GASTROINTESTINAL STROMAL TUMOR: SINGLE-CENTER EXPERIENCE WITH REVIEW OF THE LITERATURE

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ABSTRACT

Objective*: Gastrointestinal stromal tumors (GISTs) are the commonest mesenchymal tumors and these tumors stand for 0.2% of all gastrointestinal tumors. This study aimed to present the pathological and histological features, our clinical practice with surgical treatment, and the outcomes of GIST diagnosed in our center.*

Materials and methods*: A retrospective study of 48 consecutive patients with GIST treated at our institution from June 2008 to September 2015 was performed. Information regarding age, gender, tumor location, size, procedure performed, postoperative complications, and long-term follow-up were collected from the patient charts. Immunohistochemistry studies were performed to corroborate the diagnosis. The mitotic count was performed on 50 HPFs (50 consecutive high-power fields), with a wide-field ocular microscope.*

Results*: The most common primary site was stomach in 18 patients, followed by small intestine in 15. Among the study group, four patients presented with recurrent disease either isolated recurrence or metastasis. Surgery was performed in all patients. Three patients had a R2 resection and the rest of the patients had tumor-free margins (R0 resection). In our cohort we had 13 patients who received adjuvant imatinib. A variety of surgical procedures was performed. The tumor size varied from 0.8 to 22 cm. The mean follow-up period was 54.0±1.4 months. During the follow-up period, four patients had recurrence. One patient had metastasis during the follow-up. Six patients died due to GIST, four patients died due to other disease.*

Conclusion*: This study highlights the changing presentation and treatment approach, as well as the outcomes achievable for GIST tumors. These results are valuable for understanding the clinical and pathological characteristics of patients with GIST, who are diagnosed, treated and followed up in Turkey.*

Keywords*: Gastrointestinal stromal tumor, stromal tumor, follow-up, long term.*

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Introduction

Gastrointestinal stromal tumors (GISTs) are the commonest mesenchymal tumors which arise in the gastrointestinal (GI) tract and these tumors stand for 0.2% of all GI tumors[(1)]. It is thought that GISTs stem from GI pacemaker cells called as Cajal interstitial cells which are involved in the production of electrical pacemaker activity for the motility of GI system[(2)]. Hitherto, these mesenchymal tumors were categorized as leiomyomas, leiomyosarcomas, or leiomyoblastomas established mainly on their histological types. The concept of "stromal tumor" was originally created in 1983 by Mazur&Clark to define a diverse group of GI tumors[(3)]. Over 90% of GISTs occur in adults over 40 years of age, with a median age of 63 years. However, GIST cases have been reported in all ages, including children. The incidence does not differ with sex, though a study reported that there is a slight predominance of males[(4)].

GISTs are described as tumors of the GI tract from mesenchymal origin of which immunohistochemistry provide the diagnosis of certainty [posi-

tivity for KIT (CD 117) and CD34 (human progenitor cell antigen)] and highlights the markers of aggressiveness (elevated Ki67 labeling index)[5].

Usually demographic, clinicopathological, and treatment outcome data come from well-designed randomized trials. However, in real life the circumstances and outcomes might be different. We aimed to present the pathological and histological features, our clinical practice with surgical treatment, and the outcomes of GISTs diagnosed in our center.

Materials and methods

Study design

The study has been conducted by the principles of the Helsinki Declaration and approved by the local Institutional Review Board. A retrospective study of 48 consecutive patients with GIST treated at our institution from June 2008 to September 2015 was performed.

Outcome parameters

Information regarding age, gender, tumor location, size, procedure performed, postoperative complications, and long-term follow-up were collected from the patient charts. Tumor size was recorded as the largest diameter of the primary tumor.

Immunohistochemistry studies were performed [KIT (CD 117), CD 34, Vimentin, smooth muscle actin (SMA), S100, Desmin, and Ki-67 labeling index] to corroborate the diagnosis. The mitotic count was performed on 50 HPFs (50 consecutive high-power fields), with a microscope with wide field oculars (the area of a single HPF being approximately 0.5 mm^2).

Results

There were 26 males and 22 females. The mean age was 59.375 ± 12.928 (range, 35 to 84) years. The most common primary site was stomach in 18 (37.5%), followed by small intestine in 15 (31.3%), retroperiteneal in 9 (18.8%), omentum in 3 (6.3%), colorectal in 2 (4.2%) and spleen in 1 (2.1%) patient. Among the study group, four patients (8.3%) presented with recurrent disease either isolated recurrence or metastasis. Two patients showed peritoneal and one showed liver metastasis at diagnosis.

Surgery was performed in all patients. Three patients had a R2 resection and the rest of the patients had tumor-free margins (R0 resection). In our cohort we had 13 patients who received adjuvant imatinib. A variety of surgical procedures was performed. The information regarding the type of surgery are presented in Table 1. Lymph node metastasis was detected in 1 out of 48 cases (2.1%) who died due to hepatic metastasis 12 months after surgery.

