ABSTRACT

Background: Gastric GISTs account for more than half of all gastrointestinal stromal tumors and represent less than 5% of all gastric tumors. The peak age for harboring GIST of the stomach is around 60 years and a slight male preponderance is reported. These tumors are identified by expression of CD117 or CD34 antigen. Symptoms at presentation usually include bleeding, abdominal pain or abdominal mass. Endoscopically, they typically appear as a submucosal mass with or without ulceration and on CT scans an extragastric mass is usually seen. Complete surgical resection provides the only chance for cure, with only 1-2 cm free margins needed. However, local recurrence and/or metastases supervene in almost half the patients treated with surgery alone, even when no gross residual is left. Thereby imatinib mesylate was advocated as an adjuvant to surgery, which appears to have improved disease-free and overall survival.

Aim of the Work: The aim of this work was to assess clinico-pathological features of gastrointestinal stromal tumors (GIST) of the stomach and to appraise the results of treatment by surgery in patients treated at the National Cancer Institute (NCI) of Cairo between January 2002 and December 2007.

Patients and Methods: Nineteen patients with histologically and immuno-histochemically proven GIST of the stomach were treated by surgery at the NCI during the 6-year study period. Preoperative assessment included detailed history, clinical examination, full laboratory tests, endoscopy, abdominal ultrasound and CT. General medical assessment included chest X-ray, ECG and echocardiography.

Results: The patients' age ranged from 26 to 77 years with a median of 51 years. Obvious male/female preponderance was noticed (68.4% to 31.6%). Tumors were located at the upper 1/3 in 42.1%, at the middle 1/3 in 31.6% and at the lower 1/3 in 26.3%. The most common clinical presentation was related to bleeding (hematemesis, melena or anaemia) and was seen in 63.2%. No tumors were labeled as very low or low risk while there were 52.6% intermediate risk and 47.4% high risk. Wedge resection was carried out in 15.8%, partial gastrectomy in 37.8%, total gastrectomy in 5.2%, extended gastric resection in 21.1% and only biopsy in 5.2%. Lymphadenectomy was carried out in 5/19 patients to reveal negative lymph nodes in all five. Complications occurred in 73.7% of patients and only 1 case of early postoperative mortality was recorded. Two patients were lost to follow-up. The remaining 16 patients were followed-up for a period ranging from 6-34 months with a mean of 19.5±6 months and they were all alive by the end of the study, 10 were free of disease and 6 showed disease recurrence.

Conclusion: Gastric GIST can present with vague and non specific clinical picture. Therefore, thorough clinical and radiological evaluation and preoperative endoscopy and biopsy are essential to reach the diagnosis and to assess the risk for metastasis. The clinical outcome of these tumors is influenced by completeness of tumor extirpation while avoiding tumor rupture, and by the tumor malignant potential. Accordingly for tumors with adverse factors, multimodal therapy with adjuvant imatinib or one of its successors should be considered in order to improve overall and disease-free survival.

Key Words: Gastric – GIST – Surgical treatment.

INTRODUCTION

The term GIST was first introduced in 1983 by Mazur and Clark [1] to describe non-epithelial tumors of the GI tract that are thought to arise from the interstitial cells of Cajal (ICC) which are components of the intestinal autonomic nervous system and that act as pacemakers regulating peristalsis [2]. In 1998, Hirota and colleagues [3] demonstrated gain-of-function mutations of the KIT proto-oncogene in the vast majority of GISTs. This lead to identification of these tumors by the universal expression (~95%) of the CD117 antigen, part of the KIT receptor. About 60% to 70% of GISTs may show immuno-positivity for CD34 which is more common in the colorectum and esophagus [4].
Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the GI tract [4] with an annual incidence in the United States ranging between 10-20 per million [5,6]. In Egypt the relative incidence reported by the National Cancer Institute is 2.5% of all GI tumors and 0.3% of all malignancies [7]. These tumors can arise throughout the GI tract, and the stomach is the most common site, accounting for 50%-70% of GISTs [5,6,8] but representing <5% of all gastric tumors [9], with the proximal stomach being involved in about two thirds of the patients [10]. Less frequently, other GI organs may be affected such as the small intestine (25%-30%), the rectum (5%), the esophagus (2%) and other abdominal locations (5%) [11,12].

