Gastrointestinal Stromal Tumour of the Omentum: A Case Report

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Abstract

Aim

The aim of this paper is to present the first published case of a high-risk gastrointestinal stromal tumour (GIST) in Kuwait.

Case presentation and intervention

A thirty-six-year old Egyptian male patient presented with central upper abdominal pain of five-month duration. Clinically, there was an approximately 10 cm × 8 cm diffuse, non-tender, firm mass in the epigastrium. A tumour of the stomach wall was diagnosed. The mass was surgically excised. At laparotomy there was obvious peritoneal dissemination. Histopathological examination revealed a (GIST) of the omentum. Postoperatively the patient was advised to receive imatinib mesylate for a period of one year.

Conclusion

Despite significant advances in new chemotherapeutic drugs, radical surgery remains the only method offering a chance for long-term survival. Although further data are required to evaluate its use in the adjuvant and neoadjuvant settings, imatinib mesylate currently provides the most effective treatment option in the management of advanced GIST.

Key Words

Gastrointestinal, GIST, omentum, stromal tumour

Introduction

Gastrointestinal stromal tumours (GISTs) may be defined as intra-abdominal non-epithelial (mesenchymal) tumours that express the tyrosine kinase (KIT) protein or have an activating mutation in the proto-oncogene cellular tyrosine kinase (c-KIT) [(1)]. The c-KIT gene encodes the transmembrane type III tyrosine kinase, KIT protein (also known as cluster of differentiation 117 or CD117).

GISTs are commoner in the stomach and small intestine, with a minority of lesions occurring in the colon, rectum, appendix, oesophagus, mesentery or omentum [(2)].

In one series, GISTs were reported to be diagnosed at a frequency of about 15 new cases annually per million [(3)]. Tzen [(4)] and his group reported an annual incidence rate of 13.74 per million. Although rare [(5)], GISTs are considered to be the commonest mesenchymal tumours of the gastrointestinal tract [(1,2,6).]

Surgery remains to be the mainstay of treatment [(5)] and complete resection can be achieved in most cases [(5).] Even for high-risk GISTs, the only effective treatment modality has been surgical [(1)].

Imatinib mesylate is a potent specific inhibitor of KIT that has demonstrated significant activity and tolerability in the treatment of malignant unresectable or metastatic GIST [(2)]. It is proposed as therapy for high-risk GISTs after surgery [(5)]. Moreover, it is possible that the adjuvant and neoadjuvant use of imatinib (e.g. rendering initially inoperable tumours resectable) in the overall management approach to advanced GIST may contribute to surgeons'

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success in prolonging survival [2]. Postoperative recurrence or metastasis [2] occurs in 40% to 90% of all GIST surgical patients. The five-year overall survival ranges from 21% to 88% [5].

We are presenting in this paper the first published case report of a high-risk GIST in Kuwait.

Case Report

A thirty-six-year old Egyptian male presented to Hussein Makki Al-Juma Centre for Specialised Surgery, Kuwait, complaining of central upper abdominal pain of five-month duration. Associated symptoms were early satiety and feeling of fullness after eating small amounts of food. Abdominal examination revealed an approximately 10 cm × 8 cm diffuse, non-tender, firm mass in the epigastrium, deep to the anterior abdominal wall musculature.

Ultrasonography of the abdomen (Fig.1) revealed an enlarged left lobe of the liver. Computed tomography of the abdomen showed a 23 cm × 20 cm × 10 cm necrotic mass in close contact with the left lobe of the liver (Fig.2). The mass displaced the stomach backwards and the spleen and left kidney downwards. The radiological picture was suggestive of a stomach wall tumor. The levels of the alpha-foetoprotein (AFP), carcino-embryonic antigen (CEA) and cancer antigen 19.9 (CA 19.9) were within the reference ranges.

At exploration, done through a midline anterior abdominal wall incision and a left-sided transverse extension, a huge mass arising from the greater curvature of the stomach was seen (Fig. 3). The mass was compressing the left lobe of the liver towards the right side, the lumen of the stomach posteriorly, the spleen towards the left side and colon and left kidney inferiorly. Multiple tumour seedlings of varying sizes that ranged from 0.5 cm to 2.5 cm were noted all over the peritoneal cavity. Two of such nodules were seen on the superior surface of the liver. The mass was completely excised. Four of the peritoneal nodules were excised for histopathological confirmation. The patient made an uneventful recovery.

