Gastrointestinal stromal tumors are a group of neoplasms encompassing leiomyoma, leiomyosarcoma, and an epithelioid variant of leiomyosarcoma, as well as lesions expressing neural differentiation. These neoplasms are rare and account for 1% of all gastrointestinal tumors. With increasing frequency, fine-needle aspiration (FNA) has been used to diagnose intra-abdominal neoplasms before institution of definitive treatment. We encountered four patients with gastrointestinal stromal tumors diagnosed by FNA who ultimately underwent surgical excision of their tumors. The age of the patients ranged from 57 to 88 years. Smears from the aspirates were cellular and consisted of numerous small spindle cells distributed as cohesive fragments and individual cells. The dispersed cell population appeared largely as stripped nuclei. Several nuclei had perinuclear or paranuclear vacuoles, similar to the “halos” seen in sections. Cytologic evidence of malignancy (pleomorphism, nuclear irregularity, mitoses) were not identified in smears. Corresponding histologic sections demonstrated varying degrees of malignancy ranging from benign or low grade to frankly sarcomatous gastrointestinal stromal tumors. We conclude that the diagnosis of gastrointestinal stromal tumors can be made with a certain degree of confidence by using FNA findings. However, predictions about potential aggressiveness are best reserved for gross and histologic examination of the resected specimen. (Key words: Leiomyoma; Leiomyosarcoma; Gastrointestinal tumors; Fine-needle aspiration) Am J Clin Pathol 1998;109:439-443.
then removed, and the needle was manipulated back and forth, using a twist motion. Aspiration with an attached syringe and plastic tubing was used on some of the needle passes.

Material obtained from aspiration was expelled onto glass slides and divided between air-dried smears stained for immediate interpretation with rapid Romanowsky (Diff-Quik, Baxter, McGaw Park, Ill) and alcohol-fixed smears for staining by the Papanicolaou method or with hematoxylin-eosin.

All lesions studied by FNA in this series were ultimately resected. Representative sections of tissue from the respective tumors were fixed in 10% neutral-buffered formalin and embedded in paraffin, and sections were stained with hematoxylin-eosin for microscopic examination.

RESULTS

A clinical summary of the pertinent findings for each patient is given in the Table. Figure 1 illustrates a radiographic image of a lesion from a patient with a gastrointestinal stromal tumor in the small intestine. One patient (patient 1) refused diagnosis and treatment for 5 years until the mass "grew" and became increasingly symptomatic. Three aspirates in this series were from the primary lesions, and one aspirate was performed on a recurrence at the primary site which had been resected 10 years earlier (patient 2).

All smears examined were markedly cellular, consisting of a combination of small cohesive tissue fragments and a dispersed cellular population. Figures 2, A and B illustrate both patterns in a smear from patient 4. Despite marked cellularity, the smear backgrounds were relatively clean and free of excessive blood and necrotic debris. The large clusters were composed of tightly cohesive arrangements of cells. These had irregular outlines and complex branching patterns reminiscent of the "antler" pattern associated with other neoplasms (Fig 3). In alcohol-fixed smears, a fascicular arrangement was often apparent. In more loosely cohesive regions, a finely fibrillar material was present between the nuclei, representing cytoplasmic processes or matrix (Fig 4).

Individual cells were ovoid to cigar shaped, small, and relatively uniform. Dispersed cells were numerous and largely present as stripped nuclei. Cytoplasm tended to be indistinct and wispy when present. Nuclei contained bland chromatin with smooth nuclear contours and without obvious nucleoli. A cytologic equivalent of the perinuclear halo was identified as small vacuoles adjacent to some nuclei (Fig 5). Mitoses were not identified in aspirate smears.

Histologic examination of three neoplasms revealed a continuity with the muscular layers of the gastrointestinal tract. An additional lesion represented a recurrence, and an exact origin was not demonstrable. Two cases demonstrated histologically intact mucosa overlying the neoplasm (Fig 6), and one case showed focal mucosal ulceration. The borders of the neoplasms tended to be rounded and well circumscribed with a sharply delineated border between the neoplasm and

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**CLINICAL FEATURES OF PATIENTS WHO UNDERWENT FINE-NEEDLE ASPIRATION OF GASTROINTESTINAL STROMAL TUMORS**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)/Sex</th>
<th>Initial Symptom</th>
<th>Tumor Size (cm)/Location</th>
<th>Follow-Up Interval</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57/M</td>
<td>Gastrointestinal bleeding</td>
<td>16/rectum</td>
<td>6 y</td>
<td>Liver metastases</td>
</tr>
<tr>
<td>2</td>
<td>64/F</td>
<td>Gastrointestinal bleeding</td>
<td>Unknown/small intestine</td>
<td>13 y</td>
<td>Recurrence and liver metastases</td>
</tr>
<tr>
<td>3</td>
<td>70/M</td>
<td>Abdominal distention</td>
<td>25/small intestine</td>
<td>2 mo</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>88/F</td>
<td>Incidental finding</td>
<td>18.5/stomach</td>
<td>9 mo</td>
<td>None</td>
</tr>
</tbody>
</table>

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Fine-Needle Aspiration of Gastrointestinal Stromal Tumors

Fig 2. Two regions of one smear from a fine-needle aspiration of a gastrointestinal stromal tumor. A, Tight cohesive cluster of small spindle cells (Papanicolaou, x170). B, A more dispersed cellular population with a large percentage of stripped cell nuclei (Papanicolaou, x250).

Fig 3. An air-dried preparation showing a large cohesive cluster of small cells with a complex branching pattern from a gastrointestinal stromal tumor of the stomach (rapid Romanowsky, x170).