Gastric GISTs have been identified in patients ranging from 8 to 95 years of age. However, the peak age of diagnosis is around 60 years in most series, with less than 10% of the tumors found before the age of 40 years. There is a slight male predominance in adult patients, whereas most pediatric GISTs arise in girls [8].

Metastases are found at presentation in 10%-47% of cases, the most frequent locations being the liver (65%) and omentum (21%) while lymph nodes are rarely affected (2-6%). The pattern of metastatic spread is almost entirely intra-abdominal; hence bones and lungs are affected in only 6% and 2% respectively [13].

Many GISTs are asymptomatic and they are discovered accidentally upon imaging or laparotomy for other reasons. Symptomatic GISTs tend to be large, with an average size of 6cm, versus 2cm for asymptomatic tumors and 1.5cm for those detected at autopsy [14]. GISTs arising from the stomach most frequently present with GI bleeding and anaemia (54.4%), abdominal pain (16.8%), or a palpable mass; but spontaneous tumor rupture very rarely takes place (1.7%) [8].

Histologically, most GISTs are composed of spindle-shaped cells (70%). However, some GISTs are dominated by epithelioid cells (10%-20%) or contain a mixture of spindle and epithelioid morphologies (10%-20%) [8]. GISTs behavior ranges from benign to malignant and these tumors are now classified according to their size and mitotic count (MC) into one of the following categories: very low risk, low risk, intermediate risk and high risk [15]. Lesions <2cm and those with low mitotic index only occasionally demonstrate metastases [16] while those 2-5cm exhibit metastatic behavior in up to 20% of cases [17].

Upon endoscopy, the appearance of a primary GIST is that of a submucosal GI tract lesion, with or without ulceration [18]. Because of their submucosal location, FNAC or core needle biopsy with endoscopic ultrasound guidance is frequently required for tissue diagnosis [16]. CT scans (Fig. 1) are significantly helpful to determine the exact extent of the tumor and assist in both staging and grading of the tumor for pre-operative planning. An exophytic pattern of growth (Fig. 2), together with the absence of associated lymphadenopathy help to differentiate GISTs from other gastric tumors such as lymphomas or adenocarcinomas [19].

Surgical resection remains the standard treatment of choice for all resectable non-metastatic tumors since it provides the only chance for cure at the present time [13,20,21]. A 1-2cm margin was advocated to achieve adequate resection [22]. However, more recently, DeMatteo et al. [13] demonstrated that tumor size (and not wide negative microscopic surgical margins) is more important in determining survival. Positive resection margins have not been proven to compromise survival but they may result only in a higher risk of peritoneal relapse [13,20]. Therefore, the surgeon’s goal should be a complete resection with only negative gross margins. Accordingly, wedge resection has been advocated by many investigators for the majority of gastric GISTs [13,20,21]. In some cases, however, tumor size and location may dictate a more extensive surgery, including partial or even total gastrectomy [23,24]. Locoregionally advanced tumors requiring total gastrectomy or extended resections should be considered for neoadjuvant treatment with imatinib mesylate to be subsequently re-evaluated for more limited resection [25].

Laparoscopic resection of GISTs should be limited to tumors less than 2cm [23]. It provides the advantage of minimal tissue manipulation and effective diagnosis and treatment of obscure cases presenting with acute bleeding [26].

Avoidance of tumor rupture is imperative to avoid complications such as bleeding or intra-
abdominal dissemination of tumor cells with subsequent high risk of tumor recurrence [27]. Therefore, intra-abdominal open biopsy is discouraged by most experts because of the risk of tumor spillage [20].

