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STATEMENT OF EDITORIAL PURPOSE

The *Hospital Physician Oncology Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in oncology. Each manual reviews a topic essential to the current practice of oncology.

NOTE FROM THE PUBLISHER:
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Gastrointestinal Stromal Tumors in the Era of Targeted Therapy

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INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are malignancies of mesenchymal origin and represent the most common sarcoma of the gastrointestinal tract.[1] Historically, GISTs were frequently underdiagnosed because they were misclassified as other soft tissue neoplasms due to variable disease criteria and confusing nomenclature.[1] In 1 study that included 650 patients, only 28% of patients were identified as having GIST, meaning that 72% of these tumors now verified as GIST originally had been classified as other tumors. Most misclassified GISTs were identified as leiomyomas (34%) or leiomyosarcomas (18%) because they often resemble smooth muscle tumors by standard histologic techniques.[2] With the advent of modern immunohistochemical and molecular pathologic techniques, it has become clear that GIST represents a distinct clinicopathologic entity. Using these newer techniques, it is estimated that approximately 5000 new cases of GIST are diagnosed each year, a substantial increase from previous estimates of 300 to 500 cases annually.[3]

Prior to 1998, localized and recurrent GISTs were primarily managed with surgery. Attempted treatments with cytotoxic chemotherapy for metastatic disease had an extremely poor response rate, and patients frequently died of progressive, uncontrolled intra-abdominal disease. However, breakthroughs in pathologic techniques have led to a better understanding of the pathogenesis of GISTs, thereby leading to more efficacious pharmacologic therapy. The aim of this review is to summarize the remarkable advances in the diagnosis, pathologic understanding, and treatment of GIST, a disease which now serves as a model for rationally developed, targeted therapies in the management of solid tumor malignancies.

CASE PATIENT

INITIAL PRESENTATION

A 45-year-old man presents to his primary care physician with a 6-month history of progressive fatigue and decreased exercise tolerance. The patient has no significant past medical history and is not taking any medications. Physical examination is unremarkable, with the exception of guaiac positive stool by rectal examination. On additional review of systems, the patient denies chest pain, shortness of breath, headache, nausea or vomiting, anorexia, or change in bowel habits. Laboratory studies, including complete blood count, general chemistry panels, and liver function tests, are ordered.

- **What are the features of the clinical presentation of GIST?**
- **What is the role of imaging?**

CLINICAL PRESENTATION

Although GIST can occur in all age-groups, the incidence is highest in patients aged 40 to 80 years, with similar distribution between the sexes. Some studies, however, have suggested a slightly higher incidence in men.[4] Most reports indicate that large GISTs are symptomatic at initial presentation.[2] Symptoms are related to tumor size and location and may be nonspecific. Patients may present with vague abdominal pain or discomfort, weight loss, anorexia, abdominal bloating, gastrointestinal blood loss, anemia, or acute intraperitoneal bleeding or perforation.[5] It has been reported that nearly one third of all GISTs are asymptomatic, but it is possible that this reflects a selection bias for larger tumors.[2] Most asymptomatic tumors are typically small and may be found incidentally upon endoscopy or during surgery for an unrelated indication (21%) or at autopsy (10%).[2]