Benign Smooth Muscle Tumors of the Gastrointestinal Tract

A 24-Year Experience

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Between 1963 and 1987, 131 patients with benign gastrointestinal stromal tumors, primarily leiomyomas, were treated at the Massachusetts General Hospital. Eighty per cent of tumors were located in stomach or small intestine. Two thirds of the tumors were discovered in symptomatic patients before operation by a variety of diagnostic studies. A mitotic index (MI) was determined for each tumor, defined as the number of mitoses per 50 high-power microscopic fields. Only gastric and small intestine tumors had MIs more than 2. Tumors were treated by conservative excision in 67% and radical excision in 33%. At a median follow-up of 6 years there were no local recurrences. No patient with a tumor discovered incidentally has recurred. Three symptomatic patients have died of metastatic liver disease. Each patient with recurrence had a tumor with MI of 2 or more, which represents a recurrence rate of 16% in this group. We conclude that symptomatic gastric and small intestine tumors having two or more mitoses per 50 high-power fields carry a significant risk for recurrence, and that routine pathologic assessment of MI may identify a subset of patients who would potentially benefit from close follow-up and consideration for further therapy.

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BENIGN SMOOTH MUSCLE tumors of the gastrointestinal (GI) tract are uncommon entities. Symptoms occurring because of size, location, and manifestations of bleeding may prompt diagnostic evaluation, but many tumors are discovered incidentally and are resected during laparotomy for other indications. Previous studies suggest that leiomyomas with benign gross and microscopic appearance may behave in an aggressive manner, making the assessment of the ultimate malignant potential of individual tumors difficult.[1-3] We reviewed the clinical experience and independently reassessed the surgical pathology of GI smooth muscle tumors seen at the Massachusetts General Hospital during the last 24 years to gain insight into the biologic behavior and appropriate management of such lesions.

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Materials and Methods

The medical records of 131 patients diagnosed with benign GI smooth muscle tumors at the Massachusetts General Hospital between 1963 and 1987 were reviewed. Data obtained included patient sex, age at diagnosis, symptoms and physical findings leading to work-up, preoperative diagnostic evaluation, pathology reports, therapy, and further follow-up. A meticulous evaluation of specimens from the surgical pathology records was conducted independent of the clinical review. The number of mitoses seen in 50 high-power fields (HPF) was defined as the mitotic index (MI) for each tumor. Tumor size was assessed. Atypical tumors, considered to be from smooth muscle elements and not clearly sarcomas, were included. Epithelioid tumors were categorized with leiomyoblastomas. Follow-up information was obtained from the treating physician or directly from the patient. All records were included in the analysis of patient characteristics, but only those with a complete set of clinical information, pathologic data, and follow-up were considered evaluable cases for judging treatment. Outside slides sent for review and second opinion were not included unless complete clinical information and follow-up data were available.

Results

Patient Characteristics

One hundred thirty-one patients with benign GI stromal tumors were seen during the 24-year period. The median

age at time of diagnosis was 62 years (range, 19–89 years) with a slight male predominance (1.2:1). There were 103 evaluable cases in which a complete set of clinical, pathologic, and follow-up information was available. Three patients were excluded because of incomplete pathologic information. Recent follow-up information was unavailable for 25 patients.

Distribution of Tumors

As illustrated in Table 1, the majority of these tumors occurred in the stomach. Sites in order of decreasing frequency were small intestine, esophagus, rectum, and colon.

Clinical Presentation

Tumors were discovered before operation in two thirds of patients (Table 2). Esophageal lesions were symptomatic, primarily causing dysphagia and pain, in 80% of patients. Seventeen patients with gastric tumors and one patient with an esophageal tumor presented with acute hemorrhage. Three patients with small bowel tumors presented with gross bleeding, while four had more occult blood loss. Small bowel tumors presented with mechanical obstruction in only 8% of patients. Colorectal lesions generally caused no symptoms and were discovered on workup of occult bleeding or incidentally.

Diagnostic Evaluation

Upper GI endoscopy identified 60% of gastric and 50% of esophageal lesions (Table 3), but results were abnormal in only 33% of patients with small bowel tumors. Contrast studies diagnosed all esophageal and 64% of gastric lesions in patients who were evaluated; however, small intestine lesions were seen in only 25% of small bowel studies. Computed tomography was useful in a small group of patients with gastric tumors. In two patients visceral arteriography detected small bowel tumors. Colonoscopy was more useful than barium enema for detecting colorectal lesions.