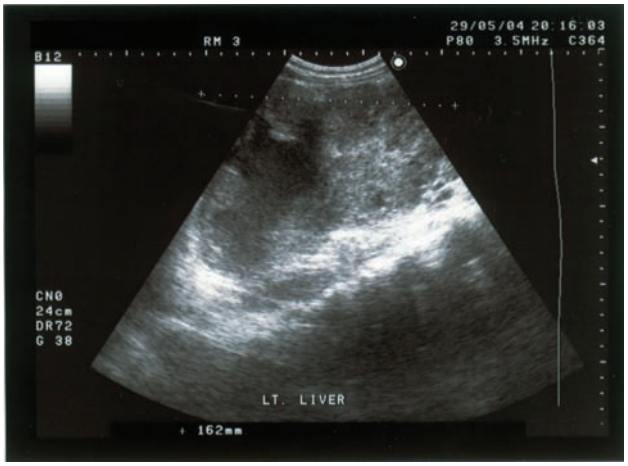

Fig. 1: Ultrasonography of the abdomen showing an enlarged left lobe of the liver.

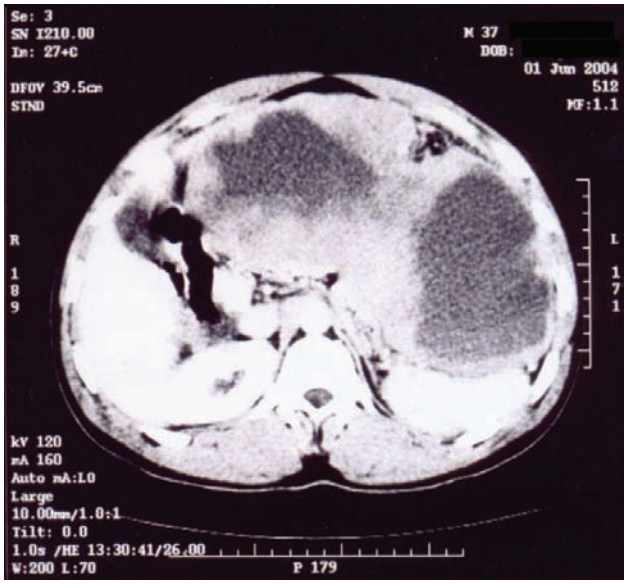

Fig. 2: Computed tomography of the abdomen showed a 23 cm × 20 cm × 10 cm necrotic mass in close contact with the left lobe of the liver.

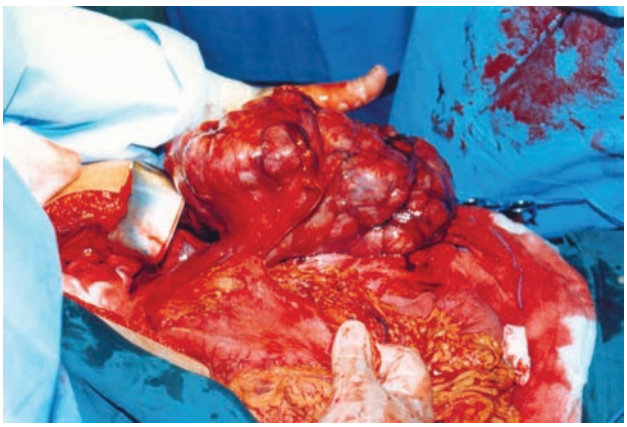

Fig. 3: Exploration of the abdomen revealed a huge mass arsing from the greater curvature of the stomach.

