hemorrhage or occasionally necrosis within the tumor.^[8] Larger tumors or malignant tumors require adjuvant therapy with Imatinib, a tyrosine kinase inhibitor, which is the first line drug. Second line tyrosine kinase inhibitors include Sunitinib, Nilotinib. Regorafenib a 2nd generation tyrosine kinase inhibitor that targets c-KIT, RET, BRAF, VEGFR, PDGFR and fibroblast growth factor inhibitor can be used in cases refractory to Imatinib/Sunitinib. PET scan can be useful to assess the response to tyrosine kinase therapy¹

2. Case Report

A 88 year old man presented to the outpatient department with 15 a day history of gross distention of abdomen. He had no any signs/ symptoms of bowel obstruction but complained of only early satiety and on examination was found to have a grossly distended abdomen with a dull note on percussion all over it with bilateral pedal edema and bilateral inguinal lymphadenopathy. USG of the abdomen and pelvis gave a differential diagnosis of omental and peritoneal metastatic deposits from unknown primary with gross loculated ascites OR wet type of abdominal tuberculosis with tubercular peritonitis and pyoperitoneum. USG guided ascitic tapping was done along with CECT of the abdomen and pelvis for further evaluation which revealed a thick walled solid cystic mass lesion in abdomen and pelvis measuring 15x26x29 cm approximately, seen infiltrating the anterior abdominal wall muscles, fat planes with urinary bladder, adjacent bowel loops and right external iliac vein appeared indistinct and was seen compressing the IVC. Ascitic fluid sample was hemorrhagic and was negative for malignancy.

Exploratory laparotomy was planned and on opening the abdominal cavity a 27 x 15 cm thick walled cystic mass containing approximately 1 liter of hemorrhagic fluid was encountered. It was seen adherent to transverse mesocolon and lesser sac superiorly extending up to aorta inferiorly and was adherent to the retroperitoneum posteriorly. There was no evidence of infiltration of mass into surrounding viscera nor any metastasis. The mass was excised in toto without damaging any viscera or vascular structures. Mass effect and distention of abdomen was relieved immediately and the specimen was sent for histopathological evaluation. Histopathology report was suggestive of Malignant epithelioid cell tumor favoring Gastrointestinal stromal tumor (GIST) with 12-15 mitoses per 50 HPF, part of the

urachus excised was suggestive of Malignant epithelioid cell tumor with peritoneal dissemination.



Figure 1: Clinical picture of the patient at presentation

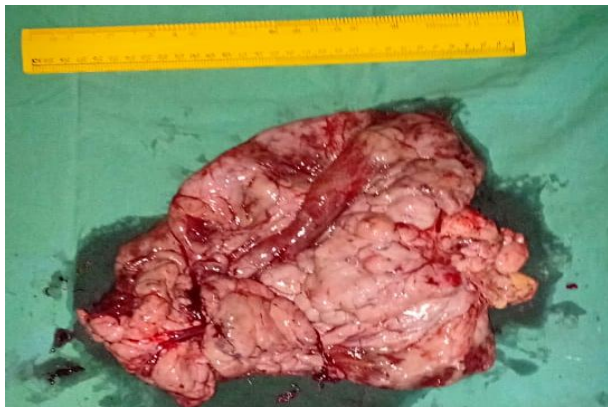


Figure 2: Excised mass measuring 27x 15 cm



Figure 3: Intraoperative picture showing attachment of the mass to lesser sac

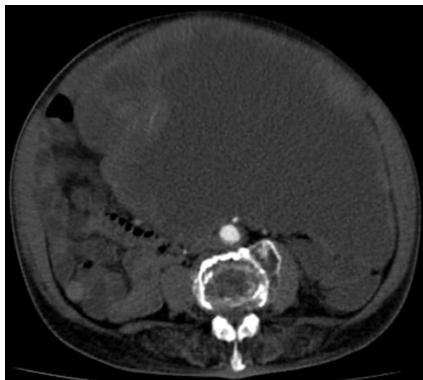


Figure 4a:



Figure 4b



Figure 4c

Figure 4: CECT images of the mass in (4a) transverse, (4b) Coronal and (4c) Sagittal planes

