Diagnosis and Treatment of Gastric Stromal Tumors: Report of 70 Cases

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OBJECTIVE To investigate the diagnosis and treatment of gastric stromal tumors (GSTs).

METHODS The clinical data from 70 cases with GSTs were analyzed retrospectively.

RESULTS Wedge resections were performed on 32 patients and major gastrectomies on 38 patients. The median tumor size was 5.4cm in diameter and 2 out of 70 cases (2.9%) indicated positive lymph node metastasis. Immunohistochemical staining showed 66 out of 70 (94.3%) were positive for CD117, 53 (75.7%) positive for CD34, 24 positive for SMA and 8 positive for Desmin and S100. Ten out of 70 cases recurred or metastasized. The 5-year survival rate in this series was 71.3%. The 5-year survival rate of benign and malignant GSTs were 92.3% and 61.8% ($P<0.05$) respectively. The 5-year survival rate for tumors of size <5 cm and ≥5 cm were 95.0% and 48.4% ($P<0.05$), respectively.

CONCLUSION The primary treatment for gastric stromal tumors is surgery. Tumor size and mitotic counts were observed to be important prognostic indicators.

KEYWORDS: stomach neoplasm, stromal tumors, diagnosis, treatment.

Clinically, gastric stromal tumors (GSTs) are rare. From January 1990 until January 2003 our hospital admitted, as well as surgically treated, a total of 70 cases diagnosed with GST, among which were 48 cases of malignant stromal tumors. We retrospectively analyzed all 70 cases to observe specifics with regard to GSTs diagnosis and treatment.

MATERIALS AND METHODS

Clinical Information

Our patient group that we analyzed consisted of 31 men and 39 women (1:1.3), with an age range of 23 to 78 years (mean 56 years). The clinical presentations were upper abdominal discomfort, 49 cases (70%); upper gastrointestinal bleeding, 24 cases (34.3%); abdominal mass, 5 cases(7.1%); and asymptomatic, 5 cases(7.1%). One patient underwent an emergency surgical procedure for intra-abdominal bleeding diagnosed as rupture of the GST.

Diagnosis and adjuvant examinations

Pre-surgery diagnosis often relies on endoscopy and X-ray imaging. Fifty-one cases underwent endoscopic examination resulting in

Received April 12, 2004; accepted May 13, 2004.

identification of a tumor, mainly appearing as a rising submucosal mass. Some were complicated by mucosal surface ulceration. Among these, 22 cases received a biopsy examination resulting in 4 positive cases (18.2%). Seventeen cases underwent an endoscopic ultrasound examination. The tumor size and range of infiltration were determined in all cases. Twenty-six of 32 cases which underwent gastrointestinal X-ray imaging were positive. There were 2 cases misdiagnosed as pancreatic mass prior to surgery, one case as a retroperitoneal mass. Four cases were discovered when the patients underwent other surgical procedures.

Treatment

All patients underwent surgical resection: 16 cases underwent distal major gastrectomy, 22 cases proximal major gastrectomy and 32 cases gastric wedge resection.There were two postoperative complications: dysfunction of gastric excretion and pancreatic fistula. No surgical mortality occurred.

Statistical analysis

Survival rate was carried out by Kaplan-Meier analysis. Univariate analysis using log-rank test, $P<0.05$ was considered statistically significant. All data were analysed by SPSS 10.0.

RESULTS

Pathological examination

To diagnose malignant stromal tumors, histologic results depend mainly upon the tumor cell mitotic count (>5/50 HPF), along with pleomorphism and invasive information. Results indicated that 22 cases were benign and 48 cases malignant. Table 1 shows the location pathogenesis and tumor size for both groups. The results of ulceration of the tumor surface stomach mucosa and peri-gastric lymph node metastasis are indicated as well. Maximum tumor size was 26 cm in diameter with an average of 5.4 cm. Two cases(2.9%) with peri-gastric lymph node metastasis were both malignant GSTs. All cases had their tissue samples examined using immunohistochemical staining, among which 66 cases(94.3%) were CD117 positive, 53 cases (75.7%) CD34 positive, 8 cases Desmin positive, 24 cases SMA positive and 8 cases S100 positive.

Follow-up

Sixty-five cases (92.9%) were followed either through written forms or at the out-patient clinic. The mean follow-up time was 53.9 months (6 to 136 months). The 5-year survival rate was 71.3%. Group analysis was conducted by dividing cases into two groups according to different surgical procedures such as wedge resection or major gastrectomy, tumor size of <5 cm and ≥5 cm, pathological results based on whether the tumor was benign or malignant. The 5-year survival-rate analysis is indicated in Table 2. Distal metastasis of malignant GSTs post surgery occurred in 6 cases and local recurrence in 5 cases. Benign GSTs resulted in no recurrence or distal metastasis. Of 2 cases with positive peri-gastric lymph node metastasis, 1 patient survived over 10 years post surgery while the other had liver metastasis within 1.5 years post surgery.