Lymphadenectomy is not routinely required since lymph node involvement is rare with GIST [13]. Nevertheless, LN dissection should be considered for patients with any suspicion of nodal metastasis [28].

Until the year 2000, chemotherapy and radiation treatments had no proven effective role in the treatment of advanced disease and the only known “effective” treatment for metastatic GISTs was surgery [29]. However, disease recurred in all patients after a very short disease-free interval and 5 and 10-year survival rates after potentially curative surgery alone were reported to be 32-78% and 19-63% respectively [13,30-33].

Imatinib mesylate was recently introduced as an integral component of GIST treatment. It is a potent and specific inhibitor of the KIT-protein tyrosine-kinase and it has been approved for the treatment of KIT (CD 117)-positive unresectable or metastatic GISTs. However, the use of adjuvant imatinib after complete resection of primary GIST is still being evaluated [34].

PATIENTS AND METHODS

Patients:

Nineteen patients with primary or recurrent gastric stromal tumor (GIST) were operated upon at the department of surgery of the National Cancer Institute of Cairo in the period between January 2002 and December 2007. This retrospective descriptive clinical study was based on studying the patients’ data retrieved from their medical records over that 6-year period.

The studied parameters included patients’ demographic characteristics such as age, gender and occupation as recorded in patient’s files (Table 1). Clinical data retrieved from patients’ records included symptoms, tumor’s location, size and histology (Table 2). Information regarding type of operation, resection margin and lymph node status (Table 3).

Preoperative assessment included CBC, liver and kidney function tests, chest X-ray and cardiac function assessment. Preoperative diagnosis was based on endoscopic, ultrasound (US) or CT imaging (Fig. 1) and guided biopsy; while metastatic work up included abdominal US and/or CT, bone scan and chest X-ray.

Evaluation:

All tumors were reviewed by experienced pathologists for histological confirmation of the diagnosis of GIST and evaluation of the morphological and immuno-histochemical characteristics. All included tumors were c-KIT (CD117) or (CD34) positive. Tumor size was evaluated on fresh specimens. The mitotic rate was assessed by counting the number of mitosis per 50 high power fields (HPF) in all patients. The tumors were classified according to the risk assessment suggested by Fletcher et al. [15] into one of 4 categories: very low, low, intermediate or high risk.

Treatment:

Different types of gastric resections were carried out and they were classified into the following categories; RO was defined as complete resection. R1 included complete resection of accompanying peritoneal seeding, omental or liver deposits. R2 entailed leaving gross residual [35]. Imatinib mesylate was administered to patients having distant metastases at diagnosis, undergoing an incomplete (R2) resection or experiencing recurrence after surgical resection.

Evaluation of treatment results:

All patients were carefully followed-up clinically at three-monthly intervals and endoscopically, by ultrasound and by CT at six-monthly intervals. The follow-up period was calculated from the date of surgery to the last month of follow-up, tumor recurrence or death. Postoperative hospital stay, complications, site and time of recurrence and survival were also noted (Table 4).

RESULTS

Nineteen patients were considered eligible for this study. They were 13 males and 6 females and their ages ranged from 26 years to 77 years (median: 51 years). Their tumor size ranged from 5 to 50 cm with a median size of 18.5 cm. Tumors measured 5-10 cm in 15 patients and 10-50 cm in 4 patients. The mitotic counts of the tumors were found to be <5/50 HPF in 10 cases, 5-10/50 HPF in 6 cases and >10/50 HPF
in 3 cases. All included tumors were c-KIT (CD-117) positive (16 cases) or CD-34 positive (3 cases). The histological types of the tumors were Spindle cell type in 13 cases, Epithelioid type in 2 cases, mixed type in 2 cases and unclassified in 2 cases. Patients were subdivided into 4 groups according to Fletcher’s risk assessment rules [15]. None were assigned to the very low or to the low risk groups, 10 cases were labeled as intermediate and 9 cases fell in the high risk category (Table 1).