3. Discussion

Gastrointestinal tumors occur anywhere in the gastrointestinal tract, many of them being small (less than 2 cm), submucosal or endophytic and asymptomatic. Few of them grow to larger sizes, (largest observed GIST is 42cm x 31cm x 23cm⁷), are extramural or exophytic and are symptomatic and may present with nonspecific symptoms of nausea, vomiting, abdominal distension, early satiety, abdominal pain, and rarely as a palpable abdominal mass. Larger tumors may cause obstruction of the gastrointestinal lumen by endophytic growth or compression of the GIT from exophytic growth leading to dysphagia, obstructive jaundice, or constipation, depending on the location of the mass. Perforated neoplasms will present with signs of peritonitis or gastrointestinal bleeding. Indolent or massive intraperitoneal bleeding is secondary to pressure necrosis and ulceration [6]. Our case here presented with a short history of distention of abdomen and early satiety with no signs /symptoms of gastric outlet obstruction or bowel obstruction. Apart from a grossly distended abdomen he had bilateral pedal edema and bilateral inguinal

lymphadenopathy. To add to the dilemma the USG findings were not confirmative and gave vague differential diagnoses of omental and peritoneal metastasis from an unknown primary with gross loculated ascites or wet tuberculosis with tubercular peritonitis with pyoperitoneum. Clinically the patient was vitally stable with no signs of acute abdomen, infection and had no co morbidities. Laboratory investigations were within normal limits with a normal total leukocyte count of 5820/ mm³. Ascitic tapping revealed hemorrhagic fluid negative for malignancy and CECT was planned for further evaluation which revealed a thick walled solid cystic mass lesion in abdomen and pelvis measuring 15x26x29 cm approximately, seen infiltrating the anterior abdominal wall muscles, fat planes with urinary bladder, adjacent bowel loops and right external iliac vein appeared indistinct and was seen compressing the IVC.

Characteristic findings on CT scan include an enhancing, exophytic mass in close association with the stomach or bowel wall. Like other sarcomas, GISTs tend to displace rather than invade adjacent structures. Occasionally, larger GISTs (>10 cm) can show heterogeneity on CT, which usually signifies hemorrhage or occasionally necrosis within the tumor. Magnetic resonance imaging can be useful in cases of rectal GIST. Although positron emission tomography (PET) is not used to diagnose GIST, it can be helpful in assessing the response to tyrosine kinase therapy. PET can also be useful in patients with metastatic disease who are being considered for surgery or those on second-line agents after failure of imatinib, in whom mixed responses may occur.⁸ Complete surgical resection with negative margins is the recommended treatment for localized GISTs. Extended anatomic resection and lymphadenectomy are not required. The goal is to achieve negative microscopic margins with an intact tumor pseudocapsule. Because GISTs spread hematogenously or by local invasion. Lymphadenectomy is not routinely required unless adjacent nodes are obviously enlarged. Resection of even locally advanced tumors is associated with improved survival. Tumor size has consistently been identified as an important prognostic factor for GIST. Mitotic activity has also been identified as an important prognostic factor and is generally categorized as fewer than 5, 5 to 10, or more than 10 mitoses per high-power field. Exploratory laparotomy with complete resection of a 27 x 15 cm thick walled cystic mass containing approximately 1 liter of hemorrhagic fluid was done for this patient. The mass was seen adherent to transverse mesocolon and lesser sac superiorly extending up to urachus inferiorly and was adherent to the retroperitoneum posteriorly. There was no evidence of infiltration into any surrounding viscera and the mass was excised in toto without damaging any viscera or vascular structures. Histopathological examination was suggestive of malignant epithelioid cell tumor favoring Gastrointestinal stromal tumor (GIST) with 12-15 mitoses per 50 HFP, large areas of tumor necrosis, plenty of lymphoid aggregates and plenty of blood vessels. Part of the urachus excised was suggestive of Malignant epithelioid cell tumor with peritoneal dissemination. All findings were consistent with malignant features of GIST.

Table 1: Guidelines for Assessing Malignant Potential of Gastrointestinal Stromal Tumors of Different Sizes and Mitotic Activity

<i>Suggested Guidelines for Assessing Malignant Potential of Gastrointestinal Stromal Tumors of Different Sizes and Mitotic Activity</i> ^[1]
Benign (no tumor-related mortality)
• No larger than 2 cm, no more than 5 mitoses/50 HPF
Probably benign (<3% with progressive disease)
• >2 cm but ≤5 cm; no more than 5 mitoses/50 HPF
Uncertain or low malignant potential
• No larger than 2 cm; >5 mitoses/50 HPF
Low to moderate malignant potential (12%-15% tumor-related mortality)
• >10 cm; no more than 5 mitoses/HPF
• >2 cm but ≤5 cm; >5 mitoses/50 HPF
High malignant potential (49%-86% tumor-related mortality)
• >5 cm but ≤10 cm; >5 mitoses/50 HPF
• >10 cm; >5 mitoses/50 HPF

There are three histological subtypes of GIST. The spindle cell form is the most common (70%) and consists of uniform, intersecting fascicles with eosinophilic cytoplasm. The epithelioid (20%) and the rare mixed type (10%) forms show more rounded cells with nuclear atypia. Approximately 95% of GISTs stain positive for KIT (CD117) by immunohistochemistry (IHC). Epithelioid GISTs tend to have weaker KIT staining than the spindle cell type. Other commonly expressed markers include CD34 (70%), smooth muscle actin (30%), and desmin (<5%). Other malignancies that can stain positive for KIT include metastatic melanoma, angiosarcoma, small cell lung cancer, and Ewing sarcoma.^[8] The histopathological findings in this patient were consistent with Epithelioid GIST containing round to oval cells with moderate eosinophilic cytoplasm, with large pleomorphic nuclei and perinuclear halo with prominent nucleoli.

