

Gastrointestinal Stromal Tumors: Diagnostic and Therapeutic Challenges

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Abstract

Background: Gastrointestinal stromal tumors (GIST) are the most common mesenchymal neoplasms of the digestive system. They originate from the interstitial cells of Cajal and are characterized by the over expression of KIT protein (Tyrosine Kinase), and they pose a diagnostic and therapeutic dilemma.

Objective: A challenge in diagnosis and treatment of GIST

Patients & Methods: This is a retrospective study of GIST cases that diagnosed and treated in our center during the past 5 years. These studies include clinical characteristics, imaging techniques, neoadjuvant therapy, surgical techniques, immunohistochemistry, and prognosis of such cases.

Results: Sixteen patients were diagnosed as having GIST (12 males/4 females) with a mean age 62 years (31-83 years). Diagnosis was made preoperatively in 11 patients (69%) and intraoperatively with histopathological confirmation in five patients (31%). The site of the tumor was detected in the stomach in 6 cases (37.5%), one in duodenum (6.25%), five in small intestine (31.25%), one in mesentery (6.25%), two in colon (12.5%) and one rectal GIST (6.25%). The main presentation of the disease was anemia, GIT bleeding and abdominal mass. Fourteen patients considered resectable and they were operated upon (87.5%) and in two patients (12.5%) neoadjuvant therapy was started with favorable response in one case and poor response in other one with advanced GIST. All patients received Imatinib as adjuvant therapy. Mean follow up period was 33 months (4-54 months).

Conclusion: GIST is a complex and challenging disease that requires a multidisciplinary approach in specialized center for better prognosis of such disease.

Keyword: Gastrointestinal stromal tumors; Neoadjuvant therapy; c-KIT treatment; Prognosis

Introduction

Gastrointestinal Stromal Tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal (GI) tract, [1,2] account for <1% of all digestive tract tumors [3,4].

GIST can develop anywhere along the whole GI tract from the esophagus to the rectum, however, stomach (60%) and small intestine (30%) are the most common locations for GIST. Only 10% of GISTs are found in the esophagus, mesentery, omentum, colon or rectum. Upto 30% of GIST exhibits high -risk (Malignant) behavior such as metastasis and infiltration [5-8].

The metastatic pattern is predominantly intra-abdominal spread throughout the peritoneal cavity and to the liver, but lymphatic spread is uncommon [9].

GIST presents overexpression of the transmembrane protein KIT (Tyrosine Kinase) Receptor, coded by c-Kit proto-oncogene located in chromosome 4 (49¹¹ - 9¹²) believed to control cell proliferation and apoptosis [10,11]. This protein expression allows the differentiation and diagnosis of these tumors using CD117 monoclonal antibody, which is positive in >95% of stromal tumors, however, in 5%, of neoplasms the result are negative for CD 117 (KIT- negative GIST) [11,12].

GIST demonstrates almost equal distribution between males and females, however some literatures suggest that there is a slight male predominance [13].

Although GIST has been reported in patients of all ages, including

children, most of them are between the age of 40-80 years at the time of presentation, with a median age of 60 years. The majority of GISTs are sporadic nonetheless; there are several cases reports of familial germline mutations in KIT proto-oncogenes [13].

The clinical manifestations of GISTs are variable and rendering accurate diagnosis challenging. The current diagnoses of GISTs are based on histological and immunohistochemical criteria, the most important of which is the expression of the receptor tyrosine kinase KIT (CD117, c kit) [14,15].

Imaging in the form of contrast-enhanced computed tomography (CECT) is the modality of choice. It is used to characterize the lesion, evaluate its extent, and assess the presence or absence of metastasis at the initial staging workup. CECT also used for monitoring response to therapy and performing follow -up surveillance of recurrence. [12,16].

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Endoscopic ultrasound (EUS) has been used in the diagnosis of GIST; it assesses the depth of invasion and is useful in obtaining a tissue sample. Preoperative percutaneous biopsy should not be used because of a significant tumor rupture or dissemination [12].

GISTs are positron emission tomography (PET) avid tumors because the receptor tyrosine kinase increases the glucose transport protein signaling [12]. PET is useful in revealing small metastasis which would otherwise not be picked up on CECT as it helps differentiate an active tumor from necrotic or inactive scar tissues [6].

