SUMMERY

The first accurate description of mesenchymal neoplasms of the gastrointestinal (GI) tract was in 1941. Traditionally, these tumors were thought to be derived from smooth muscle cells, based on their resemblance to smooth muscle tumors and they were designated as leiomyomas, bizarre leiomyomas, cellular leiomyomas and leiomyosarcomas. However, with the advent of electron microscopy, it has been shown that relatively few neoplasms showed convincing ultrastructural evidence of smooth muscle differentiation.

The application of immunohistochemistry revealed that many of these neoplasms lacked the immunophenotypical features of smooth muscle differentiation. This led Mazur and Clark in 1983 to introduce the generic designation ‘stromal tumors.

Subsequently, Herrera et al. introduced the concept of ‘plexosarcoma’ in 1984 to acknowledge the existence of a small subset of stromal tumors with autonomic neuronal differentiation which became better known as gastrointestinal autonomic nerve tumors (GANTs**).**

There was considerable controversy as to the line of differentiation, since some tumors exhibited a myogenic phenotype, others showed neural differentiation, some revealed mixed differentiation and some cases did not show any specific line of differentiation, the ‘null phenotype**.**

Gastrointestinal stromal tumors (GISTs) are rare, comprising

approximately 1% of all gastrointestinal (GI) cancers. The epidemiology of GISTs is still incompletely known, in part because GIST is a novel disease entity. These tumors were often classified as GI leiomyomas, leiomyosarcomas or leiomyoblastomas as recently as the year 2000, but are now considered a disease entity distinct from leiomyosarcoma due to important differences in clinical features, molecular pathogenesis, and responsiveness to cancer therapy.

This lack of clarity in distinguishing GIST can potentially affect clinical decision-making, because non-GIST tumors included in the differential diagnosis are sensitive to systemic chemotherapeutic treatment, whereas GIST is resistant. Indeed, surgical resection was historically the only therapy with demonstrated, albeit short-term, efficacy in true GIST. However, even complete surgical resection of primary GIST carried a substantial risk for recurrence, i.e., surgery alone rarely resulted in a cure**.**

GISTs also vary greatly in size, morphology, and malignancy potential, creating a continuum of neoplasms with uncertain malignancy potential ranging from virtually benign tumors to overtly malignant, aggressive cancers. The more indolent GISTs are typically small, sometimes incidentally found tumors that might not have surfaced during the lifetime of a patient, whereas other GISTs may present with overt metastases already at the time of the diagnosis.

Factors associated with decreased survival include 8 cm or more in size, 3 or more mitoses/HPF, positive margins or unresectability, and histopathologic grade II or higher. Surgical resection with negative margins remains the best therapy, but palliative resection is sometimes indicated to prolong survival.