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GASTRIC STROMAL TUMORS: CLINICAL PRESENTATIONS,  
DIAGNOSIS AND OUTCOME

Dildar Hussain, Hasnain Zafar and Asad Jamil Raja

**ABSTRACT**

**Objective:** To determine the clinical presentations, of gastric stromal tumors with diagnostic methods, pathology and outcome after surgery.

**Study Design:** A case series.

**Duration and Setting:** From January 1988 to December 2002 at The Aga Khan University Hospital, Karachi.

**Patients and Methods:** All patients of age 14 years and above, diagnosed histopathologically to have gastric stromal tumors were included. The data of these patients was collected retrospectively from January 1988 to December 1998, and prospectively from January 1999 to December 2002. All the patients were studied as a single group.

**Results:** There were 11 patients. Their mean age was 54 years, with 8 males and 3 females. Five patients presented with upper gastrointestinal bleeding, and 4 with lower gastrointestinal bleeding. Eight patients had pain in epigastrium and 2 had vomiting. Upper gastrointestinal endoscopy was done in all patients, and ultrasound was done in 4 patients. CT scan was done in 7 patients. Pre-operative diagnosis could be made in 6 patients. Only one patient had liver metastasis. Wedge resection was performed in 5 proximal gastrectomy with gastroesophageal anastomosis in 3, and partial gastrectomy with gastrojejunostomy in another 3 patients. The mean tumor size was 8.0 centimeters. Two patients had benign, 2 had intermediate and 7 had malignant tumors. The mean duration of follow-up was 41 months. Follow-up was completed in 8 patients, out of whom 6 were alive, and 2 patients expired due to other causes at the time of completion of this study.

**Conclusion:** Gastric stromal tumors are uncommon. Larger gastric stromal tumors are usually symptomatic with gastrointestinal bleeding as a common presentation. Immunohistochemical techniques are required for the diagnosis. Complete surgical resection is the curative therapy.

**KEY WORDS:** Gastric stromal tumors. Diagnosis. Treatment. Outcome.

**INTRODUCTION**

Gastric stromal tumors are uncommon.<sup>1</sup> Many of such tumors may not originate from smooth muscles<sup>2</sup>, therefore, these tumors may be classified as GIST i.e. Gastrointestinal stromal tumors and in relation to the stomach as gastric stromal tumors.<sup>3</sup>

These tumors were classified depending on the type of tissue from which they arise, that is smooth muscles, nervous tissue or both of them.<sup>4</sup> With the advent of the electron microscopy and immunohistochemical techniques these tumors are now classified as benign, intermediate and malignant, depending upon the tumor size and mitotic count.<sup>4</sup> Immunohistochemical techniques analyse the positivity of vimentin, desmin, anti smooth muscle antibodies and S-100 to differentiate between different tumors.<sup>5</sup> Although prediction of the biological behaviour of these tumors is often difficult, but in general malignant stromal tumors are mitotically more active, more cellular, larger in size, and having adjacent organ invasion.<sup>6</sup> The majority of gastric stromal tumors are grossly well circumscribed, even those that prove to be malignant.<sup>7</sup>

Most of the gastric stromal tumors are asymptomatic, but slowly growing tumors may present as symptomatic masses.<sup>8</sup>

Despite advances in technology, the pre-operative diagnosis of gastric stromal tumors is often difficult. Helpful investigations include: upper gastrointestinal endoscopy, ultrasonography, CT scan and endoscopic ultrasound.<sup>9</sup> As gastric stromal tumors are usually radioresistant and insensitive to chemotherapeutic agents, the only curative therapy is adequate surgical excision.<sup>6</sup> Metastatic disease is most common in liver and peritoneum.<sup>7</sup> Metastasis to local lymph nodes does not occur, thus there does not appear to be a need for lymph node dissection.<sup>10</sup>

The objectives of the study were to determine the clinical presentations, diagnostic methods and outcome after surgery of these rare tumors at The Aga Khan University Hospital, Karachi.

**PATIENTS AND METHODS**

It was a case series with combined retrospective and prospective review conducted at The Aga Khan University Hospital, Karachi from January 1988 to December 2002. The data was collected retrospectively from 1988 to 1998, and prospectively from 1999 to December 2002. All adult patients of age 14 years and above, diagnosed by histopathology, to have gastric stromal tumors were included in the study. Patients less than 14 years of age, and patients with incomplete medical record were excluded.