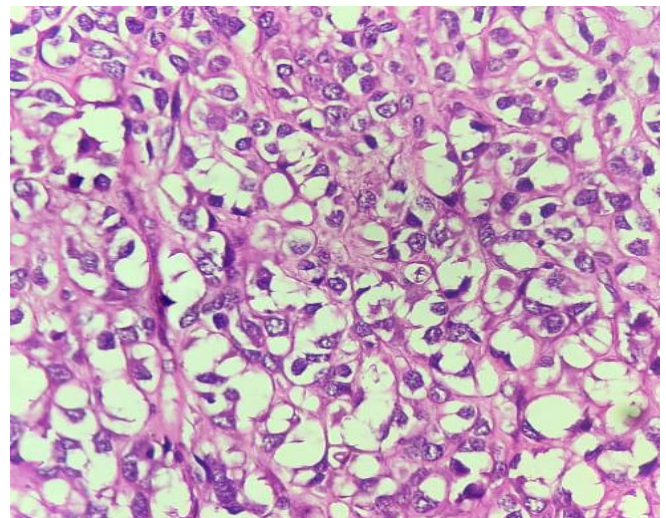


Figure 5: Histopathological image under 40x zoom showing Features of Epithelioid GIST with round to oval cells eosinophilic cytoplasm with large pleomorphic nuclei and perinuclear halo with prominent nucleoli.

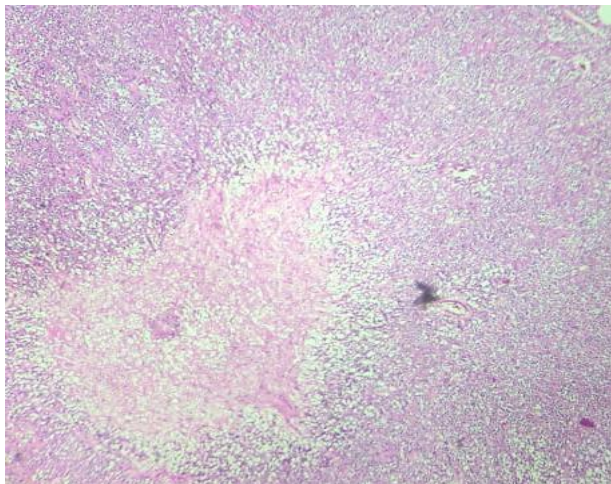


Figure 6: Necrosis, a feature of malignant GIST seen under scanner view

With surgery alone, recurrence rates approached 50% irrespective of negative margins. The approval of imatinibmesylate for the treatment of GIST, both adjuvant and therapeutic, has revolutionized the field. As a specific tyrosine kinase inhibitor (TKI), imatinib has shown efficacy in patients with both KIT and PDGFRa mutations. Imatinib is dosed orally once or twice a day and is generally well tolerated, with rash, diarrhea, and abdominal pain being the mostcommonly reported side effects. In a phase II trial led by the American College of Surgeons Oncology Group (ACOSOG), oral imatinib for 12 months after resection in patients with high-risk GISTs was shown to improve recurrence-free survival and increase overall survival compared with historical controls. High risk in this study was defined as a tumor greater than 10 cm, spillage during resection, or more than 5 tumors per patient.^[8]

Imatinib, a tyrosine kinase inhibitor, is the first line drug. Second line tyrosine kinase inhibitors include Sunitinib, Nilotinib. Regorafenib a 2nd generation tyrosine kinase inhibitor that targets c-KIT, RET, BRAF, VEGFR, PDGFR and fibroblast growth factor inhibitor can be used in cases refractory to Imatinib/ Sunitinib^[1].

4. Conclusion

Gastrointestinal stromal tumors show a myriad of presentations and cause a clinical dilemma in diagnosing and treating them. Surgical resection is the mainstay of treatment with adjuvant therapy with first line tyrosine kinase inhibitor Imatinib can be effective in large tumors. Prognosis mostly remains good with 50 % chance of recurrence within 20 years.

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