PET also differentiates malignant from benign tissues and recurrent tumor from nondescript benign changes. Changes in the metabolic activity of tumors precede anatomic changes on CECT: it is hence used to assess complex metastatic disease in patients who are being considered for surgery [17,18].

Surgery is the primary treatment of choice for all tumors which can be resected without significant morbidity. Conventional chemotherapy and radiotherapy are not usually effective. Imatinib mesylate is a potent and specific inhibitor of the KIT-Protein tyrosine kinase and has been approved for the treatment of KIT (CD117) positive irresectable or metastatic cases of GISTs as it plays an integral role in the treatment of GISTs as a neoadjuvant and adjuvant therapy [19].

Imatinib is effective in reducing the likelihood of negative margins without significant morbidity [20,21].

The purpose of this study is to present the challenges in the diagnosis and treatment of GIST cases in our institute during the past 5 years and compare the results obtained with the results of other centers.

Patients and Methods

This review retrospective study in sixteen patients with GIST, that operated upon at the department of surgery, National liver Institute, Menophya University in association with Clinical oncology department in Cairo University and Menophya University from January 2009 to January 2014.

This clinical study was based upon reviewing the patients data retrieved from the medical records with ethical and scientific approval.

Disease presentation and diagnostic methods were analyzed including upper GIT endoscopy, lower GIT endoscopy, ultrasound, endoscopic ultrasound (EUS), contrast-enhanced computed tomography (CECT), fine needle aspiration (FNAB), large core needle biopsy (LCNB) and positron emission tomography (18F-FDG-PET).

Tumors were assessed for resectability as well as complete removal of the neoplasm. Imatinib was used as a neoadjuvant therapy for the cases that diagnosed as having locally advanced or metastatic tumors, with continuation as adjuvant therapy for all cases after surgery.

Surgical techniques depend on the site of the tumor and the possibility of complete resection intra-operatively.

Histological parameters were reviewed by experienced pathologists for histological confirmation of the diagnosis of GIST and evaluation of the morphological and immunohistochemical characteristics. Tumor size and necrosis on fresh specimen was examined. The mitotic rate was assessed by counting the number of mitoses per 50 high-power field (HPF) and immunohistochemical markers (CD 117), (CD 34), Vimentin, smooth muscle actin and S-100 protein in all patients. Microscopic positive margins (<1 mm) and, in some cases, cell proliferation index measures through Ki-67. The tumors were classified according to risk prognosis using Fletcher's classification in accordance with the U.S. National Institute of Health (NIH) guidelines as very low risk, low risk, intermediate risk and high risk [12].

According to the risk prognosis guidelines and intraoperative tumor breakage, Imatinib was given postoperatively.

Follow up was carried out at 1,3,6 months after surgery then yearly using CT scan and in some cases PET scan was used in order to assess the possibility of local recurrence or distal metastasis, and disease free period.

Results

Sixteen patients were diagnosed with GIST tumors, twelve patients' males (75%) and four females (25%) with average age 62 years (31-83 years of age). Among those patients 11 cases (69%) were diagnosed as GIST preoperatively by radiological, histopathological & immunohistochemistry examination.

Five cases were diagnosed as suspicious GIST intraoperatively and confirmed postoperatively by histopathological examination of surgical specimens; these cases were classified as, one gastric GIST, one Duodenal GIST, one mesenteric GIST and two intestinal GISTs.

Tumors location of this series were as follows: six in stomach, one in duodenum, five in small intestines, one in the mesentery, two in colon and one in the rectum.

All patients presented with different signs and symptoms such as anemia in 14 cases (87.5%), gastrointestinal bleeding in 5 cases (31.25%), abdominal pain in 4 cases (25%), palpable mass in 5 cases (31.25%), nausea, vomiting and early satiety in 3 cases (18.75%), constipation in 2 cases (12.5%) and weight loss in 6 cases (37.5%), most of the patients has one or more symptoms at the time of presentation.