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The demographic data, presentations, diagnostic methods employed and the type of surgical procedure performed were studied. All the slides were reviewed by the pathologist. The tumors were classified according to the new classification system as benign, intermediate and malignant. The reasons for admission after the discharge from the hospital, and follow up of these patients were also reviewed. There were 4 patients who were studied prospectively. Since all their features were same as in the retrospective group, therefore, all patients were studied as a single group. TGM (Tumor, Grade, Metastasis) system was used to stage the disease.

## RESULTS

There were 11 patients. The mean age was 54 years. There were 8 male and 3 female patients. Ischemic heart disease was a comorbidity in 4 patients, hypertension in 3, liver cirrhosis in 1, rheumatoid arthritis in 1, smoking in 2, and goiter in 1 patient. The clinical features and the duration of these features are shown in Table I.

Table I: Clinical features and duration.

S.No.	Clinical features	No. of patients (%)	Mean duration (days)
1	Gastrointestinal bleeding	9	42
	Upper (hematemesis)	5	32
	Lower (melena)	4	55
2	Pain epigastrium	8	85
3	Vomiting	3	200
4	Dysphagia	2	75
5	Loss of appetite	2	270
6	Weight loss	2	270
7	Fever	2	105
8	Gastric outlet obstruction	1	360
9	Mass epigastrium	1	720
10	Fullness in epigastrium	1	540

The hemoglobin was less than 10 gm/dl in 3 patients, and 8 patients had hemoglobin of more than 10gm/dl at the time of admission. The liver function tests were normal in all the patients. Upper gastrointestinal endoscopy was used as a diagnostic modality in all of these patients. The yield of the upper gastrointestinal endoscopy was small and only 2 patients could be diagnosed to have gastric stromal tumors, on endoscopic biopsy. The endoscopy showed ulcer in stomach in 4 patients, nodular lesions in 2, gastritis in 3, polypoid lesion in 1, and gastric outlet obstruction in 1 patient. Ultrasonography of abdomen was done in 4 patients. It showed a mass anterior to the pancreas in one patient. The pre-operative C.T scan was done in 7 patients. In 6 patients, it revealed a mass in stomach. In one patient, it showed a mass inferior to the antral part of the stomach. No liver metastasis or ascites was detected pre-operatively in these patients.

With the help of these diagnostic modalities, the pre-operative provisional diagnosis of a gastric stromal tumor was made in 6 patients. Wedge resection with negative tumor margin was performed in 5 patients. In 3 patients, proximal gastrectomy and gastroesophageal anastomosis was performed. A partial gastrectomy and gastrojejunostomy was performed in 3 patients because the tumor was in the pylorus of the stomach. One patient was found to have liver metastasis and 3 patients had tumor rupture, detected per-operatively.

The size of the tumor ranged from 3.5cm to 21cm, with a mean diameter of 8.0cm. The slides of all these patients were reviewed by the histopathologist, and these tumors were reclassified according to a new classification system of Amin et al. Two patients had benign tumors, 2 had intermediate, and 7 patients had malignant tumors. One patient had stage I disease, 3 patients had stage II, 3 patients had stage III, one patient had stage IV A, and 3 patients had stage IV B disease.

Injury to splenic vessels occurred in one patient, during surgery, leading to hemorrhage and splenectomy was done. He was shifted to ICU, where he developed pneumonia and ARDS, leading to death. One patient developed urinary tract infection postoperatively, and he was treated with antibiotics. The mean hospital stay was 11 days.

Four patients were re-admitted with pain epigastrium due to acid peptic disease, 2 patients with upper gastrointestinal bleeding, one patient with ischemic heart disease and one patient with hepatic coma. One patient who had liver metastasis was admitted for chemotherapy.

The mean duration of follow up was 41 months. Two patients were lost to follow up, one of them was the patient with liver metastasis, and he lost to follow up after 20 months of his surgery, and another was lost to follow up 4 months after the surgery. Among the remaining 8 patients, 6 patients were alive at the time of completion of this study. One patient expired 8 years after surgery due to ischemic heart disease, and another patient expired 3 years and 9 months after the surgery, due to liver cirrhosis.

The stage of the disease, operative procedure and duration of survival is shown in Table II.

Table II: Stage of disease, operative procedure and survival.

