Revision of Gastrointestinal Mesenchymal Tumors

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Background: *Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumor of the gastrointestinal (GI) tract. The advent of target therapy (imatinib mesylate) for GISTs increases the importance of pathologic diagnosis. The previous diagnosis with smooth muscle tumor (leiomyoma or leiomyosarcoma) and nerve sheath tumor (schwannoma) become GISTs after the study with CD117 immunohistochemistry accompanying conventional histologic study in many series.*

Objective: *To identify the incidence of GISTs in the patients who were previously diagnosed with smooth muscle or nerve sheath tumors. The histology and immunoreactivity of both newly found and previously diagnosed with GISTs are also studied.*

Material and Method: *A retrospective database identified all patients seen from 1998 to 2006. Patients with mesenchymal tumors of the GI tract and intraabdominal extragastrointestinal tract were selected, 53 cases in total. Clinical and pathological data, treatment, and outcome were analyzed.*

Results: *After revision, the total number of GISTs is 42 cases. There were 33 cases previously diagnosed with leiomyosarcoma that became the diagnosis with GISTs (31 cases or 93.9%), due to CD117 positivity. Most of GISTs cases had spindle cell type (26 cases, 61.9%) and only the colon and omentum had predominant mixed cell type.*

Conclusion: *GISTs are the most common mesenchymal neoplasm of the stomach and small intestine and are relatively less frequent at other gastrointestinal sites. An increasing awareness of their histologic, immunophenotypic, and molecular features coupled with an evolving understanding of their histogenesis is facilitating our ability to identify these tumors.*

Keywords: *Gastrointestinal stromal tumors (GISTs), c-kit, CD117, Leiomyoma, Leiomyosarcoma, Schwannoma, Tyrosine kinase inhibitor, Imatinib mesylate*

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Gastrointestinal stromal tumors (GISTs) were originally introduced as a neutral term for tumors that were neither leiomyomas nor schwannomas. The designation GIST is now used for a specific group of the majority of all gastrointestinal mesenchymal tumors. These tumors are composed of most gastric and intestinal mesenchymal tumors (leiomyoma, cellular leiomyoma, leiomyoblastoma, and leiomyosarcoma).

Most gastrointestinal mesenchymal neoplasms are GIST or smooth muscle tumors. Most tumors historically called leiomyosarcoma are now classified as GISTs.

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GIST has good response with tyrosine kinase inhibitor. Tuveson et al found that tyrosine kinase inhibitor (imatinib mesylate) could inhibit the mutated KIT receptor in intact GIST cells, and further implied that imatinib mesylate should inhibit the growth of this cell line. George D. Demetri concludes that tyrosine kinase inhibitor is encouraging, as dramatic reductions in tumor size have been achieved with minimal side effects. It is the important activity of this agent in this previously untreatable malignancy.

With WHO classification of tumors of the digestive system, 1999, suggests that typical GISTs are immunohistochemically positive for KIT tyrosine kinase receptor (stem cell factor receptor).

Because GISTs dramatically respond to tyrosine kinase inhibitor, the identification of GISTs is very important. The standard method is now conventional histologic study with H&E staining and immunohistochemically positive for KIT (CD117). The present study aims to identify the incidence of GISTs in Ramathibodi Hospital. This incidence will reflect how important the immunoperoxidase method is.

Historical considerations

Gastrointestinal stromal tumor (GIST) as described in the early literature consisted of a heterogeneous group of mesenchymal tumors, primarily involving the wall of the bowel. Perhaps the best known of these early studies is the excellent paper by Golden and Stout in 1941[1]. Based on the finding that some of the tumors that they described in their series contained "myofibrils", they believed, incorrectly as it turns out, that all of these tumors were bona fide smooth muscle tumors and they became known as leiomyoblastoma, leiomyoma, or leiomyosarcoma.

The idea that GISTs were smooth muscle tumors persisted until the advent of electron microscopy and immunohistochemistry, when several observations cast doubt on the belief that all of these tumors were smooth muscle tumors[2,3]. It was noted that GISTs showed only 'partial' smooth muscle differentiation or lacked smooth muscle differentiation altogether.

Some GISTs showed peculiar neuraxonal characteristics and became known as plexosarcomas or gastrointestinal autonomic nerve tumors (GANTs)[4,5]. When immunohistochemical studies became available, it turned out that up to 41% of GISTs failed to be immunoreactive with a variety of antibodies, while others showed smooth muscle or neural differentiation[6,7].

Based on the wide spectrum of histological, ultrastructural and immunohistochemical features, the non-committed term GIST was introduced, since it did not specify a precise line of differentiation and, therefore, was consistent with what was known at the time about the histological, ultrastructural and immunohistochemical features[2]. The lack of objective criteria encouraged the inclusion of virtually any mesenchymal lesion of the gastrointestinal tract under the rubric of GIST, including desmoid fibromatosis, schwannoma, and leiomyosarcoma, among others. This situation persisted until 1998, when a conceptual breakthrough in understanding GISTs changed this field forever[3,8].