Pathology

Eighty-six per cent of tumors were benign leiomyomas. Other tumor types seen included 8 cellular leiomyomas, 6 leiomyoblastomas, 1 schwannoma, and 2 atypical, otherwise unclassifiable, smooth muscle tumors without sufficient characteristics to be called sarcomas. As shown in Table 4, 85% of tumors in this series were less than 5 cm in diameter. Eighty-four tumors had MIs of less than 2, while 19 demonstrated MIs between 2 and 7. MIs greater than 2 were seen only in gastric and small intestine tumors. All cases were originally diagnosed as benign lesions on the basis of standard light microscopy.

TABLE 1. *Site of Smooth Muscle Tumors*

Site	Number (%)
Esophagus	10 (8)
Stomach	81 (61)
Small intestine	25 (19)
Colon	7 (5)
Rectum	8 (6)

TABLE 2. *Clinical Presentation of Smooth Muscle Tumors*

Symptoms/ Signs	Percentage of Patients Affected				
	Esophagus	Stomach	Small Bowel	Colon	Rectum
Asymptomatic	20	31	44	57	29
Pain	36	20	24	0	13
Mechanical obstruction	55	0	8	14	0
Occult/frank bleeding	0	38	24	29	50
Dyspepsia	18	17	0	0	0

Therapy

All patients were treated by tumor excision, as described in Table 5. Excision with margins greater than 1 cm was performed in 34 patients (33%). No patient received adjuvant radiation or chemotherapy.

Follow-up

Information was available for 103 patients (81%). Median follow-up was 6 years; minimum follow-up was 1 year. There were three recurrences (Table 6). Tumors that recurred were all larger than 4 cm in diameter. Each was read as a benign leiomyoma on the basis of low-grade mitotic activity. Recurrence was associated with death of the three patients within 3 years after operation. There were no recurrences in patients with tumors having MIs less than 2. No recurrence of esophageal or colorectal tumors has been seen in this series.

TABLE 3. *Preoperative Evaluation*

Examination	Number Having Study (% positive)				
	Esophagus	Stomach	Small Bowel	Colon	Rectum
Endoscopy	8 (50)	52 (60)	9 (33)	7 (57)	6 (67)
Contrast studies	5 (100)	53 (64)	12 (25)	1 (0)	6 (33)
CT scan	0	6 (83)	1 (0)	0	0
Angiography	1 (0)	6 (50)	5 (40)	0	0

TABLE 4. *Tumor Characteristics*

Site	Tumor Diameter (cm)			Mitotic Index	
	<2	2–5	>5	0, 1	>2
Esophagus	2	6	1	9	0
Stomach	27	20	12	44	15
Small bowel	10	9	2	17	4
Colon	7	0	0	7	0
Rectum	7	0	0	7	0

Discussion

Although uncommon, benign smooth muscle tumors of the GI tract can present diagnostic challenges. These lesions occur with greater overall frequency than do leiomyosarcomas (about 4:1), although two series have described a similar prevalence.[4,5] Such tumors arise most commonly from the muscularis propria or mucosae of the intestinal wall, but have also arisen from smooth muscle in the tunica media of blood vessels.[6] When local overgrowth of smooth muscle cells occurs in the muscularis, expansion may be toward the bowel lumen, the serosa, or both (dumbbell tumors), as illustrated in Figure 1.

Patients with smooth muscle tumors of the GI tract may be entirely asymptomatic or may manifest symptoms referable to tumor size, growth pattern, and location. In this series one third of the tumors were discovered incidentally. Upper GI lesions were responsible for dysphagia and epigastric pain in 70% of patients. Colorectal tumors were more likely to be discovered because of gross or occult bleeding. Because of lack of bleeding or encroachment on intestinal lumen, small, primarily extraluminal tumors rarely caused symptoms. Our report confirms the distribution by site of intestinal leiomyomas as reported in other series,[7,8] with the stomach and small bowel the most common.

Preoperative detection of these GI tumors is possible by contrast studies that may define a well-circumscribed luminal defect. Endoscopy may show ulcerated or raised mucosa overlying a tumor mass.[9] CT scanning[10] and visceral arteriography[11,12] may be useful, particularly for gastric and small intestinal lesions without an endoluminal component.

