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ORIGINAL ARTICLE

Gastrointestinal stromal tumor (GIST) in southern Taiwan: A clinicopathologic study of 93 resected cases

Chien-Feng Li[a], Shih-Sung Chuang[a], Chin-Li Lu[b], Ching-Nan Lin[a,*]

[a]*Departments of Pathology, Chi-Mei Medical Center, 901 Chunghwa Road, Yung Kang City, Tainan County 710, Taiwan*
[b]*Department of Medical Research, Chi-Mei Medical Center, Tainan, Taiwan*

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Abstract

The purpose of this study was to determine the clinicopathologic features of gastrointestinal stromal tumor (GIST) in southern Taiwan. The pathology files from a medical center in southern Taiwan (1993 to 2003) were searched for primary mesenchymal tumors of the gastrointestinal tract. Hematoxylin/eosin sections and history were reviewed, and immunohistochemistry was performed using anti-CD117, CD34, smooth muscle actin (SMA), and S-100 protein. Only primary resected GISTs were included in this study. Univariate and multivariate analyses were carried out using the *T*-test to evaluate the significance of primary tumor size and mitotic activity for the prediction of recurrence and metastasis. A total of 121 surgically resected primary mesenchymal tumors were identified, and 93 of these were GISTs. These 93 patients showed a slight female predominance (male: female = 1:1.2). The clinical presentations were variable and site-dependent. The most common tumor locations were the stomach (57%) and the small intestine (39%). Microscopically, 88 tumors (95%) were composed of spindle cells, the remaining five (5%) consisted of mixed epithelioid and spindle cells. No pure epithelioid type GIST was found. In addition to CD117, 66 cases (71%) were positive for CD34, 23 cases (25%) were positive for SMA, and 19 cases (21%) were positive for S-100. In a mean follow-up time of 27.3 months (median: 26 months), 19 cases (20.6%) were clinically malignant and mainly manifested as liver metastases (seven cases, 37% of malignant GISTs). Univariate analysis revealed that both primary tumor size and mitotic activity were significantly increased in the group affected by recurrence and/or metastasis ($p = 0.001$ and 0.035, respectively). Compared to GISTs in the western countries, those in southern Taiwan are characterized by a slight female predominance, a relatively higher frequency of small intestinal localization, a higher rate of S-100 protein expression, and a less aggressive behavior. Tumor size and mitotic activity were useful predictors of malignancy.

Keywords: GIST; CD117; Leiomyosarcoma

Introduction

Gastrointestinal stromal tumors (GISTs) are by far the most common mesenchymal tumors in the gastrointestinal tract except for the esophagus, where leiomyomas are more prevalent [15]. The majority of GISTs were diagnosed previously as smooth muscle tumors (leiomyoma, leiomyosarcoma, and leiomyoblastoma) or as tumors of nerve sheath origin (schwannoma and malignant peripheral nerve sheath tumor) [1,8]. With the advance of immunohistochemistry and molecular technology, the most widely accepted criteria for GISTs are

*Corresponding author. Tel.: +886 6 2812811ext.53680; fax: +886 6 2511235.
E-mail address: angelo.p@yahoo.com.tw (C.-N. Lin).

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Table 1. Panel of antibodies used for immunohistochemical technique

Antigen	Clone	Dilution	Source[a]
CD34	QBEND 10	1:50	Serotec
CD117	—	1:300	Dako
SMA[b]	1A4	1:50	Dako
S-100	—	1:3000	Dako

High-voltage microwave boiling in citrate buffer pH 6.0 for 12.5 min for all four antibodies as the antigen retrieval method.
[a]Antibody source: Dako, Dako Crop., Carpinteria, CA, USA; Serotec, Serotec Crop., Oxford, UK.
[b]SMA, smooth muscle actin.

CD117-expressing, Kit signaling-driven primary gastrointestinal mesenchymal tumors [5,17]. Owing to the similarity of phenotypic properties and ultra-structural features between tumor cells of GIST and the pacemaker cells of gut, the so-called interstitial cells of Cajal (ICC), GISTs are regarded as tumors of ICC origin [8,22,23].

The current concept is that no GIST is truly benign. A tumor may be classified as probably benign, may have an uncertain or low malignant potential, or is defined as "probably malignant" by histopathologic criteria [15]. Malignant GISTs often manifest as local recurrence, metastasis, or intra-abdominal dissemination within a follow-up period of 24 months [6]. Many clinical, microscopic, immunophenotypic, and genetic features have been used in attempts to predict the behavior of GISTs; however, precise prognostic criteria are currently not available [12,24].

There are only a few studies that investigated GISTs in Taiwan [10,14]. The purpose of this study is to further elucidate the clinicopathologic features of GISTs in southern Taiwan and to compare them with those in the western countries.

Materials and methods

Clinicopathologic features

The pathology files of the Chi-Mei Medical Center (1993–2003) were searched for GIST, leiomyoma, leiomyosarcoma, leiomyoblastoma, smooth muscle tumor, neurilemmoma, malignant peripheral nerve sheath tumor, spindle cell tumor, and mesenchymal tumor in the gastrointestinal tract. Our hospital is a medical center in southern Taiwan, with 720 beds between 1989 and 1994, 1033 beds in 1995, and 1335 beds after 1996. Only the patients who had undergone primary surgical resection in our institute were included in the study. Patients affected by recurrent or metastatic tumors after previous surgery performed at other institutes were excluded.

The specimens of all the cases were fixed in 10% formalin, processed using routine methods, and embedded in paraffin. Sections of 4-μm thickness were used for hematoxylin and eosin and immunohistochemical study. All the original hematoxylin- and eosin-stained sections were reviewed, and new sections were necessary when there was fading in the original sections. Special stains were performed using the labeled streptavidin-biotin peroxidase method (LSAB kit, Dako Corporation, Carpinteria, CA). The antibodies used (CD34, CD117, SMA, and S-100) and the retrieval methods are summarized in Table 1. The results of immunohistochemistry and histologic diagnoses were confirmed by three co-authors, all of them surgical pathologists. The cases with reactivity for CD117 and showing proper morphologic features were diagnosed as GISTs and represented the objects of research in this study. Other cases with morphologic features suggesting GISTs, but negative for CD117, were integrated in the study of *c-KIT/PDGFRA* mutations and were also included when there were *c-KIT/PDGFRA* mutations. Clinical data and follow-up information were reviewed, including gender, age, symptoms of initial presentations, tumor location, and methods of surgical intervention, follow-up duration, disease status, and interval from initial diagnosis to the development of recurrent and/or metastatic disease.

Statistical analysis

Tumor size and mitotic activity were analyzed for their relationship to the outcome. The endpoints analyzed constituted the recurrent/metastatic event. Univariate and multivariate analyses were performed using the *t*-test to evaluate the difference in primary tumor size and mitotic activity between the tumor-free group and that affected by recurrence/metastasis.

Results

A total of 121 cases with primary gastrointestinal mesenchymal tumors were identified by initial computer