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Case Report

An unusual presentation of gastrointestinal stromal tumour arising from the Ileum and involving the urinary bladder

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ABSTRACT

Gastrointestinal stromal tumours (GISTs) are mesenchymal tumours originating usually from stomach and small intestines, at times from unusual sites without GI (gastrointestinal) tract involvement. GISTs frequently occur among men in the age range of 60 to 65 years. These tumours are rarely symptomatic usually discovered incidentally on radiology or intraoperatively, diagnosis is confirmed on histology and IHC (immunohistochemistry). This instance represents an unusual presentation in a 65-year-old male who presented with symptoms of fatigue, per rectal bleed and dysuria due to an underlying infraumbilical tumour which was later diagnosed as a GIST arising from the ileum concurrently involving the urinary bladder, managed successfully with neoadjuvant Imatinib therapy followed by surgical resection.

Keywords: Bladder gist, Extraintestinal gist, Ileal gist, Imatinib therapy, GIST

INTRODUCTION

Gastrointestinal stromal tumours (GISTs) are the commonest mesenchymal tumours originating from the gastrointestinal tract. They are usually seen in the stomach (40-70%) and the small intestine (15-44%) and are rarely seen arising from the bowel mesentery, omentum and retroperitoneal tissue (2-11%).[1] Extra GISTs (EGISTS) are tumours showing similar IHC markers like GIST, arising in the abdomen without gastrointestinal tract involvement, in the omentum (80%), mesentery or the retroperitoneal structures, with no connection to the stomach or intestinal wall.[2]

GISTs originate from the interstitial cells of Cajal. The GIST is characterized by presence of upregulation of the KIT and PDGFR (platelet derived growth factor receptor) protooncogenes in roughly 85-95% of the cases.[3]

The typical age of onset for GIST is approximately 60 years of age. GISTs are rare in children and young adults, with a higher prevalence observed in males compared to females.[1] While most GISTs occur sporadically, instances of GISTs in families with inherited KIT mutations are well-documented. Additionally, certain hereditary syndromes like neurofibromatosis type I, Carney's triad (consisting of gastric GIST, paraganglioma, and pulmonary chondroma), and Carney's dyad (comprising paraganglioma and gastric GIST) have been linked to the onset of GISTs.[3]

GIST subtypes, categorized by histological appearance, include spindle cell (70%), epithelioid (20%), and mixed (10%). The spindle cell subtype typically manifests as a sizeable, varied, enhancing mass originating from the stomach or small intestine. It commonly carries characteristic KIT and/or PDGFRA mutations, and in most instances, shows positive response to Imatinib therapy. This subtype generally carries a more favourable overall prognosis.[3]

The rarer epithelioid subtype typically originates in the stomach and is more prevalent among young females.

Unlike the spindle cell type, it often lacks the characteristic KIT and PDGFRA mutations. This subtype has a tendency to metastasize to lymph nodes, a phenomenon seldom observed in the spindle cell type, and it is associated with a poorer response to Imatinib therapy.[3]

Based on IHC, the diagnosis of GISTs is made with CD117 positivity, CD117 is positive in 95% of the cases. The prognostic factors include mitotic index, site and size.[1]

Patients with GISTs may experience symptoms such as abdominal pain, fatigue, dysphagia, a feeling of early satiety, and obstruction. They may also present with chronic gastrointestinal bleeding leading to anaemia or acute gastrointestinal bleeding resulting from erosion of the gastric or bowel mucosa. In some cases, GISTs can rupture into the abdominal cavity, leading to life-threatening intraperitoneal hemorrhage.[4] Metastases occur in approximately 50% of patients with GISTs. The liver is the most common site of metastasis (65%), followed by the peritoneum (21%). Metastases to lymph nodes, lungs, and bones are considered uncommon sites for GIST metastasis.[5] Computed tomography (CT) serves as the primary modality for accurately identifying the site, size, location, and extent of GIST. Positron emission tomography (PET) can aid in localizing secondary lesions. However, the definitive diagnosis of GIST relies on histological examination, with confirmation typically achieved through CD117 positivity on IHC. The cornerstone of treatment remains surgical resection. For patients with locally advanced tumours or metastases, neoadjuvant targeted therapy utilizing Tyrosine kinase inhibitors (such as Imatinib) can be employed.[1]

