CASE SERIES

Surgical management of gastrointestinal stromal tumors: a single centre's experience

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Abstract

Background: Gastrointestinal stromal tumors (GISTs) represent 85% of all mesenchymal neoplasms that affect the gastrointestinal track. Aim of this study is to report a case series of 18 GISTs treated surgically in a single centre and to discuss the diagnostic and therapeutic issues regarding these tumors.

Case series: A retrospective search of the unit's medical records from 2002 to 2014 was carried out, to collect all cases diagnosed and treated for GISTs. Demographics and clinical features was obtained for all relevant cases.

Results: Eighteen cases (18) of GIST were identified. Eleven tumors were located in the stomach, 3 tumors in the duodenum and 4 tumors in the jejunum. The mean age at diagnosis was 62.5 (range 42-81) years, while the male to female ratio was 1.57/1 (11 males/7 females). Patients presented with a variety of symptoms and all underwent surgery. The 5-year-survival rate of these patients was 50%.

Conclusion: Due to non-specific presentation of GISTs, initial diagnosis of these tumors may be delayed. High clinical suspicion and knowledge of their characteristics are essentials in order to achieve an early diagnosis and lead patients to surgery as soon as possible. Hippokratia 2015, 19 (1): 73-75.

Keywords: GIST, mesenchymal tumors, surgical management, c-KIT, imatinib

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Introduction

Although gastrointestinal stromal tumors (GISTs) represent 85% of all mesenchymal neoplasms, they are considered rare tumors that arise predominantly in the gastrointestinal track. They were first described as a separate group of mesenchymal tumors in 1998, after the discovery of gain-of-function mutations in the c-KIT protoncogene that characterize and distinguish them from the rest mesenchymal tumors. Presenting symptoms of GISTs can vary from vague abdominal pain to severe acute life threatening bleeding. Due to non-specific presentation of the disease, initial diagnosis of GIST may be delayed. Contrast enhanced computed tomography (CECT) is considered to be the imaging modality of choice for GIST diagnosis while its surgical removal is the primary choice of treatment. Adjuvant treatment with revolutionary molecularly-targeted therapies, such as imatinib mesylate, can reduce significantly the frequency of disease recurrence and prolong the life-expectancy of these patients.

Aim of this study is to report a series of eighteen cases of GISTs treated surgically in a single centre and to discuss the diagnostic and therapeutic issues of these tumors, as well as the morbidity and mortality rates of these patients.

Case series

A retrospective search of the unit's medical records from 2002 to 2014 was carried out, regarding cases diagnosed and treated for GISTs. Data obtained for all relevant cases included demographics and clinical features (sex, age, presenting symptoms, surgical treatment and survival). Despite the rarity of these tumors, 18 cases of GISTs were identified (Table 1). The mean age at diagnosis was 62.5 (range 42-81) years, while the male to female ratio was 1.57/1 (11 males/7 females). Patients presented with a variety of symptoms. Ten patients suffered from vague abdominal pain, anorexia and weight loss, three patients were operated urgently due to severe upper gastrointestinal (GI) bleeding, four patients presented with melenas and anemia, while one patient was diagnosed with GIST incidentally, during routine gastroendoscopy. CECT was performed preoperatively in all 18 patients, which demonstrated accurately the location and extent of the tumors. Gastroendoscopy was performed in 14 patients, as in the other four patients, tumors were located in the jejunum. Eleven tumors were located in the stomach, 3 in the duodenum and 4 in the jejunum. Ten patients underwent subtotal gastrectomy, while 1 patient underwent total gastrectomy. All three patients with GIST located in the duodenum were admitted urgently due to severe upper GI bleeding and underwent emergency surgery. The first patient underwent pylorus-preserving pancreaticoduodenectomy, due to an ulcerated bleeding mass that was found in the second part of the duodenum, located very close to the ampulla of Vater. Ulcerated bleeding masses, located

Table 1. Demographics, surgical procedure and tumor characteristics for the 18 patients treated in our centre for gastrointestinal stromal tumors (GISTs).