Operation	Number
Resection of small intestinal loops	15
Partial gastrectomy	7
Excision of retroperitoneal tumors	7
Total gastrectomy	4
Omentectomy	3
Partial gastrectomy+ omentectomy	2
Transverse colectomy+ small intestinal loops	2
Resection of recurrent masses	2
Partial gastrectomy+ splenectomy+ omentectomy	2
Colectomy	1
Transverse colectomy+ small intestinal loops+ hepatic metastatectomy	1
Splenectomy	1
Partial gastrectomy+ splenectomy+ omentectomy+ retroperitoneal tumor excision	1
Total	48

Table 1: Surgical treatment in patients with GIST.

The size of the tumor varied from 0.8 to 22 cm. A definitive diagnosis of GIST was made after surgery by examination of the resected specimen. GIST diagnosis was determined by tumor cell morphology and immunohistochemistry characteristics, mainly a positive staining for KIT (Table 2). Forty-four of 48 specimens (91.6%) were KIT (CD 117) positive, 37 of 48 specimens (77.1%) were CD34 positive, 23 of 24 specimens (95.8%) were vimentin positive, 21 of 42 specimens (50%) were SMA positive, 8 of 45 specimens (17.7%) were S100 positive, 1 of 42 specimens (2.4%) was desmin positive. Ki-67 labeling index was studied in 42 of 48 specimens and was 11.74±15.49%. Of these 42 patients, 14 have Ki-67 labeling index > 10%. Twenty-two of 48 (45.8%) patients had mitotic counts of > 5/50 HPFs.

The mean follow-up period was 54.0±1.4 months. During the follow-up period, four patients (8.3%) had recurrence. One patient had metastasis

during the follow-up. Six patients died due to GIST, four patients died due to other disease.

Immunohistochemistry	No.
KIT (CD 117)	44/48 positive
CD 34	37/48 positive
Vimentin	23/24 positive
SMA	21/42 positive
S100	8/45 positive
Desmin	1/42 positive

Table 2: Immunohistochemistry of tumor samples.

Discussion

Even though the GIST incidence is increasing in the Asian inhabitants, existing data on this topic is yet limited, particularly reports with significant sample-size in a single center.

More than 90% of GISTs appear in adults older than 40-years of age, with a median age of 63 years. Nevertheless, patients with GISTs have been described in all ages, as well as children[6,7]. The present report revealed that GIST rates culminate amongst individuals in their 50s & 60s. In our series, the youngest patient was female aged 35 years with gastric GIST and the oldest patient was a male aged 84 year with small intestine GIST. Even though in the majority of available literature, there is no well-defined sex predilection[5], several papers showed that there was a minor male dominance[7]. Our data correspond with the latter. In the present report, there were 26 males and 22 females, with a mean age of 59.4 years.

GISTs may rise from any organ in the GI tract and also in extragastrointestinal sites involving retroperitoneum, mesenterium, and omentum[8].

In the present study, the commonest GI site of the GISTs was stomach, followed by small intestine. Liver metastases and intra-abdominal spread are the two major pathways of extent of malignant GISTs (8). Distant metastasis to the lymph nodes, lungs, and bones may occasionally be observed (9). Among the study group, four patients presented with recurrent disease either isolated recurrence or metastasis. Two patients showed peritoneal and one showed liver metastasis at diagnosis.

During the follow-up period, four patients (8.3%) had recurrence. One patient had metastasis during the follow-up.

Surgical treatment of the GIST is the gold standard treatment for operable GISTs. Total resection should be performed deprived of GIST capsule rupture and spread of tumor cells into the abdominal space[10]. Imatinib is the accepted treatment for individuals with recurrent, locally advanced, or metastatic diseases[11]. Surgery was performed in all patients. Three patients had a R2 resection and the rest of the patients had tumor-free margins (R0 resection). In our cohort we had 13 patients who received adjuvant imatinib. A variety of surgical procedures was performed.

Positive immunohistological staining for CD34 and CD117 has been revealed to support the detection of tumors originating from Cajal cells[12]. CD34 protein is shown in nearly 40-70% of GISTs whereas CD117 protein in nearly all cases[13]. Further indicators, such as SMA, display varying expression in 20-30% of GISTs and S100 in nearly 10% of GISTs, while desmin is faintly expressed in nearly 2% of individuals only. Forty-four of 48 specimens (91.6%) were KIT (CD 117) positive, 37 of 48 specimens (77.1%) were CD34 positive.

The natural manners of GISTs is multifaceted and variable. Size of the tumor and mitotic counts are thought to be two main factors for foreseeing the clinical progression and recurrence risk[14,15]. The size of the tumor varied from 0.8 to 22 cm. Twenty-two of 48 (45.8%) patients had mitotic counts of > 5/50 HPFs.

Lymph node metastasis of GISTs is uncommon, with incidence ranging from 0 - 5%; so standard lymph node dissection is not essential[16,17]. Lymph node metastasis is usually considered as a morphological feature associated with malignancy and poor prognosis, as supported in our data[18,19]. Lymph node metastasis was detected in 1 out of 48 cases (2.1%) who died due to hepatic metastasis 12 months after surgery.

This study highlights the changing presentation and treatment approach, as well as the outcomes achievable for GIST tumors. These results are valuable for understanding the clinical and pathological characteristics of patients with GIST, who are diagnosed, treated and followed up in Turkey.

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