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Surgical resection for a giant gastrointestinal stromal tumor: A case report

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Abstract

Gastrointestinal stromal tumors (GISTs) are a rare tumor originating from stromal cells inside or outside of the digestive tract. The treatment for GISTs is surgery-centered. However, for a resectable GIST with a large size, the therapeutic options are debatable. Here, we report a female patient with a giant GIST that was surgically removed without complications. Currently, the patient has been tumor-free for 8 months since surgery. It is safe to surgically remove a large GIST, but further investigations are warranted to compare the long-term prognosis of surgical resection and neoadjuvant therapy for GISTs with a large size.

Keywords

gastrointestinal stromal tumors; stromal cells; digestive tract

Introduction

Gastrointestinal stromal tumors (GISTs) account for only approximately 5/million population, or 1% of tumors in the gastrointestinal tract, but are the most common tumor arising from mesenchymal cells in the gastrointestinal system [1,2]. GISTs occur predominantly in the adulthood, with a median incidence in the fifth decade of life. It has been reported that men have a slightly higher incidence than women. GISTs are usually found in the stomach or small intestine, but can occur at any sites of the gastrointestinal tract, and even extra-gastrointestinal locations. Surgical resection is a prioritized therapeutic option for GISTs, although it is challenging to remove GISTs with huge volumes. Here, we report a case with a giant GIST that was successfully removed by surgery.

Case Report

A 58-year old female patient complained of a mass in the abdomen since one year. The original size of the mass was described to be like an adult fist. Since 6 months earlier, the mass became bigger gradually to the size of a newborn's head. The patient sought help from another hospital, where she received an ultrasound-guided biopsy. Histological examinations of the biopsy sample indicate a tumor composed of spindle cells, and then a diagnosis of GIST was suspected. The patient declined the suggestion of surgery provided by that hospital. Since one month, the mass has increased in size more rapidly and the current size is approximately 25 cm in diameter. No apparent body weight loss occurred during the history of

present illness. The patient also complained of bloating, difficulty in defecation, appetite loss, fatigue, and dyspnea. The patient was subsequently admitted to our department aiming to a surgical resection.

The physical examination revealed a large mass in the right upper quadrant (Figure 1). Palpation of the tumor indicated a firm non-mobile tumor in the right upper quadrant. The surface was smooth. The larger diameter was approximately 25 cm. The edge was clear. No tenderness could be triggered. No pulsatile was felt. Percussion revealed dullness of the tumor. No vascular murmurs could be heard during auscultation.

Clinical imaging was ordered to assess the tumor and its relationship with adjacent organs. Computerized tomography (CT) scans with intravenous contrast showed a large tumor in the peritoneal cavity with a larger diameter of 21 cm (Figure 2). The adjacent organs were shifted due to the tumor's huge volume. There seemed to be no vascular invasion. Three-dimensional reconstruction of CT demonstrated the possible invasion to the inferior vena cava (between the level of the right renal vein and that of the right renal lower edge, (Figure 3). A decision for surgical treatment was made and an open laparotomy was performed. During the procedure, the tumor was found to invade the abdominal wall and ileocecal junction. Subsequently, the final surgical decision of an en block resection of the tumor, right colon, and partial abdominal wall was made. The entire procedure took 3 hours, with 200 ml of blood loss. The post-surgery measurement indicated the greatest dimension of the tumor was 22cm, and the weight was 3.3 kg. The post-operative recovery was uneventful. The histopathological assessment revealed high grade GIST (mitotic rate is larger than 5/50 per high power field, Figure 5). Immunohistochemistry assessments indicated CD117 (+), SMA (+), Cyrokeratin (+), and Vimentin (+). Therefore, the final histological diagnosis and stage were GIST, $T_4N_0M_0G_2$, Stage IIIB, and high-risk of recurrence. The patient was scheduled for a routine administration of imatinib mesylate (Glivec, 400 mg PO, qDay). The patient is being followed up since surgery. She remains symptom- and tumor-free for 8 months.

Discussion

GIST as a term was first used to describe an intra-abdominal tumor that was not carcinoma and that exhibited a histologic feature of smooth muscle or nerve cells by Mazur and Clark in 1983 [3]. It has been proposed that the origin of GISTs might be different among patients: approximately one third of GIST lesions are original from smooth muscle lineages (immunohistochemistry positive for smooth muscle actin); one third of GISTs differentiate from nerve cells (positive for S100); and the lineage of the final third cannot be determined (negative for both of the above markers) [4]. Assessed by immunohistochemistry, more than 95% of GISTs characteristically express CD117, also named by mast/stem cell factor receptor (SCFR) or c-KIT [5].