CT scan with oral & intravenous contrast was used as a gold standard diagnostic test for all patients (Figure 1). UGI endoscopy plus biopsy was used in 4 patients (25%) with positive for GIST in only 2 cases (Figure 2). Endoscopic ultrasound (EUS) was used in 3 patients (18.75%) (Figure 3). Large core needle biopsy (LCNB) was done in 2 cases (12.5%) in large tumor to confirm the diagnosis and to start neoadjuvant therapy.

Fluoroxyglucose positron emission tomography (18F-FDG-PET)

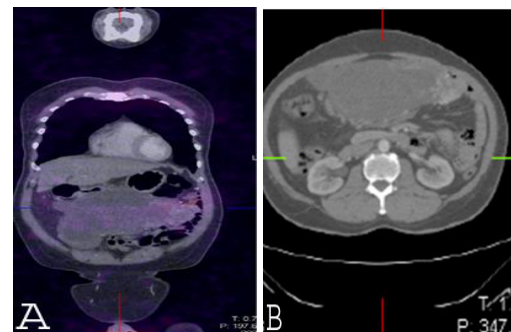


Figure 1: Abdominopelvic CT scan for Gastric GIST Tumor 33 cm in Diameter A. Coronal Section B. Axial Section (Huge intrabdominal swelling occupied the abdomen and pelvis).

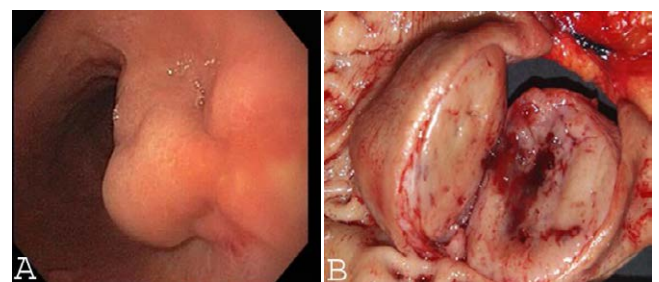


Figure 2: Gastric GIST Tumor A. Upper Endoscopy B. Tumor bisected after Excision.

was carried out before starting and after-neoadjuvant Imatinib therapy for follow up response in 5 cases (31.25%).

Fourteen patients were diagnosed as resectable tumors and were operated upon (87.5%). Nine patients were diagnosed preoperatively and 5 patients were assessed for resectability intraoperatively. In two patients that were considered unresectable at the initial assessment (12.5%) one had advanced tumor and the other had metastatic spread at the time of presentation therefore they received 400 mg/day Imatinib as neoadjuvant therapy for 6 months, with good response in one patient with huge gastric GIST (about 33 cm in diameter) revealed by PET scan and the patient become a surgical candidate (Figure 4). On the other hand the second patient had metastasis with poor response to neoadjuvant therapy and still on the treatment since 2 years.

Surgery was the treatment of choice for 15 patients (93.75%) aiming to remove the disease in all cases. The type of surgery depends upon the location of the tumor: 4 patients did partial gastrectomies, 2 patients did distal gasterctomies (Figure 4) one duodenopancreatectomy (Whipple's operation) (Figure 5), one mesenteric excision with adjacent intestinal resection, (Figure 6) 5 intestinal resection, (Figure 7) one transverse colectomy, and one anterior resection for rectal GIST ,with all negative safety margins (Table I).

