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General Surgery

Giant Gastrointestinal Stromal Tumors

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Abstract **Case Report**

Gastrointestinal stromal tumors in interstitial Cajal cells of myenteric plexus of the muscularis propria are the commonest gastrointestinal mesenchymal tumors, not exclusively, appearing in the stomach. This case report documents management of a giant gastric stromal tumor of a 75 year-old female patient presented with generalized, vague, constant abdominal pain and melena, both of a week's duration. She had early satiety with dizziness, feeling weak, and fatigue. She had a good appetite and no weight loss, hematemesis, or vomiting. She was apyrexial, with normal vital signs. The abdomen was soft, with a palpable large mass in epigastrium and central abdomen; an abdominal CT showed a heterogeneous mass lesion of antrum of stomach. Subtotal gastrectomy with roux-en-y gastrojejunostomy was performed. Histopathology showed epithelioid high grade gastrointestinal stromal tumor. The cornerstone therapy is a full operative removal of the tumor, with adjuvant therapy with selective receptor tyrosine kinase inhibitors.

Keywords: Tumors: Giant Gastrointestinal stromal; case report.

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most frequent mesenchymal tumor of the GI tract, ranging 1% - 3% of all gastrointestinal tumors. The term GIST was initiated in 1983 for a distinct mesenchymal tumors of the GI tract with no ultrastructural aspect of smooth muscle differentiation [1]. The real cell of origin of these tumors is a pluripotent mesenchymal stem cell designed to differentiate into interstitial cajal cells, the GI tract "pacemaker cells" - responsible for starting and coordinating GI motility [2]. Gastrointestinal stromal tumor may appear anywhere in the gastrointestinal tract. Submucosal lesions, which commonly increase endophytically or exophytically, ranging in size between small (1 cm) to large (40 cm). The majority (50-75%) of tumors appears in the stomach, with a fifth (20%) in the small intestine and they appear less frequently in the colon and rectum. Brunner's gland hamartomas of the duodenum are similar in the radiological and endoscopic aspect of GIST. GIST is more common in males than in females, and in those aged 40-60 years. Clinical features range from an incidental radiological finding to intestinal obstruction, upper or lower GI bleeding or melena, and an emergent idiopathic spontaneous intra-abdominal bleeding or a palpable abdominal lump.

The most critical moment that differentiated GIST as a unique clinical entity was the discovery of c-kit proto- oncogene gain-of-function mutations in these tumors in 1998 [3]. Molecular targeted management including adjuvant and neoadjuvant protocols using tyrosine kinase inhibitors like imatinib mesylate was initiated. These act by competing for the ATP binding site on the target kinase, inhibiting tyrosine kinase and decreasing cellular proliferation.

PATIENT AND OBSERVATION

Patient Information

A 75 year old female patient.

Clinical Findings and Timeline

Patient presented to A&E with generalized abdominal pain of 1 week duration, which was vague in nature but constant. This was associated with melena of the same duration. She had early satiety and complained of dizziness, feeling weak, and fatigue; however, she had a good appetite and no weight loss, hematemesis, or vomiting.

She had been admitted a month previously with a history of melena, during which she received a transfusion and had an upper endoscopy, which revealed multiple small ulcers and erosions in the stomach, with a larger ulcer at a greater curvature with blood oozing from the edges. The ulcer edges were injected with adrenaline.

Diagnostic Assessment

She was lost in follow- up and did not attend any of her clinical appointments. She had no comorbidities apart from osteoarthritis (on NSAIDs). On examination, she was apyrexial, with normal vital signs. The abdomen was soft, with a palpable large mass in the epigastrium and central abdomen. Per rectum examination showed no blood and no masses.

Blood and radiological workup: She had an abdominal CT which showed a heterogeneous mass lesion arising from antrum of stomach associated with pneumoperitoneum, suggestive of perforated tumor. Her clinical profile supported the diagnosis a sealed perforation, and conservative management was applied to optimize her condition and plan for surgery. She was transfused a total of 4 units of blood, and after cautiously reintroducing oral feeding, she was given high protein drinks.

Diagnosis

She improved clinically and was later investigated with repeated abdominal CT scan, which showed resorption of the intra-abdominal free gas and no collections (Figure 1); the PET scan showed no distant metastasis. Planned laparotomy was done and luckily there was no invasion to other structures, as demonstrated by her images.