All patients were symptomatic at presentation. The main presenting symptoms were abdominal pain in 10 patients, a palpable abdominal mass in 7 cases and gastrointestinal bleeding (hematemesis or melena) in 2 cases. In addition, 10/19 patients were found anaemic with a Hemoglobin of <12g/dl.

Only 14/19 patients were diagnosed as GIST pre-operatively. Three had been previously operated outside the NCI and were admitted for excision of abdominal recurrence. Five patients were diagnosed through upper GI endoscopic biopsy, two because of upper GI bleeding and three because of persistent anemia. The remaining six were diagnosed by CT guided core needle biopsy. The undiagnosed cases preoperatively were explored with the suspicion of gastric lymphoma or adenocarcinoma (in 3 cases), retroperitoneal sarcoma (in 1 case) and splenic hilar mass (1 case).

All 19 patients underwent surgery, where wedge resection of the stomach was carried out in 3 patients (Figs. 2,3), partial gastrectomy in 7, total gastrectomy in 1, extended resection in 4 (including splenectomy in 2 cases and omentectomy in 2 cases). Excision of local recurrence was carried out in 3 and only exploration and biopsy was performed in 1 patient who had extensive liver metastasis. Laparoscopic assisted antrectomy was undertaken in only 1 patient with a small (5 cm) tumor (Table 2).

On the whole, fourteen patients had R0 resection; three had R1 and two had R2 resection. During follow-up, liver metastases occurred in 3 patients undergoing R0 resection, peritoneal and liver metastases supervened in one of three patient undergoing R1 resection; while Local recurrence occurred in both patients undergoing R2 resection (Fig. 4). Regional lymphadenectomy was undertaken in 5 cases because of grossly enlarged lymph nodes and all were proved to be LN–ve on pathological examination. Two patients were found to harbor metastases at laparotomy, one in the liver and the other in the greater omentum. In the first patient no resection was done and only biopsy was taken, while in the other additional omentectomy was carried out together with hemi-gastrectomy. Tumor rupture occurred in 6/19 patients. Among these, 4 patients developed recurrence 2 locally, 1 in the liver and 1 in both (Fig. 5).

The duration of surgery ranged from 100-290 minutes with a mean operative time of 190±65 minutes. Blood transfusion was required in 12 patients with a median of 3 units/patient (range: 1-5 units). The median length of hospital stay was 10 days (range 5-26 days).

Early postoperative complications occurred in 9 patients from whom 1 patient died of fatal massive pulmonary embolism on postoperative day 6 and five cases developed transient atelectasis and/or pneumonia. Minor anastomotic leakage occurred in 3 cases while a major gastrocutaneous fistula developed in 1 case. The former three were treated conservatively; while the latter was successfully treated surgically. Late postoperative complications consisted of incisional hernia in 4 cases. Three of those were repaired with prolene mesh while the fourth patient refused surgery (Table 2).

Two of our patients were lost to follow-up and we had one early (D6) postoperative mortality. The rest (16 patients) were followed-up for a period ranging from 6-34 months with a mean of 19.4±3.6 months. By the end of the study, none of the 16 followed patients had died of their disease and 10/16 (62.5%) were alive and free of disease. The remaining 6/16 (37.4%) of the followed cases showed treatment failure consisting of liver metastases in 3 patients, local recurrence in 2 and both peritoneal recurrence and liver metastases in 1.

Fifteen patients had tumors smaller than 10 cm, 3 of them developed recurrence (2 in the liver and 1 locally) while four had tumors larger than 10 cm and 3 of them showed disease recurrence (1 in the liver, 1 locally and 1 in both liver and tumor bed) (Fig. 6). Among the 10 patients with <5/50 mitoses per HPF, only 1 patient (10%) showed disease recurrence in the liver, while among the 6 cases with 5-10 mitoses/HPF, 3 patients (50%) developed recurrence two locally and one in the liver and among the
3 cases with >10/50 mitoses per HPF, 2 patients (66.7%) developed recurrence one in the liver and the other both on the peritoneal surface and liver (Fig. 7 and Table 2).