Imatinib functions as a selective, small molecule inhibitor targeting three receptor tyrosine kinases: the transmembrane receptor KIT, the chimeric BCR-ABL fusion oncoprotein associated with chronic myeloid leukemia, and PDGFRA. Previously referred to as STI 571, Imatinib works by competitively inhibiting the activity of these tyrosine kinases at the adenosine triphosphate (ATP)-binding site of the enzyme.[6] This action leads to the inhibition of tyrosine phosphorylation in the proteins involved in signal transduction pathways.[7]

Neoadjuvant therapy with imatinib is both feasible and advisable, with a recommended duration of at least 6 months. It has been shown to induce a notable reduction in tumour mass, consequently lowering operative morbidity. In the adjuvant setting, patients at a significant risk of relapse are recommended to undergo a 3-year course of imatinib treatment.[7] There are other drugs used in Imatinib refractory or resistant cases such as sunitinib, regorafenib, ripretinib, avapritinib.[7]

This is a case study involving a 65-year-old man who experienced symptoms of general weakness, per rectal bleeding, and urinary discomfort, which were later attributed to a rare tumour. Subsequent diagnosis revealed the tumour to be a GIST concurrently affecting the ileum and the fundus of the urinary bladder.

This case report aims to encourage fellow surgeons to adopt a more vigilant approach when dealing with unusual presentations of small bowel GISTs that invade other organ systems. It also aims to highlight the critical role of genetic mutation studies in managing GISTs to ensure successful surgical outcomes in such atypical cases.

CASE REPORT

A 65-year-old man, farmer by occupation visited the outpatient ward of medicine department at our tertiary care hospital with complaints of generalised weakness, poor appetite, fatigue since two months and was under treatment for anaemia, on presentation the patients vitals were as follows heart rate of 92 beats per minute, blood pressure of 120/90 millimeters of mercury, oxygen saturation of 98% on room air, his blood work revealed a hemoglobin level of 7, indicative of microcytic hypochromic anaemia, with normal total leukocyte count (TLC) and platelet counts upon admission. The remaining panel of relevant blood work and urine investigations were within normal limits, showing no apparent pathology. The patient also had complaints of pain in abdomen, blood in stools, frequent urination and complaints of mild dysuria for which he was referred to surgery department.

The patient had tenderness and a palpable lump in hypogastric region, per rectal examination showed no fissures or hemorrhoids, blood staining was seen on examining finger.

Further work up in form of radiological investigations as ultrasound sonography (USG) and contrast enhanced computerised tomography (CECT) to revealed a large (14×10×10 cm) solid mass lesion in lower infraumbilical region compressing the ileal loops with obscured fat planes between the lesion and urinary bladder. The preoperative CT guided biopsy done was indicative of a mesenchymal tumour with myxoid stroma, the IHC report was suggestive of CD117 positive, DOG1 positive, CD34 positive and Desmin positivity, which confirmed the diagnosis of GIST and the patient was given neoadjuvant Imatinib targeted therapy for 6 months, and was advised follow up after completion of therapy. The urinary bladder involvement of the tumour was persistent post therapy as suggested by subsequent imaging so the patient was planned for surgical resection.

After requisite preoperative optimization the patient was posted for elective exploratory laparotomy and a 14×10×10 cm tumour arising off the antimesenteric surface of ileum and involving the fundus of urinary bladder was revealed intraoperatively.