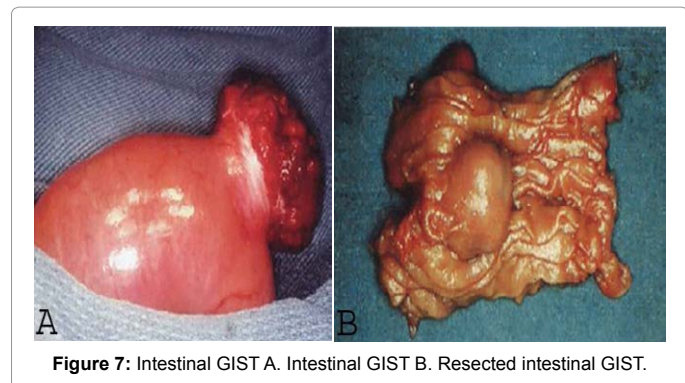
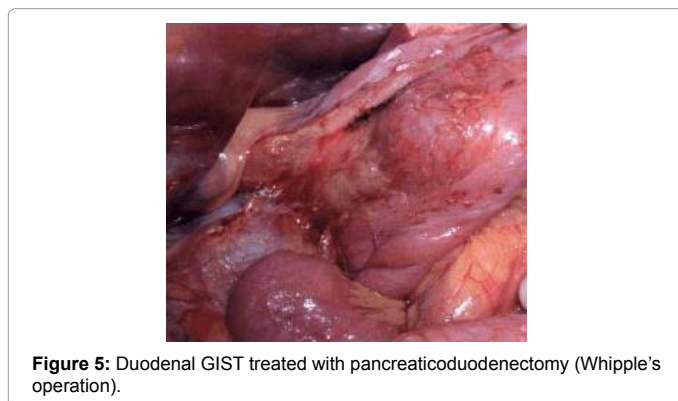
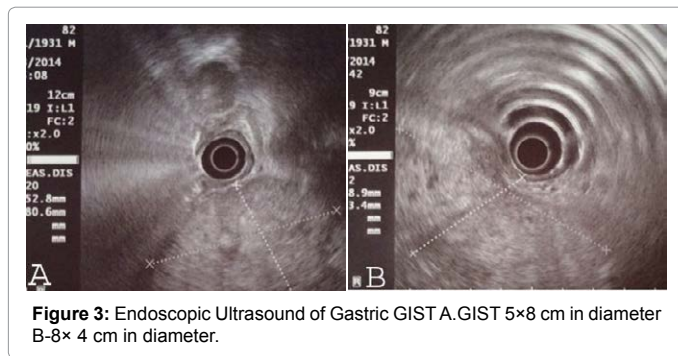


Table I: Operative procedures performed in 15 GIST Tumors out of 16 Tumors.

Origin of GIST	Type of Resection	No. % 15 cases
Stomach (6)	-Partial or wedge gastric resection	(4)26.66%
	-Distal gastric resection	(2)13.33%
Duodenum (1)	-Pancreaticoduodenectomy (Whipple's operation)	(1)6.66%
Intestine (5)	-Small bowel segmental resections	(5)33.33%
Mesentery (1)	-Mesenteric excision with adjacent intestinal segmental resection	(1)6.66%
Colon (1)	-Transverse colectomy + Segmentectomy seg.7 (Metastectomy)	(1)6.66%
Rectum (1)	-Anterior resection	(1)6.66%

Histological analysis revealed: 8 tumors (50%) had a mitotic index <5 mitosis/50 HPF, 5 tumors (31.25%) had a mitotic index >10 mitosis/HPF and 3 tumors (18.75%) had necrosis. Classification of tumors according to Fletcher prognostic scale was as follow 5 tumors (31.25%) with low risk, three tumors (18.75%) with moderate risk and eight tumors (50%) with high risk (Table II).

According to the cell type 10 tumors (62.5%) were fusiform (spindle) cell, 4 tumors (25%) were epithelioid cell and 2 tumors (12.5%) were mixed types (Figure 8).

Average tumor size was ranged from 3.5 cm to 33 cm in diameter. The average tumor weight from 200 mg to 11 kg.

Immunohistochemistry study revealed 14 neoplasms (87.5%) positive for CD 117 and CD 34, five patients positive for vimentin and actin (31.25%) and four patients positive for S-100 protein (12.5%) (Figure 9).

Average hospital stays 6.5 days (4-20 days)

There was no mortality in this series but there was 3 morbidity (one patient with wound infection, one patient with lung collapse both treated conservatively and one patient with incisional hernia treated surgically with mesh)

Five patients (31.25%) received 400 mg /day Imatinib as

Table II: Fletcher Prognostic Classification of 16 GIST Tumors.