Fig. (1): Abdominal CT showing exophytic GIST arising from gastric body.

Fig. (2): Same case of exophytic gastric GIST at laparotomy.

Fig. (3): Same tumor after wedge gastric resection with grossly free margin from Stomach wall.

Fig. (4): Recurrence in relation to type (R) of gastric resection.

Fig. (5): Recurrence in relation to tumor rupture.

Fig. (6): Recurrence in relation to size of tumor.
Gastric GISTs account for more than half of all gastrointestinal stromal tumors and represent less than 5% of all gastric tumors. These tumors are identified by expression of CD117 antigen which is a part of KIT receptor. Symptoms at presentation usually include bleeding and anaemia, abdominal pain and/or abdominal mass. Complete surgical resection provides the only chance for cure, with only 1-2 cm free margins needed. Nevertheless, local recurrence

Table (3): Surgical treatment and outcome in 19 patients with gastric GIST.

<table>
<thead>
<tr>
<th>Surgical intervention</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wedge Gastrectomy</td>
<td>3</td>
<td>15.8</td>
</tr>
<tr>
<td>Partial Gastrectomy*</td>
<td>7</td>
<td>36.8</td>
</tr>
<tr>
<td>Total Gastrectomy</td>
<td>1</td>
<td>5.3</td>
</tr>
<tr>
<td>Extended Gastrectomy</td>
<td>4</td>
<td>21.1</td>
</tr>
<tr>
<td>Excision of local recurrence</td>
<td>3</td>
<td>15.8</td>
</tr>
<tr>
<td>Exploration &amp; Biopsy</td>
<td>1</td>
<td>5.3</td>
</tr>
</tbody>
</table>

Microscopic margin**:
- Free: 16, 88.9%
- Close: 1, 5.6%
- Involved: 1, 5.6%

* 1/7 patients underwent laparoscopic antrectomy.
** Only 18 patients were included because 1 patient was irresectable and only wedge biopsy was taken.

Table (4): Results of treatment in 19 patients with gastric GIST.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest infection</td>
<td>5</td>
<td>26.3</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td>5.3</td>
</tr>
<tr>
<td>Anastomotic leakage</td>
<td>4</td>
<td>21.1</td>
</tr>
<tr>
<td>Incisional hernia</td>
<td>4</td>
<td>21.1</td>
</tr>
</tbody>
</table>

Recurrence*:
- Site
  - Local: 2, 12.5%
  - Liver: 3, 18.8%
  - Both: 1, 6.3%

- Time (months):
  - 0-6: 0, 0%
  - 7-12: 2, 12.5%
  - 13-18: 1, 6.3%
  - 19-24: 3, 18.8%

* Only 16 patients were included because 1 patient died on D6 and 2 patients were lost to follow-up.

DISCUSSION

Gastric GISTs account for more than half of all gastrointestinal stromal tumors and represent less than 5% of all gastric tumors. These tumors are identified by expression of CD117 antigen which is a part of KIT receptor. Symptoms at presentation usually include bleeding and anaemia, abdominal pain and/or abdominal mass. Complete surgical resection provides the only chance for cure, with only 1-2 cm free margins needed. Nevertheless, local recurrence
and/or metastases supervene in almost half the patients treated with surgery alone, even when no gross residual is left [4,8].

The present study reviewed the clinico-pathological features of gastrointestinal stromal tumors (GIST) of the stomach in 19 patients treated surgically at the National Cancer Institute of Cairo during the 6-year period between January 2002 and December 2007. We also tried to appraise the results of treatment in relation to patients’ criteria, tumors’ characteristics and extent of surgery and their effect on disease recurrence.