It has been reported that CD117 is expressed in the majority of GIST patients (95%). A breakthrough of the GIST research area was the discovery of the over activation of CD117 in GIST patients. In 1998, Hirota and colleagues [6] first reported the uncontrolled ligand-independent activation of CD117 in GIST patients. The same group also found that patients with familial GISTs carried a germline mutation of CD117 that is over-activated [7]. Nude mice bearing CD117 mutation that induced ligand-independent CD117 activation had a malignant phenotype, indicating the direct roles of CD117 gain-of-function mutations in tumor initiation. The most common mutations of CD117 have been

observed to be in the exon 11, which encodes the intracellular juxta membrane domain of CD117. Besides CD117 mutations, GIST can be induced by other signaling pathways, for instance, the mutations in exon 18 of platelet-derived growth factor receptor-alpha (PDGFRA) [8]. However, there are still a certain number of GIST patients with wild-type CD117 and PDGFRA.

Imatinibmesylate (Gleevec in the United States, Glivec elsewhere) is the major medication for the adjuvant and neoadjuvant therapy for GISTs. Imatinib mesylate potentially inhibits the tyrosine kinase activity of both CD117 and PDGFRA, which consequently blocks the constitutive activation of these signaling pathways, arrests cell proliferation, and induces apoptosis [9].

GISTs mainly arise from the stomach (60%-70%), following the small intestine (20%-30%), and other organs in the gastrointestinal tract (less than 10%) [10]. GISTs can also originate from extra-intestinal abdominal or pelvic sites, including the omentum, mesentery, retroperitoneum, even pancreas [11]. In this case report, the original site of GIST of this patient remains unclear. We think this GIST might occur from the cecum or the retroperitoneum. Given to the invasive manner of this case, the original site cannot be determined. However, we used the staging system for GIST not originating from the stomach to guide the adjuvant therapy and follow-ups. GISTs can occur as multiple lesions, so it is imperative to carefully explore the entire peritoneal and pelvic cavity to exclude multiple lesions and/or metastatic tumors.

Surgery remains the prioritized treatment for patients with primary localized GISTs. Usually, GISTs do not involve the regional lymph nodes, so extensive lymph node resection is not suggested. GISTs are rich in vascular vessels and often exhibit a pseudocapsule, so surgeons should avoid tumor rupture and subsequently peritoneal spread. Surgical margins should also be examined macroscopically and microscopically. More recently, laparoscopic and endoscopic resections are being performed more often, but the outcomes, especially long-term outcomes, need to be evaluated further. Considering the large volume of the tumor in this case, we performed open laparotomy to remove the tumor. Although the indications of potentially surgically removable GISTs are still being debated in the surgical community, our experience of this case indicates that even large tumors can be safely removed by operation with a good prognosis. Our tricks for removing large GISTs are to resect tumors inside the pseudocapsule to avoid injuries of adjacent organs, as our initial observations showed the composition of the pseudocapsule is only fiber tissues without evidence of invading tumor cells (unpublished observation). Therefore, we believe maneuvers inside the pseudocapsules provide a safe and effective surgical path for GIST resections.

Radiotherapy and chemotherapy for GIST patients after surgery appear to have no beneficial roles in preventing recurrence. It is appreciated that administration of imatinib mesylate after surgery potentially delays tumor recurrence. The indication for the adjuvant therapy of imatinib includes large tumors, high risk of recurrence, and metastatic tumors. Risk levels can be measured using AJCC staging systems, or simply the 5's rules, which are tumors larger than 5 cm in greatest dimension and 5 mitoses per 50 nuclei per high-power field [12]. In a randomized trial assessing the benefit of imatinib adjuvant therapy (Z9000 trial) [13], administration of imatinib following resection of primary localized GISTs significantly increased the recurrence free survival rate from 83% to 98% at 1 year compared to placebo. In a recent European cohort, imatinib mesylate therapy starting 1 to 12 weeks postoperatively for 3 years

significantly improved overall survival than1 year of administration (92.0% v.s. 81.7%) [14]. Therefore, it has been suggested by the National Institute of Health of the United States that GISTs patients with moderate to high risk of recurrence should receive imatinib mesylate adjuvant therapy for 3 years.