Therapeutic intervention: Subtotal gastrectomy with roux-en-y gastrojejunostomy was performed (Figure 2, Figure 3). The patient recovered well postoperatively and was discharged with a prescription of imatinib (400mg daily).

Follow up and outcome:Histopathology showed high grad gastrointestinal stromal tumor of epithelioid type. (Mitotic rate 34MF/5mm, tumor size 20x14x10 cm, pathological stage pT4 N1). Immunohistological markers showed positive CD117, DOG1, and negative SD100.

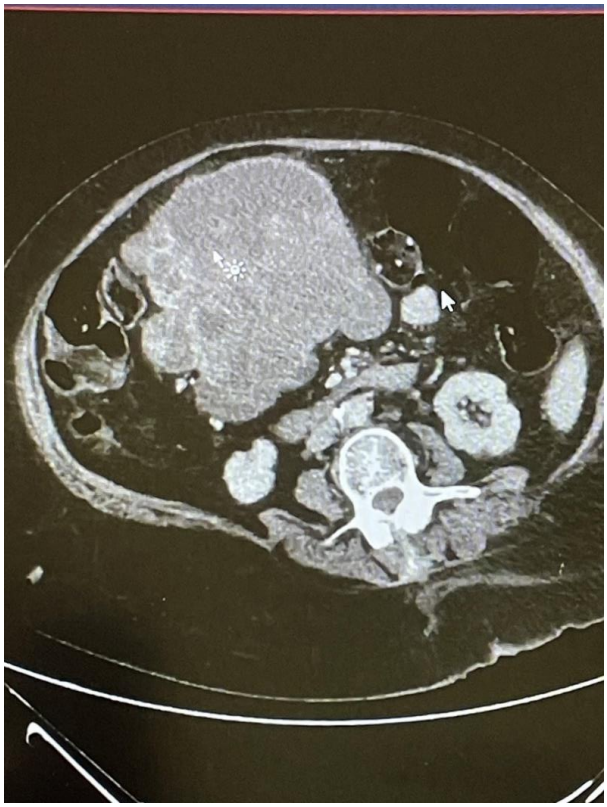

Figure 1: Abdominal CT scan showing resorption of the intra-abdominal free gas and no collections and no distant metastasis

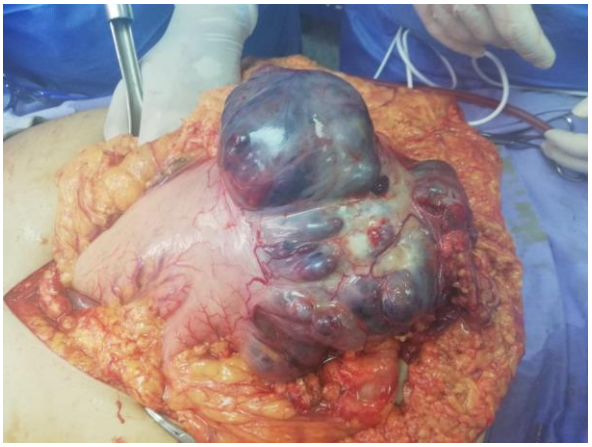

Figure 2: Subtotal gastrectomy with roux-en-y gastrojejunostomy (I)