Table 1. Comparison of pathological specifics between benign and malignant gastric stromal tumors

	Benign GSTs(n)	Malignant GSTs(n)	*P* value
Tumor size			
>10cm	0	10	
5-10cm	3	21	<0.05
<5cm	19	17	
Mucosal ulceration			
present	4	28	<0.05
absent	18	20	
Tumor site			
lower	6	6	
middle	5	19	>0.05
upper	11	23	
LN metastasis			
positive	0	2	-
negative	22	46	

Table 2. Relationship between GSTs prognosis and different surgical procedures, size and characteristics of 65 cases

	Cases	5-year survival rate (%)	*P* value
Gastric wedge resection	30	73.2	<0.05
Major gastrectomy	35	69.7	
Tumor diameter <5cm	34	95.0	<0.05
Tumor diameter ≥5cm	31	48.4	
Benign GSTs	20	92.3	<0.05
Malignant GSTs	45	61.8	

DISCUSSION

Gastrointestinal stromal tumors (GISTs) are a common

type of gastrointestinal nonepithelial neoplasm, and may be located throughout the entire gastrointestinal tract, most often occurring in the stomach(60-70%).[1,2] The term GSTs was first used by Mazur and Clark in 1983 to describe gastric non-epithelial neoplasms that lacked the immunohistochemical features of Schwann cells, but did not have the ultrastructural characteristics of smooth muscle cells. The discovery of gain-of-function mutations in the c-kit proto-oncogene in GISTs by Hirota and colleagues in 1998 was of crucial importance in terms of the genesis and classification of these tumours.[3] Recent studies show GISTs share immunohistochemical, ultrastructural and histogenesis with interstitial Cajal cells , both express c-kit.[4,5]

The early stages of the disease are often asymptomatic. Therefore clinical diagnosis is often achieved only in the developing stages where gastrointestinal dysfunctions or bleeding or rupture of the neoplasm occur, as well as during diagnosis while undergoing other surgical procedures or examinations.

Pre-surgical examinations of GSTs often rely on endoscopy and X-ray imaging. In using the endoscope one often observes a submucosal mass varying in size, sometimes accompanied by ulceration of the mucosal surface. Endoscopic biopsies are often superficial, hence it is difficult to obtain neoplastic tissue and thus the report is negative. Endoscopic ultrasound examinations can specifically determine tumor size and range of infiltration, acting as a valuable input in diagnosis. Pre-surgical ultrasonography and CT examinations are relevant in regards to larger sized tumors, as well as to assess whether or not liver metastases exist.

Diagnosis of benign and malignant GSTs were determined according to tumor cell nuclear mitotic counts, pleomorphism and invasive information as well as pathological characteristics. Further analysis indicated variation in both groups in terms of tumor size and presence of stomach mucosal ulceration. Malignant GSTs are often larger in size than benign and often are complicated by tumor surface stomach mucosal ulceration. Gastric location of both benign and malignant GSTs indicated no obvious deviation.

Currently, there is no obvious histo-pathological standard to predict the behavior of GSTs. Some researchers reported 20-30% of benign GSTs may result in malignancy.[6] The primary choice of treatment for GSTs is surgery,[7,8] gastric wedge resection is sufficient for benign GSTs while major gastrectomy is required for malignant GSTs. Due to the fact that it is often difficult to determine malignancy prior to surgery, diagnosis is obtained during surgery according to tumor size, presence of surrounding organ and tissue infiltration as well as whether or not there are distal metastases. For tumors of size ≥5 cm in diameter, major gastrectomy is suggested, if infiltration of surrounding tissues exist, unified resection of organs should be performed.

GSTs distal metastases often occur as liver metastases seeding into the peritoneum, but rarely occur as peri-gastric lymph node metastases. Sources report lymph node metastasis rates of 1.7-6%.[9] Our study indicates a lymph node metastasis rate of 2.9%. However in order to reduce post surgical recurrence and metastatic rates, strict procedure guidelines along with "no-touch" and "en-bloc" principles should be followed during surgery. Laparoscopic gastric wedge resection is an alternative choice for smaller sized GSTs. Matthews et al. [10] reported no obvious difference in comparison of laparoscopic resection with open surgery with regards to safety and post surgical survival rate, however surgical trauma and post surgical recovery were greatly improved.

GSTs is not sensitive to routine standard chemotherapy and radiotherapy. However in recent years, molecularly targeted therapy with imatinib mesylate (Gleevec, STI571)-a selective inhibitor of the c-kit receptor tyrosine kinase-has been shown to successfully block the proliferation and growth of GSTs tumor cells.[11] Demetri et al.[12] reported a response rate of 54% among 147 patients with inoperable or metastatic GIST, and 28% had a minor response or stable disease.

The factors influencing prognosis of GSTs are tumor size, mitotic count and whether or not there exists rupture of the tumor, and not as dependant upon tumor growth types, presence of mucosal ulceration and type of surgical procedure.[13,14] In our study the benign GSTs 5-year survival rate was 92.3% and the malignant GSTs 5-year survival rate was 61.8% , resulting in a significant difference ($P<0.05$). The comparison between 5-year survival rates of patients with tumors size <5 cm and ≥5cm in diameter indicates an obvious difference, respectively being 95.0% and 48.4%. In our study 24.4% of patients with malignant GSTs were recurrence or metastases. Post surgical follow up is imperative.

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