It is wise to consider neoadjuvant therapy with imatinib for patients with large GISTs that cannot be removed safely without residue. Clinical trials have indicated that neoadjuvant therapy with imatinib mesylate is effective in reducing the tumor size [15]. The treatment response should be monitored closely by ^{18}F-FDG PET scans. The maximal response to imatinib usually occurs between 3 and 6 months after the initial administration. In the current case, the biopsy before surgery could not confirm the diagnosis of GIST, and the patient refused the neoadjuvant therapy concerning side effects and uncertain responses, therefore we did not administer imatinib mesylate prior to surgery.

Conclusion

In conclusion, this case report shows that it is feasible to surgically remove large GISTs. However, further investigations are warranted to compare the long-term prognosis of surgical resection and neoadjuvant therapy.

Figures

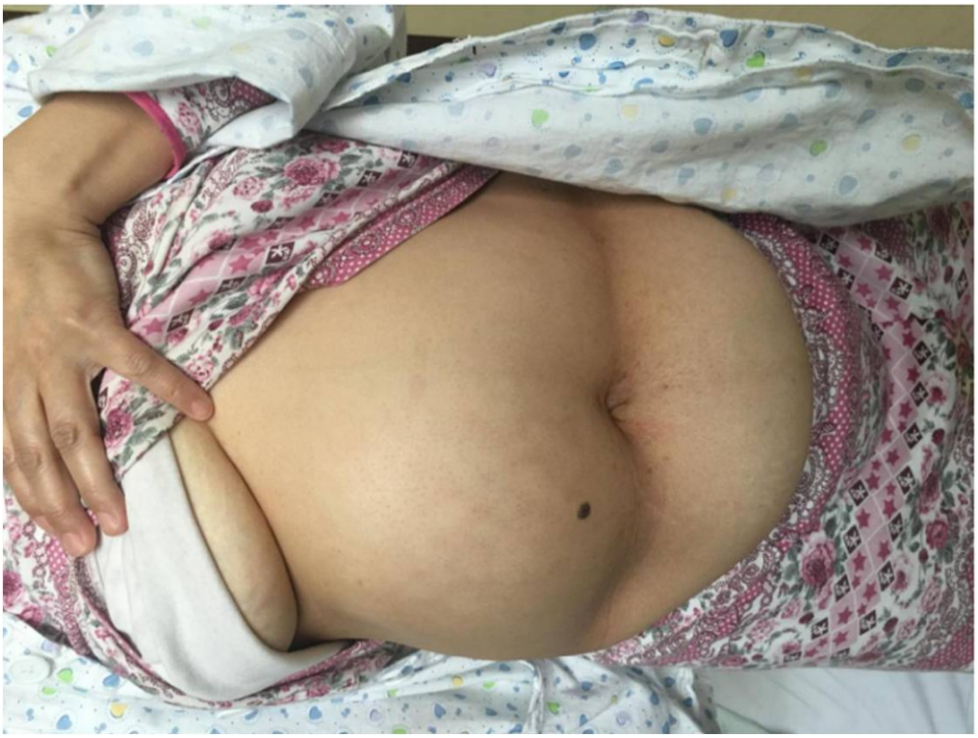

Figure 1: A mass was observed in the right upper quadrant of the patient.

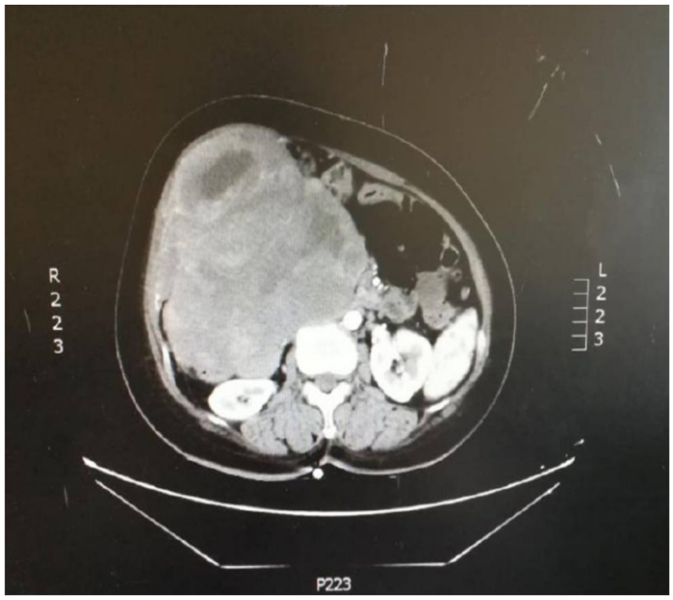

Figure 2: CT scans with intravenous contract indicated a huge tumor in the peritoneal cavity.