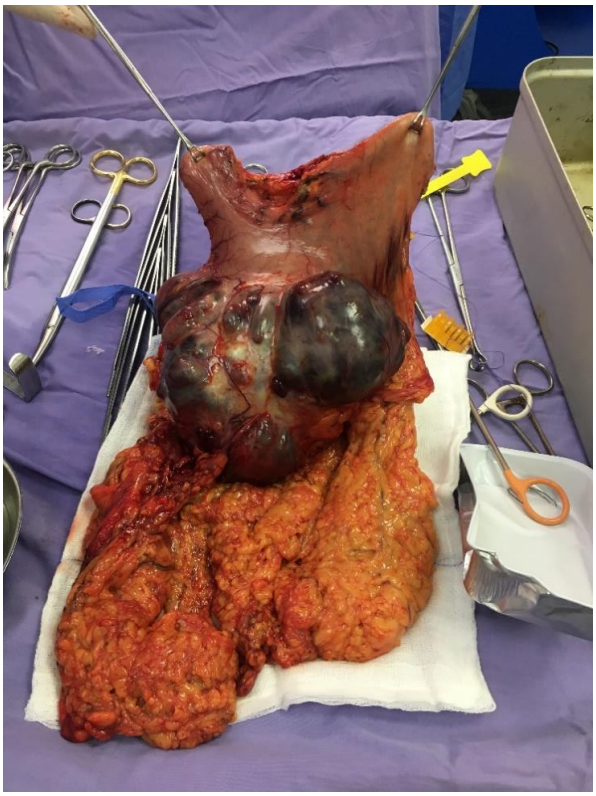

Figure 3: Subtotal gastrectomy with roux-en-y gastrojejunostomy (II)

DISCUSSION

In adults, GISTs most frequently occur in the stomach (60%) and small intestine (30%). On very rare occasions, GISTs can originate from the mesentery, omentum, or retro peritoneum outside the gastrointestinal tract [4].

GIST tumors may present in a wide array of symptoms depending on their sizes and locations. Less than 5% of GISTs are found as part of syndromes like, neurofibromatosis type I (NF I), Carney triad or familial GISTs syndrome [5, 6]. There is a correlation between the risk of recurrence and metastases having variance to the anatomical site of the initial GIST; a previous study found that 38.5-62.5% of the high risk group had recurrence or metastases, and Fletcher risk scheme is a good anticipator of recurrences and metastases [7].

Although abdominal ultrasound is the primary imaging in a patient with abdominal pain or mass, the tumor is often problematically large (making the organ of origin unrecognizable), manifest in a huge mass filling the abdomen, of heterogeneous reflectivity and common necrosis. CT attains the confirmation and staging. Tumors are of varying densities, with patchy enhancement following intravenous contrast. Various degrees of necrosis are commonly shown in the mass. The CT attains fast evaluation of the size of the primary tumor , and metastatic disease is found at the outset. CECT abdomen solid pseudo papillary neoplasm of the pancreas might share the radiological aspect of GIST.

GISTs may appear in a huge size before confirmation with cystic change correlated with a rim of the viable enhancing tumor. Necrosis causes enteric fistulation, and calcification in the tumor is identified in correlation with tumor necrosis. The curative therapy is operative excision with a clear margin (R0). The prognosis primarily relies on the risk factors of the size of the tumor and its mitotic activity. There is a high risk of malignant potential and recurrence in tumors of more than 5-10 cm in size, with a mitotic count of more than 10/50 hpf. There is up to 80% recurrence in high risk groups.

The cornerstone of therapy is operative excision; traditional chemotherapy and radiotherapy are not effective. The protocols for therapy of GIST by the ESMO and ASCO groups are outlined as follows:

Small esophagogastric or duodenal nodules less than 2 cm are low risk, while excision is used for tumors increasing in size or becoming symptomatic. Excision biopsy is for nodules less than 2 cm. If surgery involves multivisceral resection, multiple core needle biopsies are done. Imatinib is prescribed for 6-12 months to attain cytoreduction if R0 excision is not possible. There is a high risk of tumor rupture (spontaneously or during excision). Most metastases or recurrences involve the peritoneum and liver. PET scans are useful to spot tumor response to neoadjuvant. Imatinib mesylate with sunitinib is used for metastatic GIST and for the prevention of recurrences in operated GIST for intermediate and high risk groups. Imatinib mesylate is a multitargeted c-KIT, PDGF–R, and c-ABL inhibitor of T–cell proliferation. Imatinib binds preferentially to ATP binding sites of c-KIT proto-oncogene product, platelet-derived growth factor receptor (PDGF-R), and Abelson kinase (c-ABL), impeding the ensuing signal transduction.

The risk of recurrence is increased if tumor spillage runs intraoperatively. Patients with histological profile of intermediate, moderate, or high risk, and those with R1 and R2 (microscopic and macroscopic tumor residue) or tumor rupture, must be given long-term imatinib

CONCLUSION

It is agreed that the cornerstone therapy for giant GIST is a full operative removal of the tumor with adjuvant management with selective receptor tyrosine kinase inhibitor. Before surgery, R0 resection must be attained individually.

COMPETING INTERESTS

The authors declare no competing interests.

AUTHORS CONTRIBUTION

The author has read and agreed to the final manuscript

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