Fig 4. Fixed smear of an aspirate from patient 2 in this series showing dispersed and cohesive cells. Individual cells are small and elongated or comma shaped. In this aspirate a fine fibrillar material is seen between the cell nuclei (Papanicolaou, x200).

Fig 5. Individual dispersed cells with stripped nuclei and vacuoles believed to represent the cytologic equivalent of the perinuclear halo (rapid Romanowsky, x400).

Fig 6. Gastrointestinal stromal tumor originating from the muscularis of the gastric wall (hematoxylin-eosin, x68).
the adjacent normal structures. All of the stromal tumors were very cellular and showed focal areas of necrosis or hemorrhage. A pattern of small and medium-sized vessels was present throughout all gastrointestinal stromal tumors. Tumor cells were arranged in whorls and bundles with a marked tendency to palisade in all sections examined. Clear spaces or halos were identified adjacent to or surrounding nuclei in representative sections of all cases. Individual tumor cells appeared relatively uniform with the exception of one lesion with obvious pleomorphism, numerous mitotic figures, and nuclear atypia. This tumor (patient 3) was the largest in our series, measuring in excess of 25 cm. The remaining three neoplasms showed only subtle nuclear irregularity and occasional mitotic figures (Fig 7). Nuclear irregularity and mitoses, indicators of higher grade lesions, were not reflected in the corresponding aspirates obtained from these patients.

DISCUSSION

The histogenesis of gastrointestinal stromal tumors is controversial. The controversy has centered around immunohistochemical studies demonstrating at least focal positivity for the marker of neural differentiation, S-100 protein, in tumors classified as leiomyoma or leiomyosarcoma.\textsuperscript{12-14} The recognition of possible neural differentiation led to the broadening of the definition of gastrointestinal stromal tumors. Before their reclassification these lesions were usually classified as leiomyoma or leiomyosarcoma based on size\textsuperscript{15,16} and histopathologic features, such as grade and number of mitoses.\textsuperscript{2,3,5,15,16} Current recommendations include separation of low- and high-grade gastrointestinal stromal tumors by a threshold of 1 to 5 mitotic figures per 10 high-power fields and size greater than 4 cm.\textsuperscript{5,15-18} An epithelioid variant of leiomyosarcoma accounts for 16% of gastrointestinal stromal tumors and is usually located in the stomach.\textsuperscript{14,15} Although it is a histologically distinct neoplasm, the epithelioid variety does not seem to confer a particularly unique prognosis.\textsuperscript{17}

The cytopathologic characterization of gastrointestinal stromal tumors has been limited. In a study of the FNA characteristics of 51 cases of smooth muscle tumors from various sites, Tao and Davidson\textsuperscript{11} described criteria to separate benign and malignant neoplasms. Their series included 16 smooth muscle tumors of the stomach and gastrointestinal tract. In their series, the features of malignancy included the presence of loose groupings and solitary cells, as well as the presence of multinucleated cells, blood vessels, and stripped nuclei.

Das and Pant\textsuperscript{10} described their findings in FNA experience with 78 gastrointestinal tract lesions, using ultrasonographic guidance for 52.\textsuperscript{10} This review consisted largely of adenocarcinoma and lymphoma, which accounted for 23% and 11.5% of cases examined by FNA, respectively. Also included in this series were 2 cases of leiomyosarcoma; the diagnosis was determined unequivocally by FNA findings. Descriptions and illustrations are of a cellular aspirate composed of spindled cells with cigar-shaped nuclei with rounded ends. An additional case of a gastrointestinal stromal tumor diagnosed by FNA with the aid of transmission electron microscopy was reported by King et al.\textsuperscript{9}

The collective cytopathology literature contains additional FNA descriptions of leiomyosarcoma in primary soft tissue\textsuperscript{19} and assorted other sites, including the renal pelvis,\textsuperscript{20} the kidney,\textsuperscript{21} the prostate,\textsuperscript{22} the orbit,\textsuperscript{23} the lung,\textsuperscript{24} and the liver.\textsuperscript{25} Most of these reports emphasize the obvious cytologic features of malignancy, including hyperchromatism and pleomorphism. The corresponding histologic descriptions and illustrations are of tumors with a much more obvious sarcomatous appearance than the gastrointestinal stromal tumors we describe. The FNA findings of epithelioid leiomyosarcoma from the soft tissues of the extremities have been described in two cases.\textsuperscript{26}

The current study of the FNA biopsy findings of gastrointestinal stromal tumors demonstrates many of the same cytologic features reported in previous descriptions of benign or low-grade smooth muscle tumors. These include a relatively bland population.

\textbf{Fig 7.} High-power photomicrograph demonstrating subtle nuclear irregularity of one gastrointestinal stromal tumor. (hematoxylin-eosin, ×400.)
of uniform spindled cells without obvious pleomorphism, mitoses, or cellular anaplasia and hyperchromatism. Although we identified histologic evidence of potential aggressiveness in one of the tumors (numerous mitoses and occasional pleomorphic cells), no evidence was seen in the corresponding aspirate of this neoplasm. This neoplasm, and one other without these features, metastasized.

This lack of correspondence between the cytologic features of malignancy and the malignant behavior has been noted by others in the study of soft tissue tumors. In the current study, reliance on FNA findings for prediction of biologic behavior would have underestimated the malignant potential in at least two cases. We conclude that the diagnosis of gastrointestinal stromal tumors can be made with a certain degree of confidence by using the FNA findings. However, predictions about potential aggressiveness are best reserved for histologic examination or, better yet, the patient's ultimate outcome.

REFERENCES