Risk	Size (cm)	Proliferation index (Mitotic count)	(No= 16) %
Very low	< 2 cm	< 5/50 HPF	(n= 0) 0%
LOW	2- 5 cm	< 5/50 HPF	(n= 5) 31.25%
Medium	< 5 m 5-10 cm	6- 10/50 HPF < 5/50 HPF	(n= 3) 18.75%
High	> 10 cm Any	Any > 0/50 HPF	(n= 8) 50%

HPF, high power field

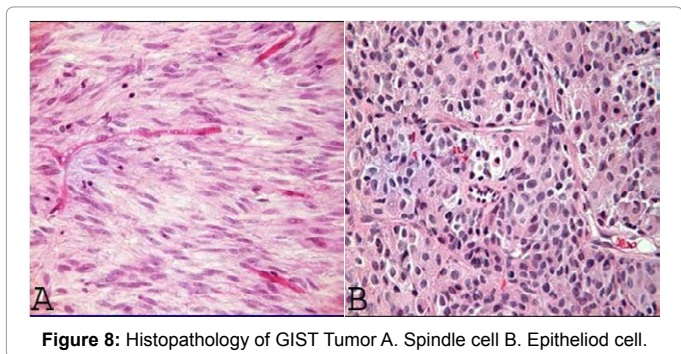


Figure 8: Histopathology of GIST Tumor A. Spindle cell B. Epithelioid cell.

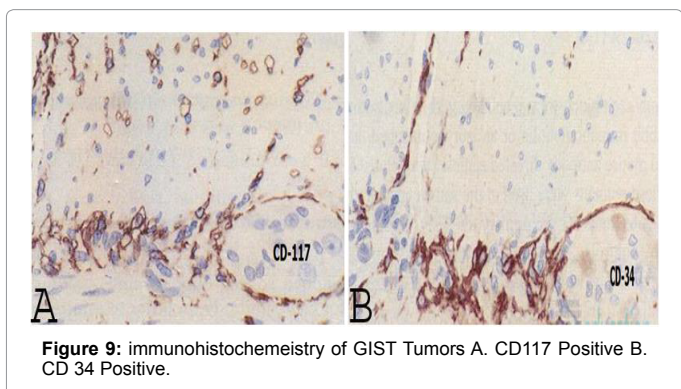


Figure 9: immunohistochemistry of GIST Tumors A. CD117 Positive B. CD 34 Positive.

neoadjuvant therapy for 3-6 months to decrease the size of the tumor preoperatively and then surgical intervention depends on the response to therapy. All patients received Imatinib postoperative as adjuvant therapy for 6 months. One patient considered not a candidate for surgery due to advanced and metastatic disease, received Imatinib for 24 months and still on treatment.

Average follow up was 33 months (4-54 months) during follow up period two patients developed metastasis in the liver. One patient did transverse colectomy for colon GIST presented with metastasis in the segment VII of the right lobe of the liver for which segmentectomy of segment VII (Metastatectomy) was done (Figure 10), the other patient had huge liver metastasis central in the liver about 20x 25 cm in diameter 6 months after intestinal GIST resection and the patient put on Imatinib therapy for 1 year with poor response, but the course still stationary (Figure 11).

Discussion

Gastrointestinal stromal tumors (GISTs) are common mesenchymal tumors that arise predominantly in the gastrointestinal tract (GIT). In the past, there has been considerable debate regarding its nomenclature, cellular origin, diagnosis and prognosis [22-24]

Due to their similar appearance by light microscopy, GISTs were previously thought to be smooth muscle neoplasms and most were classified as leiomyomas, leiomyoblastomas, leiomyosarcomas or schwannomas [24]. It was in 1998, after the discovery of gain-of function mutations in the c-KIT proto-oncogene that these tumors

were reliably distinguished from other histopathological subtype of mesenchymal tumors [22,25].

GISTs represent the most common mesenchymal neoplasms of the GIT with an incidence 0.1-3.0 % for malignancy transformation [26,27]. It is thought that these tumors differentiate from intestinal pace maker cells, also known as interstitial cell of Cajal [28].

They affect mostly males between the ages of 50 and 70 years, but it can be discovered incidentally at young age groups. Large or advanced lesions may present with a variety of clinical findings, include bleeding, abdominal pain, early satiety, bowel obstruction or perforation [29,30].

The most frequent location of GIST is the stomach (60-70%) followed by the small intestine (20-30%), colorectal (<5%), esophagus (<2%), with lower frequency in the peritoneum, mesentery and omentum [31]. Our series showed a higher prevalence in the stomach (37.5%) followed by small intestine (31.25%) and colon (12.5%) ,which constitute with what has been reported in the literatures.