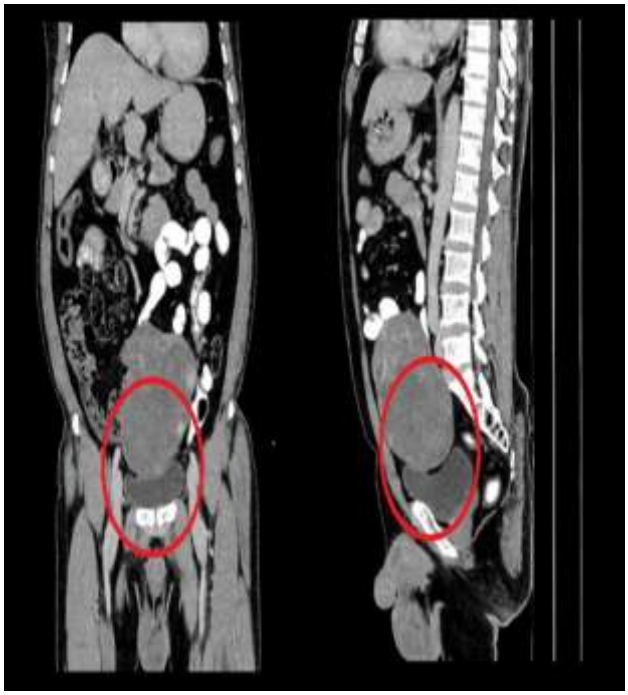

Figure 1: CECT abdomen + pelvis films showing involvement of bladder.

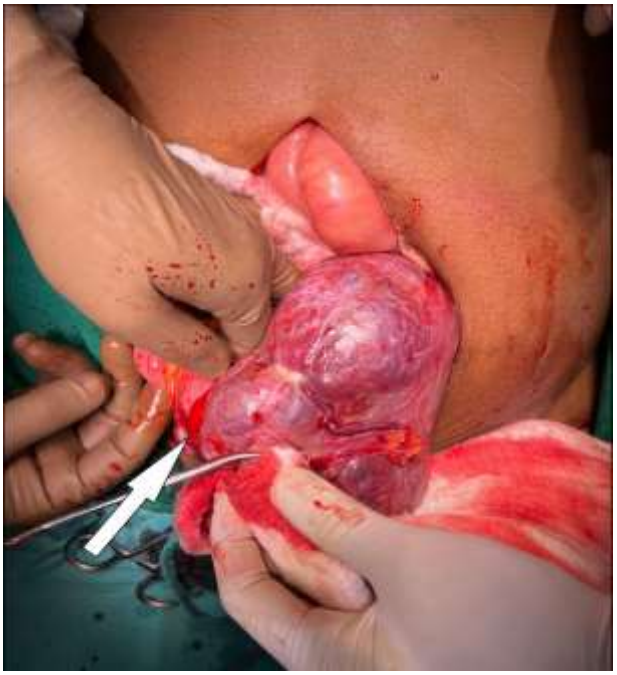

Figure 2: Intraoperative image showing origin of the tumour from antimesenteric border of small bowel loops (ileum).

Removal of the tumour with wedge resection of the involved wall of ileal loop and excision of the tumour surface involving fundus of bladder was done. The ileal defect was closed primarily and primary closure of the defect in urinary bladder was done in two layers. The patient was vitally stable throughout procedure and tolerated the resection and primary repair well.

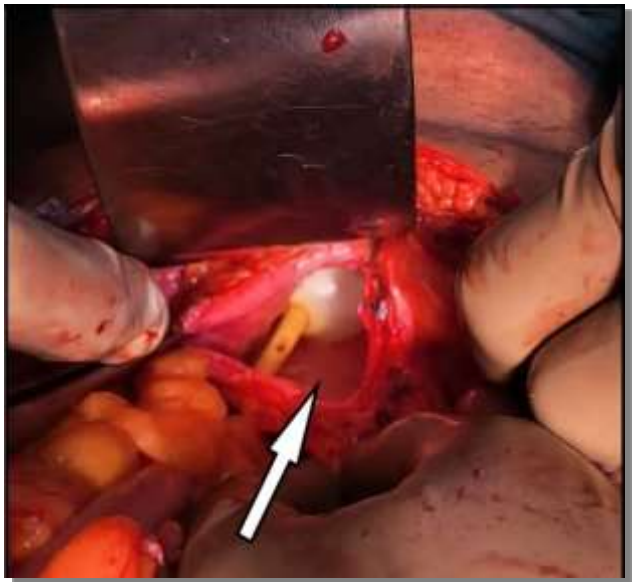

Figure 3: Intraoperative picture post excision of specimen showing a defect in Urinary bladder with visible bulb of foleys catheter.