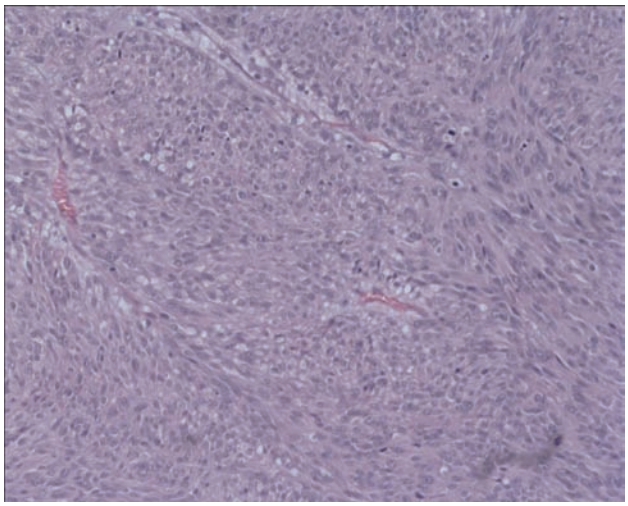

Fig. 4: High power magnification of spindle-cell tumour. The tumor is densely cellular and formed tight fascicles of cells. The cells show marked nuclear hyperchromasia and pleomorphism.

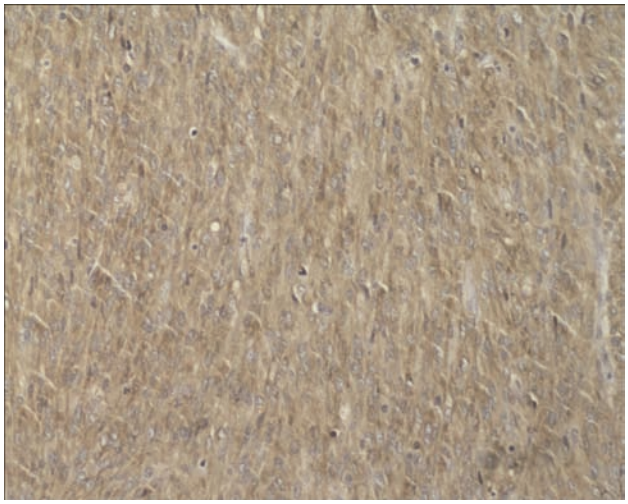

Fig. 5: Strong CD34 immunoreactivity in the malignant omental stromal tumour.

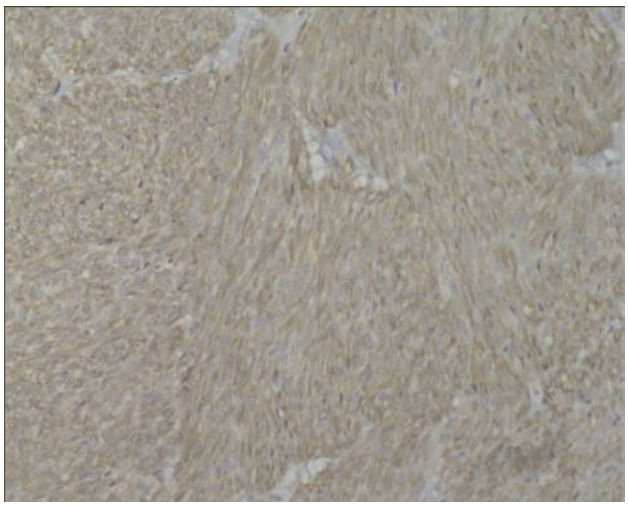

Fig. 6: Strong CD117 immunoreactivity in the malignant omental stromal tumour.

The gross specimen consisted of a mass at the greater curvature and body of the stomach; it measured 25 cm × 23 cm × 12 cm. There was an attached sleeve of stomach measuring 14 cm in length. The tumour measured 11 cm x 7 cm x 6 cm and appeared encapsulated with one area of breach at its attachement to the left copula of the diaphragm. The outer surface was nodular with foci of congestion. When the tumour was sliced, areas of haemorrhage and necrosis were noted. The tumour was friable. On opening the sleeve of the stomach, the mucosa was unremarkable. There was a plane of cleavage between the wall of the stomach and the tumour. The tumour was not reaching the resection margins.

The frozen-section histopathological examination revealed a malignant spindle-cell tumour. Microscopically, multiple sections showed a spindle-cell tumour, in a fascicular pattern of arrangement (Fig. 4). At places, there was a peritheliomatous arrangement. The tumour cells had plump spindled nuclei with moderate eosinophilic cytoplasm. There was moderate nuclear pleomorphism and more than 10 mitotic figures per high power field (HPF). Areas of necrosis were also seen. The background showed foci of myxoid change.