Pathologists have long been aware of the difficulties in differentiating benign from malignant smooth muscle GI tumors, which can be the case for soft-tissue leiomyomas in other locations. Although the mitotic activity of a GI stromal tumor remains the most critical prognostic factor, tumors have been seen to recur locally and to metastasize even with rare or absent mitotic figures.[13] According to Golden and Stout,[2] "one can never be entirely certain that any leiomyoma is necessarily benign, except the small

TABLE 5. *Surgical Therapy*

Site	Margin of Excision		No. of Recurrences
	<1 cm	>1 cm	
Esophagus	7	2	0
Stomach	40	19	1
Small bowel	12	9	2
Colon	4	3	0
Rectum	6	1	0

TABLE 6. *Recurrences*

Site	Size	MI	Recurrence	Time to Death
Stomach	4 cm	7	liver	2 years
Duodenum	5 cm	2	liver	2 years
Jejunum	13 cm	4	liver	3 years

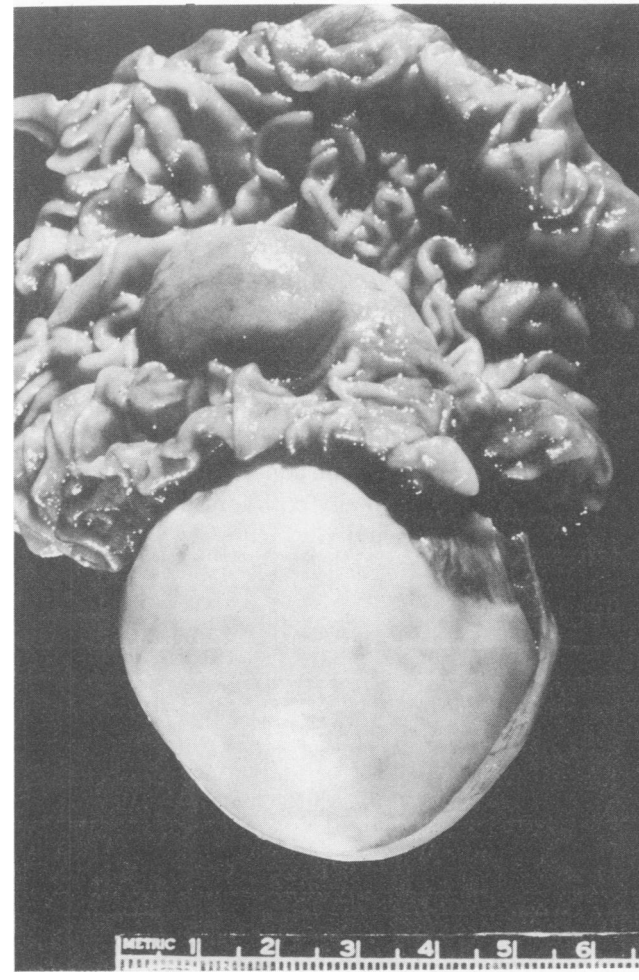

FIG. 1. Dumbbell leiomyoma of small intestine, illustrating both intraluminal and extraluminal components. In this instance, the extraluminal component predominates.

intramural tumors that are chance findings at autopsy or operation." They favored the designation malignant leiomyoma in this setting instead of sarcoma to denote a lesion with a lower degree of malignant potential. Ranchod[14] emphasized the importance of considering new criteria for the diagnosis of leiomyosarcoma in nonuterine smooth muscle tumors and believed that five or more mitoses per 10 HPF in gastric and small bowel tumors were indicative of malignancy. Appleman and Helwig[3] and Akwari[15] found that tenand five mitoses per 50 HPF, respectively, indicated a tumor with malignant potential. In the former series, 13% of patients with gastric leiomyomas with one to five mitoses per 50 HPF developed metastases.[16] In the current series, 3 of 19 patients (16%) with 2 or more mitoses per 50 HPF died of metastatic liver disease.

Gastric and small bowel leiomyomas with benign gross appearance have the potential, as seen in this study, to be aggressive lesions. Our only recurrences were in this group, and one fourth of gastric and small bowel tumors had MIs more than 2. No tumor involved lymph nodes, making regional node dissection not a necessary component of therapy.[8] In this study we observed no local recurrences, regardless of margin of surgical excision. Tumors with adherence to adjacent structures should be treated with *en bloc* resection of the adjacent structure to achieve excision of the entire tumor. For these tumors, this sort of adherence is an uncommon finding. The most important factor allowing prediction of subsequent recurrence proved to be the mitotic index. Darling and Welch[17] reviewed 46 benign and 86 malignant small bowel tumors and noted that a preoperative palpable mass was almost always indicative of malignancy. A palpable mass was not seen in any of our patients. All tumors that recurred in our series were initially symptomatic. We found no recurrences in patients with tumors discovered incidentally at laparotomy. We recommend conservative local excision for tumors found incidentally both for diagnosis and for evaluation of mitotic activity.

Esophageal and colorectal tumors in this series were less common lesions, had low MIs, and were also not associated with recurrence, regardless of margin of excision. Conservative local excision should suffice as therapy.

We recommend a higher index of suspicion for the malignant potential of symptomatic gastric and small intestinal leiomyomas, particularly those that have more than two mitoses per 50 HPF.

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