The histopathological examination of the excised specimen, measuring 14×10×10 cm and weighing 650 gm, revealed a circumscribed, solid, lobulated mass with a smooth, grey white pseudo capsule covered with blood vessels and adipose tissue interspersed at places. The specimen exhibited two raw areas at the sites of resection: 1) a 3×2.5 cm tubulonodular region, likely of intestinal origin, and 2) a 6.5×5.5 cm irregular roughened surface located over the inferior convexity of the tumor.

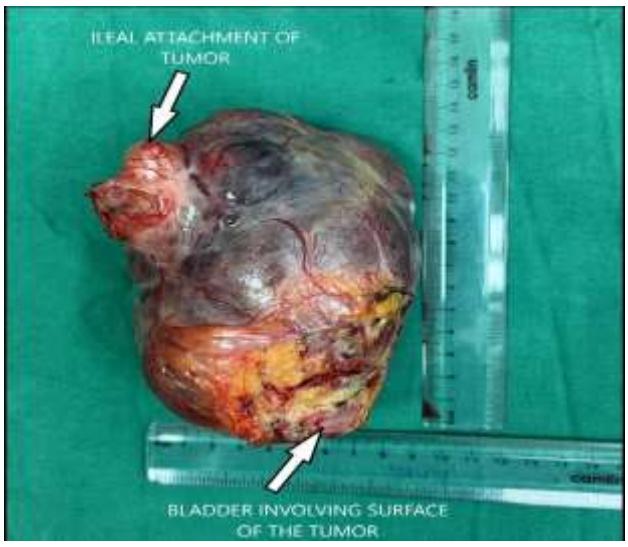

Figure 4: Excised specimen of the tumour showing ileal and bladder attachments.

The lymph node biopsy sent from the mesentry of involved bowel loop showed reactive sinus histocytosis, no evidence of lymphoreticular spread of malignancy.

The microscopic findings were consistent with GIST arising from small intestine probably ileal in origin with no mucosal invasion, no tumour necrosis, abnormal mitoses or vascular invasion.

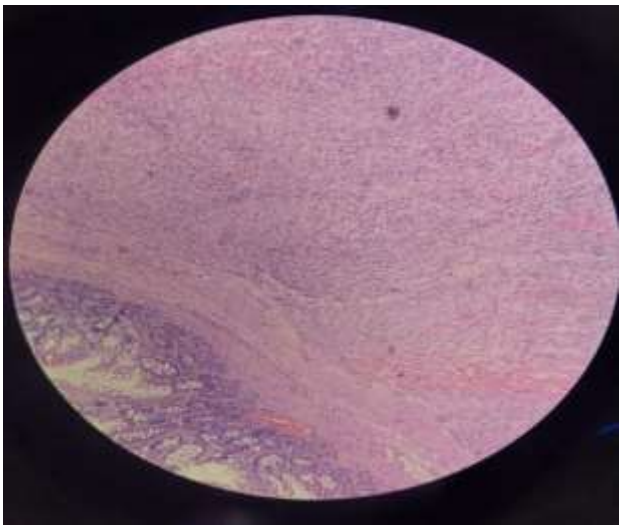

Figure 5: Histopathological slide of the tumour specimen showing normal small intestinal mucosa with a submucosal well circumscribed mass composed of spindle cells arranged in fascicles, no evidence of tumour invasion into the intestinal mucosa.

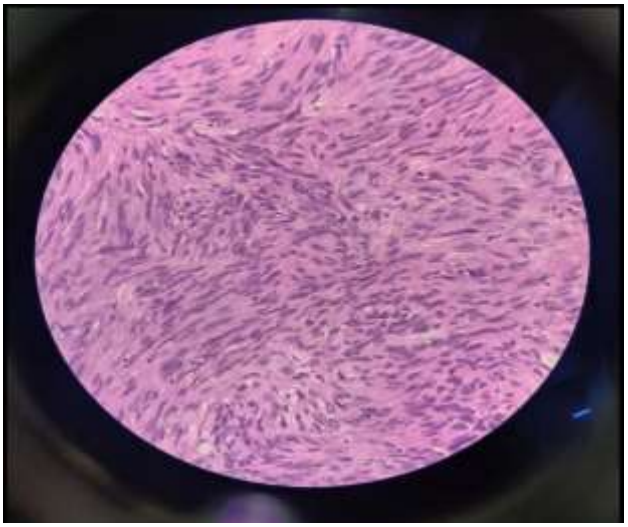

Figure 6: High magnification slide of the excised specimen showing no evidence of marked atypia, tumour necrosis or abnormal mitosis.