Sections from tissue labelled as nodule at the gastrosplenic ligament, mass at the mesentery of the jejunum, nodule over the mesentery of the sigmoid colon and peritoneal nodule at the rectum showed a similar tumour. Tissue labelled as liver adhesion did not show any malignancy. The stomach mucosa was unremarkable.

Immunohistochemistry stains were positive for CD34 (Fig. 5), CD117 (Fig. 6) and S100, focal positive for smooth muscle actin (SMA) and negative for desmin. The overall features were of a malignant GIST of the omentum. All the excised peritoneal nodules were shown to be tumour deposits of similar histological features as the primary tumour.

Postoperatively, it was decided to give the patient imatinib mesylate for at least one year and to follow him up closely. However, the patient was lost to follow-up.

Discussion

Gastrointestinal mesenchymal tumours were previously categorised into two subgroups of benign and malignant smooth muscle tumours. Today, some of these tumours are classified as GISTs. The term GIST was first coined by Mazur and Clark in 1983 [7] to include a heterogeneous group of non-epithelial neoplasms affecting the gastrointestinal tract. Typically, GISTs are immunohistochemically positive for the KIT (CD117) receptor which is perhaps their single best defining feature. The histologic origin of these tumours has recently been suggested to be the interstitial cells of Cajal (ICC). ICC are the unique pacemaker cells that are normally present in the myenteric plexus. GISTs were suggested to originate from ICC, because of their cell surface expression of CD34 and KIT (CD117) receptors. GISTs carry gain-of-function mutations in genes encoding the KIT (CD117) receptor or platelet-derived growth factor receptor α, both of which are involved in cell survival, development and proliferation.

GISTs can occur anywhere along the gastrointestinal tract, but they most commonly arise in the stomach (65%) or small intestine (25%). About 5%–10% of GISTs are located in the colon and rectum and approximately 5% are found in the oesophagus. A minority of lesions occur in the mesentery or omentum [2]. In other words, GIST of the omentum is a minority subcategory of a rare disease. Nearly all GISTs are sporadic [8].

GISTs are far more common in adults. The average age of patients presenting with the tumour ranging between 40 and 60 years. In a report, which focused on the epidemiology of GISTs and included 1458 cases, no patient below the age of 20 years was reported [9,10]. Other large sample-size retrospective studies confirm that GISTs are mostly observed in adults and are rare in children [10]. The reported male to female ratio was 3:1.

Fletcher et al. classified GISTs into very low, low, intermediate and high-risk categories, according to the tumour size and mitotic count [Table 1] [5]. According to this classification, our reported case belongs to the high-risk category (tumour size 11 cm and > 10 mitotic figures per HPF).

The most reliable prognostic factors are the size of the primary tumour and mitotic index. The latter measures the proliferative activity of the cells. Other prognostic factors include specific histologic subtypes (epitheloid versus spindle cell), the degree of cellular pleomorphism and age of the patient.

Tumour size (cm)	Mitotic Count (50 per HPF)	Risk
< 2	< 5	Very low
2 – 5	< 5	Low
< 5	6 – 10	Intermediate
5 – 10	> 5	Intermediate
> 10	Any	High
Any	> 10	High

Table 1: Fletcher Classification of GIST Tumours

The preoperative diagnostic modalities include ultrasonography, computed tomography (CT), upper gastrointestinal endoscopy, video-capsule endoscopy, isotope scintigraphy and angiography [10].

Furthermore, 18F-Fluorodeoxyglucose (FDG) -positron emission tomography (PET) is a useful technique for assessing GIST. The FDG uptake is considered to predict the malignant potential of GIST [11]. The functional imaging in GISTs with FDG-PET can give additional information that can assist clinicians in the management of patients.

In addition, combined PET and CT offer several advantages over PET. The use of this technique has spread widely over the past few years. Some studies have described PET/CT imaging of GISTs. The sensitivity has been found to be 93% for CT and 86% for PET for the diagnosis of GIST. A false negative on PET scan appears to be related to small lesions. The minimum lesion detected has been reported to be 0.4 cm [11].