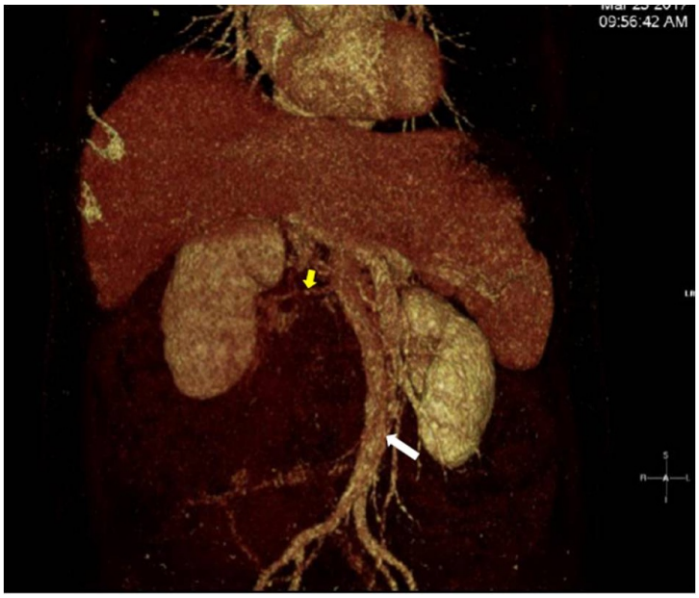

Figure 3: Three dimensional construction of CT demonstrated the invasion to the inferior vena cava. Yellow arrow: the right renal vein. White arrow: the vena cava.

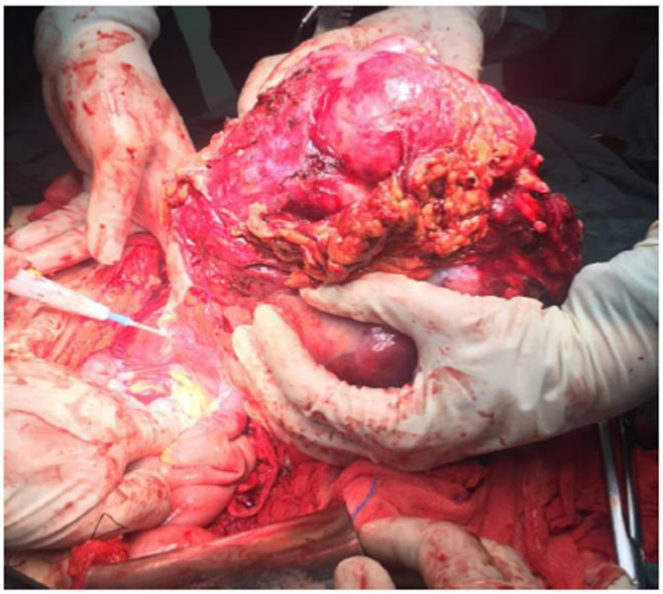

Figure 4: The tumor was removed in an enblock resection from the peritoneal cavity.

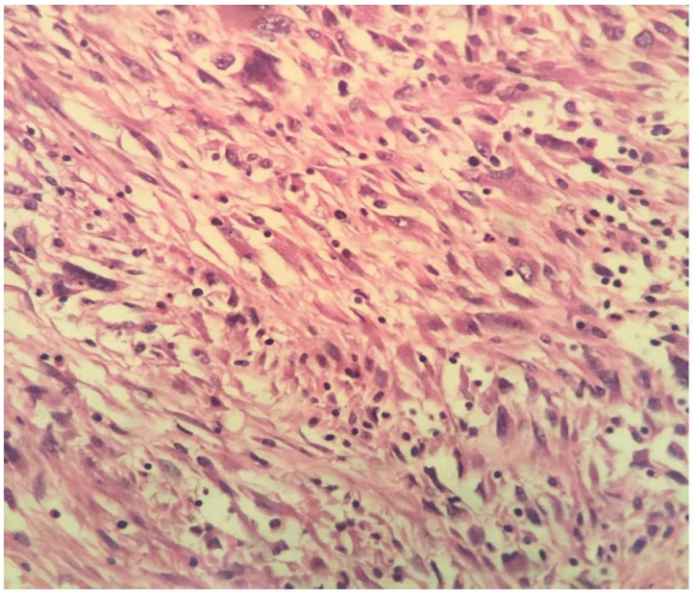

Figure 5: Histological image of the patient, Hematoxylin & Eosin staining 400×.

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