The patient was transferred to the intensive care unit (ICU) for postoperative hemodynamic stabilization and later moved to the general ward. He showed a rapid recovery in the general ward and was discharged thereafter. Currently, the patient is undergoing adjuvant Imatinib targeted therapy for one year, as recommended by oncologists. There has been no recurrence of symptoms postoperatively, and the patient's condition remains stable.

DISCUSSION

During the review of literature for our report, we came across a very few reports in the literature regarding GISTs invading the urinary bladder. Although it is very rare for GISTs to invade other organs outside the gastrointestinal tract, adhesion to adjacent organs may be commonly seen. The incidences of small intestinal GISTS involving the urinary bladder in form of compression of bladder, isolated involvement of bladder, or delayed invasion of urinary bladder, although rare have been previously documented in cases of massive GISTS, recurrence of GISTs, syndromic GISTs and metastatic GISTS.[5,8,9] Urinary bladder involvement by a secondary tumour occurs as either a metastasis or a direct tumour extension from advanced tumours of adjoining pelvic organs or distal gastrointestinal tract.[2] As per literature the urinary bladder is known to harbour metastases of primaries originating in breast, stomach and lung, rare cases of metastatic GISTS invading bladder have also been documented.[9] The small intestinal GISTS invading the bladder may not always present with urinary symptoms obscuring their diagnosis.

EGISTS (extra intestinal GISTS) are defined as tumours arising from intraabdominal structures other than the stomach or bowel wall mimicking IHC positivity of the GISTS.[2] The tumour behaviour, genetics and prognosis of EGISTs themselves is an enigma yet to be decoded, labelling our case as extra intestinal GIST would be rather controversial, hence we refer to our case as invasion of urinary bladder by a small intestinal (ileal) GIST.

In our case preoperative imaging and evaluation revealed a solid lesion arising from ileal loops adherent to the urinary bladder. After biopsy confirmation of the tumour as GIST, a trial of neoadjuvant targeted therapy was given aiming to achieve tumour regression so as ensure minimal mutilation of involved organs during resection. As per recommendations FDG-PET-CT is gold standard for the early detection of tumour response to molecular targeted therapy or neoadjuvant therapy.[5] Due to the unavailability of FDG-PET scans at our center, a post-therapy CECT imaging was performed, which showed no reduction in the tumour involvement of the urinary bladder. Mutational studies of the tumour specimen could not be performed due to the lack of availability at our center.

Mutational analysis can be crucial in diagnosing GIST, as mutations in KIT and PDGFRA can confirm the diagnosis when it is uncertain. Mutational studies of GISTs suggest that KIT exon 9 mutant GISTs of the small intestine and colon tend to be more aggressive compared to tumours with a KIT exon 11 mutation.[4,5] Several risk stratification factors have been proposed to predict the risk of aggressive clinical behaviour in primary GISTs, including the national institute of health (NIH) consensus criteria (Fletcher criteria), the modified

NIH consensus criteria (Joensuu criteria), and the Armed Forces Institute of Pathology criteria (Miettinen criteria). These criteria incorporate factors such as tumour size and location, mitotic count per high-power fields (HPFs), and tumour rupture.[5]

CONCLUSION

Overcoming the lack of advanced analytical facilities at our centre, we opted for elective laparotomy surgery as the next best management option for the case. The tumour was excised with wedge resection of the involved wall of ileal loop and excision of the tumour surface involving fundus of bladder was done, followed by primary closure of defect in the ileal loop and double layered repair of the defect in urinary bladder. The extensive adhesions of the tumour to the bladder wall and the lack of regression after neoadjuvant therapy may be due to unfavourable genetic mutations that could have been identified through mutational studies. We are pleased with the positive surgical outcome of this case, that our patient tolerated the procedure well and is now living a symptom-free and healthy life postoperatively.

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