Since not all intramural lesions of the gastrointestinal tube are GISTs, a preoperative pathological diagnosis should be obtained. However, even when a biopsy is performed during a conventional endoscopy, the diagnosis may be missed because GIST usually is covered by normal mucosa, leading to insufficient endoscopic biopsy specimens from the deeper layers. Endoscopic ultrasonography, enabling intramural scanning of the gastrointestinal tract, has been reported to be useful in the diagnosis of submucosal tumour and in differentiating submucosal tumour from extraluminal lesions. Nevertheless, the diagnosis on the basis of endoscopic ultrasonography is presumptive and cannot replace a histological diagnosis of GIST. Therefore, definitive tissue diagnosis of submucosal tumour and extra-intestinal lesions is not clear without surgery, and a less invasive method of obtaining tissue diagnosis is desirable. Endoscopic ultrasound-guided fine-needle aspiration has emerged as a minimally invasive technique that allows identification and sampling of various submucosal tumour and extra-intestinal mass lesions.

Definitive surgery remains the mainstay of treatment for patients with localized, primary GIST [5]. Since every GIST is now considered as potentially malignant, all GISTs may need to be resected, even small intramural lesions of the gastrointestinal tract. At surgery every effort should be made to identify the origin of the tumour and related anatomic structures. Complete surgical removal should be the goal, as despite significant advances in new chemotherapeutic regimens, radical surgery is the only method offering a chance for long-term survival [5,12].

Following surgery, high-risk GISTs are treated with selective KIT inhibitors, such as imatinib mesylate [5,12], as they may improve the clinical outcome of the patients with metastasis or recurrence [12,13]. In fact, imatinib has had a significant impact on the management of advanced GIST, which has traditionally had a poor prognosis. Patients with metastases at laparotomy have a significantly lower 5-year survival rate [6].

GIST resistance to conventional chemotherapy has led to a search for more effective systemic therapy in the setting of advanced disease. Imatinib mesylate demonstrated excellent results by controlling tumour growth in up to 85% of advanced GISTs in the phase I, II, and III trials reported to date [8]. This excellent response rate led to the establishment of imatinib as the treatment modality of choice for metastatic GISTs and it allowed investigation of its use in a neo-adjuvant fashion for the management of marginally resectable primary tumours when, because of the size and location of the tumour, resection would require the risk for severe organ dysfunction or when negative margins would be difficult to achieve. Recent reports are demonstrating an increasingly important role for surgery in the multimodality management of GISTs following initial imatinib therapy [8].

Primary resistance to imatinib is rare, affecting only 15% of patients. Half the patients, who initially respond, however, become resistant by 2 years after imatinib initiation. The most common mechanism of acquired resistance is secondary c-KIT mutation [8].

Although further data are required to evaluate its use in the adjuvant and neoadjuvant settings, imatinib currently provides the most effective treatment option in the management of advanced GIST. In a recently published study, Raut et al. [14] reported 69 patients with advanced or metastatic GISTs who were treated with imatinib or sunitinib followed by surgical resection.

In the current case, peritoneal dissemination was discovered intraoperatively. The definitive diagnosis of GIST was made postoperatively. Therefore, there was no way to consider neo-adjuvant imatinib. The patient was lost to follow-up and could not be put on adjuvant imatinib mesylate. Fortunately, the immediate postoperative course was uneventful.

The initial site of recurrence involves the liver in 65% of cases, the peritoneal surfaces in 50% of cases, and both in about 20% of cases [8]. Recurrence and survival rates have also been reported to correlate with the location of the

primary GIST lesion, with small bowel tumours showing a somewhat worse prognosis.

The overall 5-year survival rate for patients with primary gastric GISTs who underwent complete resection ranges from 20% to 63%, with a recurrence rate of 17% to 76%. Miettinen [15] reported that small GIST (< 2 cm) developed no metastasis in 1765 cases categorized into prognostic categories, with follow-up information. In other words, complete surgical resection of GIST smaller than 2 cm is associated with 100% cure.

Conclusion

In the treatment of GISTs, especially high-risk ones, complete surgical extirpation should be the ultimate aim, as radical surgery is the only treatment modality offering a chance for long-term survival, despite significant advances in new chemotherapeutic regimens. If surgery is impossible, imatinib mesylate is offering a hope for advanced and metastatic GISTs. Although further data are required to evaluate its use in the adjuvant and neoadjuvant settings, imatinib currently provides the most effective treatment option in the management of advanced GIST.

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