Sex distribution among our patients showed a clear male predominance (2.2:1) compared to most reported series which found no appreciable sex difference in adults [8,10,11]. This observation needs to be studied more thoroughly in a larger series.

Tumor location was found in the upper 1/3 of the stomach in 8 cases (42.1%), the middle 1/3 in 6 cases (31.5%) and the lower 1/3 in 5 cases (26.3%). These figures correlate with other studies reporting that gastric GIST usually affects the proximal stomach in over two thirds of cases [10].

All our patients were symptomatic at presentation. This could be explained by the large size of our tumors ranging from 5-50 cm (median: 18.5 cm). In contrast, most western studies reported that only 50-70% of patients are symptomatic [8,11,36]. Three studies done one at Mayo clinic [36], another at Cleveland [37] and a third at Irvine [38] in the USA, reported that their tumors’ size ranged from (1.5 to 7.0 cm), (0.5 to 10.5 cm) and (2.8 to 7.1 cm) respectively. In the first study, not a single patient presented with symptoms. Kindblom [14] found that symptomatic GISTs tend to be larger (average size of 6 cm) versus 2 cm for asymptomatic GISTs. In a study published by Miettinen and colleagues [8], 54.4% of patients presented with symptoms related to GI bleeding (most commonly anemia) and a smaller fraction of patients (16.8%) presented with upper abdominal pain. Slightly higher figures were found in our study where 63% of the patients presented with symptoms related to bleeding such as hematemeses, melena or anaemia. This could probably be explained by more frequent mucosal ulceration caused by our larger tumors.

Upon histological examination of the specimens, 68.5% of the tumors, were found to be spindle cell, 10.5% were epithelioid, 10.5% were mixed (spindle and epithelioid) and 10.5% were unclassified. This compares favorably with the described incidence in other studies. Levy et al., reported that 20-30% of gastric GISTs have epithelioid morphology and that some show both elements [39]. In this study, no cases were assigned to the very low or to the low risk groups, while 52.6% of the cases were labeled as intermediate risk and 47.4% as high risk. Our cases showed higher risk when compared to other studies dealing with gastric GIST. Berindoague et al. [9] reported the low, intermediate and high risk groups to account for 44.4%, 33.3% and 22.2% respectively. This could also be due to the large tumor size at presentation in our cases.

It has been reported that 10%-47% of patients with GIST harbor distant metastases at presentation [13,35]. In this study, only 2/19 patients (10.5%) presented with metastatic disease. This low incidence in association with high prevalence of high risk cases needs to be further explored. Nevertheless, relative metastatic distribution was close to other reports [13,33,35,40] since it involved the liver in 5.3% and the omentum in 5.3%.

Five of our patients underwent nodal dissection but no lymph node metastases were histologically found in any of them. Again, this finding compares favorably with other studies [13,20,41] where positive nodes were rarely reported. Our results consolidate the general consensus that lymphadenectomy is warranted only when evident nodal involvement is found [20].

Most studies on GIST advocate that vital structures such as the stomach should not be sacrificed if grossly free margins can be achieved, since the status of microscopic margins does not seem to affect survival [13,42]. A wedge resection of the stomach with tumor-free margins is satisfactory in most gastric GISTs while gastrectomy is reserved for tumors involving the pylorus or the esophago-gastric junction [40]. In accordance with this principle of organ preservation, total gastrectomy was undertaken, in this study in only one case (5.2%) and this was due to the large size of the tumor involving approximately the whole stomach.
Microscopic margins were infiltrated in 1 case and close in 1 case. The former patient developed local tumor bed recurrence after 8 months while the latter stayed free for 13 months (till the end of the study). Among the remaining 13 patients with free surgical margins, only 2 patients developed local recurrence. This matches with the finding by Gold and DeMatteo [43] that the presence of residual tumor is significantly related to early recurrence and short survival. Similarly, Pierie et al. [42] and DeMatteo et al. [13] reported a significantly longer 5 year survival rate when GISTs were completely removed (42% and 54% respectively, versus 9% for incomplete removal according to the former study).