Only 70% of patients with GIST are symptomatic while 20% are asymptomatic in which the tumors are detected incidentally, 10% of the lesions are detected only at autopsy, symptoms and signs are not disease specific, and are related more to the site of the tumor [27,32]. Anemia considered a predominant sign for all cases of GIST [33,34] and this constitutes with our series as anemia represent 87.5% of the cases. Bleeding comprises the most common symptoms after anemia (30-40%), and it is attributed to the erosion into GIT lumen causing hematemesis, melena, or anemia which is usually more chronic on presentation [27-32].

The symptoms reported in our series were similar to those reported in the literatures.

Diagnosis was occasionally incidental while studying another disease through imaging studies , suspected cases intraperatively or through histological study from surgical specimen obtained as



Figure 10: Metastatectomy of segment VII of the liver after transverse colectomy for Colonic GIST.

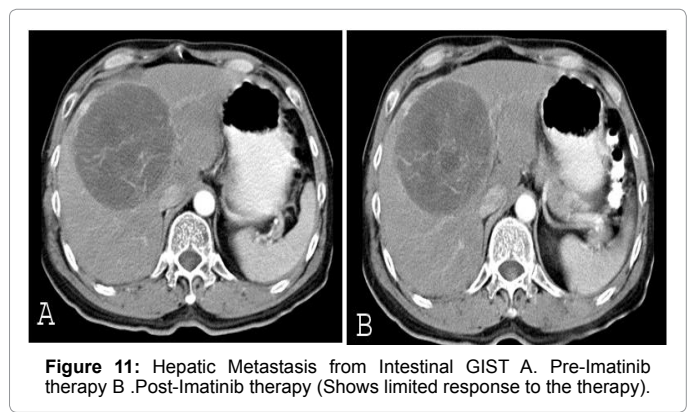


Figure 11: Hepatic Metastasis from Intestinal GIST A. Pre-Imatinib therapy B .Post-Imatinib therapy (Shows limited response to the therapy).

occurred in (31.25%) in our cases, but the diagnosis was confirmed preoperatively in (68.75%) of cases.

CT scan using oral and intravenous contrast is the method of choice for patients with suspected abdominal tumor. CT scan reveals exophytic heterogenous, vascular tumors associated with hemorrhage and necrosis [35].

In our series CT was the method of choice for diagnosis and follow up.

Upper GIT endoscopy for gastro-duodenal or esophageal cases usually shows a protruding submucosal lesion with or without mucosal ulcer [36].

Endoscopic biopsy usually does not provide sufficient evidence to establish GIST diagnosis because of its submucosal nature [37].

This also occurred in our study as endoscopy was carried out in 4 cases of gastro duodenal GIST with submucosal lesion and endoscopic biopsy confirm the diagnosis of GIST only in two out of 4 cases.

Endoscopic Ultrasound (EUS) can detect small GIST tumors (round or oval, hypoechogenic and those found in muscularis propria), allowing the study of the relationship between different sheets of the gastrointestinal wall. Echo endoscopic puncture has a better outcome than endoscopic biopsy with a success rate of 80%-90% [38]. Only 3 patients of our series with suspected GIST in the gastric wall were subjected to EUS and the diagnosis of GIST tumor was confirmed by FNAB guided through EUS.

The Task Force Report (NCCN GIST) does not recommend carrying out preoperative biopsy from easily resectable tumors because this may lead to hemorrhage and dissemination [34,35]. However, locally advanced tumors that might be treated using Imatinib required immunohistochemical study on CD 117. Two cases of our series (12.5%) that had locally advanced tumors required large core needle biopsy (LCNB) to achieve the diagnosis of GIST. Imatinib started as a neoadjuvant therapy to down stage the tumors. One patient had a good response after treatment with Imatinib for 6 months, and the GIST become surgically resectable, the other one had poor response to the treatment.

PET-18F-FDG offers information about metabolic activity and allows the estimation of neoplastic malignancy because a higher glucose uptake represents higher metabolic activity and, therefore, this suggests a more aggressive tumor [36]. Also, this technique has high sensitivity in assessing early-and long-term response to Imatinib in patients with advanced GIST positive to CD 117 [39,40]. However, CT scan is more cost-effective in suspected abdominal tumor.