No	Age	Sex	Location	Surgical procedure	Mitotic rate	Maximum diameter	Surgical margins	Lymph nodes (positive/total)	Grade of malignancy
1	62	M	2nd portion of duodenum	PPPD	>5/50	2 cm	free	0/9	high
2	77	M	Jejunum	Enterectomy	5-10/50	7.3 cm	free	1/9	moderate
3	49	M	Stomach	Subtotal gastrectomy	<5/50	3 cm	free	0/34	low
4	60	F	Stomach	Subtotal gastrectomy	<5/50	6.5 cm	free	0/7	moderate
5	69	M	Stomach	Subtotal gastrectomy	5-10/50	7.2 cm	free	0/2	high
6	61	F	Stomach	Subtotal gastrectomy	5-10/50	1.6 cm	free	1/16	moderate
7	67	M	Stomach	Subtotal gastrectomy	>5/50	1 cm	free	0/18	moderate
8	44	F	Jejunum	Enterectomy	2/50	6.6 cm	free	0/3	moderate
9	47	M	Jejunum	Enterectomy	4-5/10	4.2 cm	free	0/4	low
10	75	F	Stomach	Subtotal gastrectomy	5-10/50	0.8 cm	free	0/9	low
11	42	M	Stomach	Subtotal gastrectomy	<5/50	3.3 cm	free	0/20	low
12	81	M	Stomach	Subtotal gastrectomy	<5/50	3 cm	free	0/13	low
13	75	F	Stomach	Total gastrectomy	>5/50	13 cm	free	0/10	high
14	54	F	3rd portion of duodenum	Segmental duodenal resection	>5/50	2cm	free	0/14	high
15	62	M	4th portion of duodenum	Segmental duodenal resection	5-10/50	1.8 cm	Free	1/7	high`
16	49	M	Stomach	Subtotal gastrectomy	>5/50	13 cm	free	0/20	high
17	80	M	Jejunum	Enterectomy	5-10/50	8 cm	free	0/12	moderate
18	71	F	Stomach	Subtotal gastrectomy	5-10/50	10.3 cm	free	0/8	moderate

F: female, M: male, PPPD: pylorus-preserving pancreaticoduodenectomy.

in the fourth and third part of the duodenum, were found in the second and third patient, respectively. Segmental resection of the third and fourth portion of the duodenum was performed in both patients. All four patients with GIST located in the jejunum underwent segmental resection of jejunum. The mean size of these tumors was 5.26 cm (0.8-13 cm). Metastatic tumors were found intra-operatively in two patients with mesenteric infiltrations and liver metastases. Based on the histopathological findings, tumor's size and mitotic rate, six patients were found to have of high grade, seven of moderate grade and five of low grade of malignancy. According to these result, a therapy with imatinib was initiated in 13 patients (high and moderate grade patients). Follow up included CT scan every 3-6 months for all patients with high and moderate grade, while those with low grade of malignancy underwent CT scan once a year. The two patients with metastatic disease died in 6 and 8 months, respectively after surgery due to diffuse peritoneal carcinomatosis. Recurrence of disease occurred in four patients with high grade of malignancy during the first two years, while seven (with moderate and low grade of malignancy) patients are free of disease 5 years on follow up. Two patients died due to severe cardiovascular disease. The 5-year-survival rate of the current case series patients was 50%.

Discussion

In the past, GISTs were classified as leiomyomas, leiomyoblastomas and leiomyosarcomas and it was only recently that GISTs were considered as a separate entity. Immunochemistry demonstrated that these tumors lacked features of smooth muscle differentiation and while some had markers of neuronal differentiation, some other had neither[1-3]. Mazur *et al* first introduced the term "gastrointestinal stromal tumor" in 1983[3] but it was Hirota *et al*, in 1998 who managed to reliably distinguish GIST from other histopathological subtypes of mesenchymal tumors. They reported that GISTs contained activated c-KIT mutations, which play a central role in its pathogenesis, and that mutations of c-KIT resulted in gain of function of the enzymatic activity of the KIT tyrosine kinase receptor, a glycoprotein expressed by the interstitial cells of Cajal[4-6].

GISTs represent the most common (85%) mesenchymal tumors that affect the gastrointestinal track[7] and have an annual incidence of 11-14 per 10,000,000, and form 0.1%-3% of gastrointestinal malignancies[8]. In the reported cases, the median age of patients was 62.5 (range 42-81) years, with a small male predominance (1.57/1; 11 males/7 females) which is in accordance with the reported in the literature[9,10].