S.No.	Stage of disease	Operative procedure	Survival in months
1	1	Wedge resection	45 (expired)
2	11	Wedge resection	66
3	11	Wedge resection	04 (lost to follow-up)
4	111	Prox. gastrectomy with gastroesophag. anastomosis	96 (expired)
5	111	Wedge resection	54
6	111	Partial gastrectomy and gastrojejunal anastomosis	26
7	1VA	Proximal gastrectomy with gastroesophag. anastomosis	20 (lost to follow-up after 20 months)
8	1VB	Partial gastrectomy with gastrojejunal anastomosis	35
9	1VB	Proximal gastrectomy with gastroesophag. anastomosis	49
10	IVB	Partial gastrectomy and gastrojejunal anastomosis	21

## DISCUSSION

Tumors of smooth muscle origin account for 0.3% of gastric lesions.<sup>11</sup> Many of such tumors may not originate from smooth muscles<sup>2</sup>, and therefore, these tumors are called gastric stromal tumors. A significant number of patients have their tumors discovered during operation when they present with bleeding, perforation, or obstruction.<sup>7</sup> The surgeon is required to formulate adequate therapy usually in an acute condition for a rare disease. Most of these tumors are

asymptomatic. Symptomatic tumors have varied presentations. Gastro-intestinal bleeding was the common presentation in this study, occurring in 9 patients. This was followed by pain in epigastrium, vomiting, dysphagia and anorexia. The incidence of gastrointestinal bleeding as reported in the literature is up to 70%.<sup>12</sup> However, these are usually nonspecific and depend upon the size and location of lesion.<sup>13</sup>

As pre-operative diagnosis of these tumors is often difficult, in the literature pre-operative diagnosis could be made in upto 15% of the cases.<sup>12</sup> In our series the pre-operative provisional diagnosis of gastric stromal tumors was made in 6 patients. Endoluminal ultrasonography has sensitivity of 80% to 100% in detecting gastric stromal tumors and it also differentiates benign from the malignant stromal tumors, as described in the literature.<sup>9</sup> A demarcated hypoechoic mass that is contiguous with the muscularis propria layer of the stomach is characteristic of a stromal tumor.<sup>9</sup> Fine needle aspiration and core biopsy are also described as pre operative diagnostic methods.<sup>14</sup> These modalities were not used in our patients.

Surgical resection of localized gastric stromal tumors is the preferred treatment modality. Historically a 1 to 2 cm margin was thought to be necessary for adequate resection. Recently it is demonstrated that the surgical goal should be complete resection with negative resection margins, without lymphadenectomy.<sup>14</sup> In some cases, tumor size and location may require extensive surgery, including partial or total gastrectomy. Removal of all the gross disease improves the outcome even in patients with advanced disease. The regional lymphadenectomy would not result in beneficial effects<sup>10</sup> because majority of these patients present with systemic metastasis.<sup>15</sup> In the present series, removal of all the gross disease was done in 10 patients and one patient had liver metastasis. Tumor rupture is said to have an adverse influence on the survival of the patients.<sup>7</sup> In this study, 3 patients had tumor rupture, because the tumor had already ulcerated prior to surgery.

Currently a laparoscopic resection of gastric stromal tumors is performed in some centres. A study done by Novitsky *et al* showed a laparoscopic approach to surgical resection of gastric stromal tumors was associated with low morbidity and short hospital stay.<sup>16</sup> The long-term follow-up (mean 36 months) in this study showed a disease-free survival of 92%.

The mean diameter of the gastric stromal tumors as described in the literature is upto 7.3 centimeters. In this study, the mean diameter is 8.0 centimeters. This seems that patients presented in the advanced stage of the disease. The mean follow-up was 41 months, which is better than the study of Ludwig.<sup>12</sup> The local recurrence has been reported upto 10% to 12% in the literature, but in our study no patient had local recurrence. The rates of curative resection for gastric stromal tumors ranges from 68% to 90%, and 5 years survival ranges from 32% to 63%.<sup>14</sup>

A case reported by Shiwani showed 4 years postsurgery follow-up in a patient operated for gastric stromal tumor, without chemo-radiotherapy that did not show any evidence of disease.<sup>17</sup> In this study one patient expired 8 years after the surgery due to ischemic heart disease, but having no evidence of the tumor recurrence.

The role of radiotherapy has yet to be determined. Presently, there is no data available to support the administration of radiotherapy to these patients. Currently, it is described that C-kit receptor tyrosine kinase is expressed in these tumors. The tyrosine kinase inhibitor Glivec is the first rationally designed molecular targeted drug therapy for gastric stromal tumors or with metastatic disease.<sup>19</sup> In one study, after surgical resection, Glivec caused stabilization or regression of the tumor in 84% of patients.<sup>20</sup> True efficacy is unknown until the results of the ongoing prospective trials. Glivec was not given to patients in this study.

## CONCLUSION

Gastric stromal tumors are uncommon. Larger tumors are usually symptomatic. Immunohistochemical techniques are required for the diagnosis. Complete surgical resection can lead to prolongation of life, and may be a potential cure for patients with gastric stromal tumors.

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