Tumor response is assessed for other entities as size decrease according to RECIST criteria (Response Evaluation Criteria in Solid Tumor. However, these criteria may underestimate response for GIST neoplasms because there are several changes revealed by CT scan in addition to tumor size changes, especially the addition of intratumoral nodules or decreased vascularization [41].

Choi et al concluded that CT scan is sensitive and specific to assess metastatic GIST response to Imatinib, considering response as size decrease >10% or tumor density decrease >15% at 2 months after the initiation of therapy with a 97% sensitivity, and 100% specificity, when compared to PET response [17].

The consensus conference of Lugano [35] established that PET should be used when an early assessment of tumor response to Imatinib is required to consider surgery or when there is some confusion that raises suspicion of metastasis. In our series, only five patients were diagnosed and follow up using PET pre-neoadjuvant Imatinib therapy

and follow up response of this therapy. The rest of patients were studied using CT scan with 100% sensitivity. MRI provides more valuable information than CT scan for rectal GIST [36]. In our series, one case of rectum the MRI used in evaluation and follow up.

GIST vary greatly in size from a few millimeters to more than 30 cm, the median size being between 5cm-8cm. Macroscopically, GIST usually has an exophytic growth and a common intra-operative appearance is that a mass attached to the stomach, projecting into the abdominal cavity and displacing other organs [26,32]. On gross appearance they are smooth gray, and white tumors which are well circumscribed, usually with a pseudo capsule. A small area of hemorrhage or cystic degeneration and necrosis may be visible [32]. In our series one tumor size reaches 33 cm in diameter and weight up to 11 kg which constitute with other reports in literatures.

Because there is a wide range of differential diagnosis of GIST histology, these tumors are confirmed through immunohistochemical and molecular biological techniques with c-KIT overexpression (CD117) as the key marker. Approximately >75% of tumors are c-KIT positive for CD117, whereas 60-70% are positive to CD 34, 30-40% positive to Vimentin & smooth muscle Actin, 5% to S-100 protein and 1-2% to desmin or Keratin [5,7,9,32]. In our series 87.5% of cases positive for CD117 & CD34, 31.25% for Vimentin & Actin while 25% positive for S-protein, which is similar to the results reported in other literatures.

GIST has three essential histological patterns, 70% fusiform (spindle) apparently with the best survival rate, 20% epithelioid and 10% mixed. C-KIT negative GIST are usually epithelioid and extra-intestinal [42]. In our cases, fusiform (spindle) histological pattern are the predominant type (62.5%), followed by the epithelioid type (25%) and mixed type (12.5%).

Based on studies by Fletcher et al. [12] the two most important prognostic variables for GIST are tumor size (<2 cm, 2-5 cm, >5 cm) and mitosis index per 50 high-power fields (HPF) (<5 mitosis/50 HPF or >5mitosis/50 HPF), therefore ,tumors are classified according to the prognostic risk as 'very low Risk'(<2 cm and <5 mitosis/ 50HPF),'low Risk' (2- 5 cm and <5 mitosis/50HPF), 'Medium Risk' (<5 cm and 6- 10 mitosis/50 HPF or 5-10 cm and <5 mitosis/ 50 HPF) and 'high Risk'(>5 cm and >5 mitosis/50HPF, 10 cm/any mitosis index or any size and >10 mitosis/50HPF). Considering the prognostic risk in our series there were 5 tumors with low Risk (31.25%). 3 tumors with moderate Risk (18.75%) and 8 tumors with high Risk (50%). Other poor prognostic factors are necrosis, infiltration, metastasis and hypercellularity [43,44]. In our series there were 3 cases (18.75%) that had necrosis with poor prognosis.