Treatment failures are known to affect almost half of GIST patients treated by surgery alone [4,5] and tend to be found in the liver in 65%, the peritoneal surface in 50% and in both in about 20% [13]. In agreement with these findings, tumor recurrence occurred in 6/16 of our followed patients (37.5%). It was in the liver in 50%, local on the peritoneal surface in 33.3% and it occurred synchronously in both in 16.7%. We probably had slightly smaller figures because of our smaller number of patients and shorter follow-up period. On the other hand, this study involved only gastric GISTs which have been reported to follow a less aggressive course compared to small bowel tumors of the same size [39,44].

Tumor rupture occurred in 6/19 cases. Among these 66.7% developed disease recurrence (Fig. 5). This finding confirms the recommendation of Mochizuki et al. [27] to avoid tumor rupture since it was associated with intra-abdominal dissemination of tumor cells and subsequent high risk of local tumor recurrence.

Lillemoe et al. [44] found that recurrence was predicted by tumor size as well as mitotic count. Comparable findings were found by Boni et al. [45]. Our results are in accordance with these findings. In the present study, patients with tumors >10 cm in diameter developed disease recurrence more frequently than those with smaller tumors measuring <10 cm (75% and 20% respectively) (Fig. 6). Also, low number of mitotic count was found to correlate with less risk of recurrence. The recurrence rate for patients with <5/50, 5-10 and >10/50 mitoses per HPF, was 10%, 50% and 66.7% respectively (Fig. 7).

In our study macroscopically complete resection was undertaken in 17/19 cases (89.5%). One patient was found inoperable and was just biopsied and another patient showed an involved resection margin. The latter patient developed local peritoneal recurrence 8 months postoperatively in spite of adjuvant treatment with imatinib. This is in agreement with findings by Boni et al. [45] that the presence of residual tumor is significantly related to early recurrence and short survival. The negative effect of macroscopic residual tumor is well known since many authors [13,42] found a significantly longer 5 year survival rate when GISTs were completely removed (42% versus 9%).

The median time to recurrence was 15.8 months (range: 8-24 months) which is shorter than other studies reporting median intervals to recurrence of 19 and 25 months [13,42]. This can be explained by the relatively large number of high risk cases in our study.

It is generally agreed that neoadjuvant imatinib is not warranted unless the expected decrease in size by the tumor will noticeably affect surgery [20]. Following this strategy, none of our patients received neoadjuvant treatment with imatinib since all but one patient were treated with gastric preservation. The only patient who undertook total gastrectomy had not been diagnosed as GIST preoperatively. Postoperatively, Imatinib was given only to patients who had liver metastases at surgery (10.5%), those who underwent an incomplete resection (10.5%) or those experiencing recurrence after surgical resection (31.5%).

Conclusion:

The clinical outcome of gastric GIST is influenced by many factors, the most important of which are tumor malignant potential and completeness of tumor extirpation. Gastrointestinal stromal tumors of the stomach can present by vague and obscure symptoms; therefore prompt diagnosis by abdominal CT and endoscopy is required to detect small tumors amenable to cure. Radical gastrectomy is not required, but only complete tumor resection without lymphadenectomy and with only 1-2 cm free margins is sufficient. However, local recurrence and/or metastases supervene in almost half the
patients treated with surgery alone, hence, multimodal therapy warrants consideration for tumors with adverse factors. It is thought that larger prospective randomized studies are needed to precisely identify significant prognostic factors and to clarify whether adjuvant treatment with imatinib or one of its more recent successors can improve overall and disease-free survival in high risk GISTs.

REFERENCES


Gastrointestinal Stromal Tumors (GIST) of the Stomach