GISTs have uncertain biological behavior, high phenotypic polymorphism and show a wide range of clinical phenotypes from indolent-benign to malignant with high metastatic capacity. They can vary greatly in size from a few millimeters to more than 30 cm but their median size is between 5 cm and 8 cm[9,10]. In the reported case series the mean diameter was 5.26 cm, ranging from 0.8 to 13 cm.

Macroscopically, GISTs often display an exophytic growth pattern, projecting into the abdominal cavity and displacing other organs[9,10]. GISTs can develop anywhere in the gastrointestinal track, but the most common locations are stomach (60%) and small intestine (30%). In the reported case series, the tumor was located in the stomach in 11 patients (61.1%), including three tumors with exophytic growth, in the duodenum in 3 patients (16.6%) and in the jejunum in 4 patients (22.2%), all the later with exophytic growth.

Up to 30% of GISTs show high malignant behavior such as metastasis and infiltration of adjacent organs. They usually give metastatic spread throughout the peritoneal cavity and to the liver, while lymph nodal infiltration is very rare[10,11]. In the reported case series, two patients were found intra-operatively with mesenteric in-

filtrations and liver metastases.

Only 70% of the patients with GIST are symptomatic; 20% are asymptomatic and diagnosed incidentally while the remaining 10% of GISTs are found only in autopsies. Symptoms may vary greatly and depends on the size and location of the tumor[8,9,12].

Initial diagnosis of GIST may be delayed due to the non-specific presentation of the disease. CECT is considered to be the imaging modality of choice, as it can characterize the lesion, evaluate its extent and assess the presence of metastasis. It can also be used for monitoring response to therapy and for follow-up surveillance for recurrence[13]. Endoscopic Ultrasound (EUS) has been used in the diagnosis of GIST as it can assess the depth of invasion and can be useful in obtaining a tissue sample. The efficacy of EUS guided fine needle aspiration (EUS-FNA) has been pointed out in several studies and the reported accuracy is reported to be 80%-85%[13,14]. GISTs are positron emission tomography (PET) avid tumors[15], so PET is useful in revealing small metastases which would otherwise not been showed by CECT. PET can also help to differentiate an active tumor from necrotic or inactive necrotic tissue and malignant from benign tumor[16].

Surgical removal is the primary treatment of choice in localized or potentially resectable GIST. These tumors are considered to be very fragile, so they must be handled with care in order to avoid tumor rupture, and achieve complete tumor resection with their pseudocapsule intact. Lymphadenectomy is not required as GISTs have a low incidence of nodal metastases[7,13]. In the present case series, complete resection was achieved in all patients. From the histopathological findings, regarding the size of the tumor and the mitotic rate, six patients were found to be of high, seven of moderate and five of low grade of malignancy. According to these result, a therapy with imatinib was initiated to 13 patients.

During follow up, 50% of patients with GIST will develop recurrence of their disease or metastasis following complete surgical resection[10,13,17]. The 5-year survival rate is approximately 50%, while the median time to recurrence after resection of primary high grade GIST is two years. In the reported case series, 5-year survival rate was also 50% and the median time to recurrence after resection of primary high grade GIST was 2 years, in accordance with the international literature. Knowledge of GIST pathology and better understanding of gain-of-function mutations in the c-KIT protoncogene led to discovery of revolutionary specific, molecularly-targeted therapies such as imatinib mesylate[18]. Imatinib mesylate is a tyrosine kinase inhibitor which prevents and slows down GIST progression and has been shown to improve progression free survival and overall survival[19,20].

Conclusion

GISTs are rare mesenchymal tumors that affect the gastrointestinal track and can present with a variety of usually non-specific symptoms. Due to non-specific presentation, initial diagnosis of these tumors may be delayed. High clinical suspicion and knowledge of their characteristics are essentials so as to achieve an early diagnosis and lead patients to surgery as soon as possible. Molecularly-targeted adjuvant therapies, such as imatinib mesylate, are currently used in order to improve overall survival.

Conflict of interest

Authors declare no conflict of interest.

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