Surgery is the primary treatment of choice in localized or potentially resectable GIST. It is important to avoid tumor rupture. The tumors are fragile and should be handled with care, aiming to achieve complete gross resection, with an intact pseudocapsule. Multivisceral and radical surgery should be avoided whenever possible: segmental or wedge resection with an aim to obtain histologically negative margin is sufficient. Resection should be accomplished with minimal morbidity. Lymphadenectomy is not required as GISTs have low incidence of nodal metastasis [9,12,16]. In our series, 15 patients (93.75%) underwent surgery with complete surgical excision, 4 had partial gastrectomies, 2 had distal gastrectomies, one had local mesenteric excision with adjacent intestine, 5 had intestinal resection, one transverse colectomy, one anterior resection and one duodeno-pancreatectomy for duodenal GIST.

All surgical interventions were open techniques. Laparoscopic approach was not used in our cases, as some authors don't recommend laparoscopic surgery for tumor >2 cm or extra-wall neoplasm because of the increased risk of tumor breakage and peritoneal dissemination,

[36] however, other authors consider this as a valid alternative in addition to open surgery [34].

Overall report 5-years survival rate after complete surgical resection of primary GIST is from 40%-55% [13,36].

Disease free survival is associated with tumor size and mitosis index. Therefore, low risk GIST has a 5-year disease free survival of 96%, median-risk of 54% and high-Risk of 20% [45].

Disease free survival in our series was 87.5% at 4.5 years in all cases. Only 2 cases had liver metastasis, one case had small metastasis in segment VII of the right lobe of the liver in which segmentectomy (metastatectomy) was carried out. The second one was huge liver metastasis therefore put on Imatinib therapy since 2 years with little response.

Advanced and metastatic GIST (peritoneal dissemination or long distant metastasis (liver/lung) represent a treatment challenge. Until recently, overall survival of these patients was <1 year and 5-years survival was only 20% [46].

Imatinib Mesylate, a tyrosine kinase inhibitor, plays a key role in the management of GISTs. It can be used as neoadjuvant therapy, adjuvant therapy and to treat tumor recurrence [47]. Its mechanism inhibits c-KIT tyrosine-kinase, which has a positive effect over c-KIT positive GIST. Several studies confirmed the beneficial effect of this medication in advanced GIST.

Consensus [35] and expert guidelines indicate Imatinib therapy may increase survival in patients with c-KIT-positive advanced GIST, allowing some patients to undergo primary surgery then to start as initial dose of Imatinib 400 mg/day (except for exon q mutation on c-kit, changing dose to 800 mg/day).

Early response will be assessed after 2-4 weeks of therapy using CT and PET scan (ideally) in order to determine functional response. In case of response, treatment will be continued until maximum response is achieved (3-6 months) and patient will undergo surgery if total resection is possible [48].

In this series, we have 5 patients who received Imatinib 400 mg/day for 6 months as neoadjuvant therapy one of them had advanced gastric GIST, after 6 months of Imatinib therapy there was a dramatic response and the patient became candidate for surgical resection.

Postoperative Imatinib therapy has been reserved for patient with high risk of recurrence although there is insufficient evidence about optimal length of such therapy [49]. In our series all patients received Imatinib as adjuvant therapy for at least 6 months.

Metastatic GIST in the liver in the commonest site followed by peritoneal cavity, but can also occur in bone, skin, soft tissue and lymph node [50].

Patient with hepatic metastasis who is medically fit and with surgically accessible but focally progressive disease should be considered for resection. The rationale behind this approach is to eliminate of drug-resistance clones that will allow ongoing therapy with Imatinib [51].

Surgery in metastatic liver patients is a case based decision. Residual tumor resection is safe but multifocal resection is not recommended without considering the patient's performance status and personal situation [51,52].

When surgery may not be possible, limited evidence exists that similar benefits could be obtained from other nonsurgical ablative techniques such as radiofrequency ablation or embolization [53,54].

In our series we have 2 patients with liver metastasis one of them cured with surgical resection and adjuvant Imatinib therapy, the other case had huge focal hepatic metastasis from colonic GIST and was not considered a candidate for surgery, had received the Imatinib therapy with poor response.

Conclusion

Gastrointestinal stromal tumor (GIST) is a complex and challenging disease requiring an effective multidisciplinary management team involving integrated specialties such as a pathologist, radiologist, gastroenterologist, oncologist, and a surgeon for better outcome of such cases.

Conflict of interest

The authors have no conflict of interest to report.

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