The KIT revolution

C-KIT (KIT), also known as CD117, is a type III receptor tyrosine kinase (RTK) that is involved in the development and maintenance of erythrocytes, mast cells, melanocytes, germ cells and interstitial cells of Cajal (ICC)[9,10]. KIT is a transmembrane protein with an extracellular ligand-binding domain and an intracellular kinase domain.

The ligand for KIT is known as stem cell factor (SCF)[11,12]. Binding of SCF results in KIT dimerization D oligomerization and autophosphorylation D activation through phosphorylation of critical tyrosine residues. Subsequent to autophosphorylation D activation, KIT phosphorylates other signal transduction proteins, many that also have kinase activity, resulting in modulation of cellular behaviors including cellular proliferation, chemotaxis, and apoptosis[13,14]. Loss of function KIT mutations result in anemia, loss of mast cells, white coat 'spotting' due to failure of migration of dermal melanocytes, sterility due to a block in gametogenesis and gastrointestinal abnormalities due to loss of ICC[12,13,15].

ICC are unique "pacemaker" cells that are interposed between the autonomic nervous system and the muscular wall of the bowel and are responsible for coordinating peristalsis[3,16]. Based on the findings that loss of function KIT mutations result in loss of mast cells and gain of function KIT mutations are found in mast cell neoplasms, some authors postulated that gain of function KIT mutations might result in ICC neoplasms[8,14,17]. Since both ICC and GISTs are immunoreactive for KIT and CD34, they wondered if GISTs might be ICC neoplasms and harbor KIT mutations.

They determined the entire coding sequence of the KIT gene in six GISTs and found that five of the six lesions harbored KIT mutations. The mutations, whether they were missense mutations or deletions, were predicted to encode virtually full-length KIT. This suggested that KIT activity was preserved, which would be predicted if KIT was involved in the pathogenesis of GIST.

Furthermore, they showed that the GIST-type KIT mutations conferred ligand-independent KIT phosphorylation /activation in BaF3 lymphoid cells, and these cells were tumorigenic in nude mice. If there was any doubt about the important role that KIT played in the pathogenesis of GIST, this was put to rest by the finding that affected family members within a familial GIST kindred that developed GISTs in an autosomal dominant pattern of inheritance possessed

germline KIT mutations of the type found in sporadic GISTs[11,18,19]. After the initial findings by Hirota[8] et al in 1998, there has been a virtual explosion of data regarding GIST. What follows is the current understanding regarding GISTs.

Histogenesis:

The immunophenotypic (CD117 positive) and ultrastructural resemblance of GISTs to the interstitial cells of Cajal, gastrointestinal pacemaker cells which control gut motility, suggests a histogenesis from the latter cells[3]. Furthermore, one study has shown that an embryonic form of smooth muscle myosin in GIST is similar to that found in Cajal cells[20].

Cajal cells are known to originate from common intestinal mesenchymal precursor cells that also give rise to smooth muscle cells and it has been proposed that CD117 is required for differentiation into Cajal cells[16]. This would explain the morphological resemblance of GISTs to smooth muscle tumors and the occurrence of the GISTs outside the bowel wall, in the omentum and mesentery, where Cajal cells are not normally found[21].

Research question:

Are GISTs' incidence underestimated? How are the epidemiology, histology and immunohistochemical reactivity of GISTs?

Expected advantage:

The patient who is diagnosed with GISTs can receive those specific treatments that give them a better prognosis than the usual prior treatment.

Study design:

Retrospective descriptive study.

Place: Department of Pathology, Ramathibodi Hospital.

Timing: 17 February 1998 to 17 July 2006.

Sample:

Inclusion: - tumors of gastrointestinal tract and intraabdominal extragastrointestinal tract (esophagus, stomach, small bowel, large bowel, liver and vermiform appendix), retroperitoneum, omentum, and mesentery that were previously diagnosed with leiomyoma, leiomyosarcoma, leiomyoblastoma, cellular leiomyoma, epithelioid leiomyoma, schwannoma, malignant schwannoma, mesenchymoma, stromal tumor and malignant stromal tumor.

Exclusion: - tumors of non-gastrointestinal tract that were previously diagnosed with leiomyoma, leiomyosarcoma, leiomyoblastoma, cellular leiomyoma, epithelioid leiomyoma, schwannoma, malignant schwannoma, mesenchymoma, stromal tumor and malignant stromal tumor.

Material and Method

Clinical and pathologic data were taken from the database, and the information was augmented with a chart review and follow up history.

Patient data collected include age, sex, clinical presentation, and history of treatment. Treatment and outcome data collected included type of resection, adjuvant treatment, development of loco-regional recurrence or distance metastasis and status at last follow up. No analysis of the effect of adjuvant therapy was attempted.

Pathologic data included tumor size, resected margin, multiple sites of disease, presence or absence of necrosis, and mitotic count (number of mitosis per 50 HPF). The present study was independently reviewed by a single pathologist to confirm the diagnosis of GIST and to allow regarding of the tumor according to the most current pathologic standards.

Resection was considered to be complete when all grossly evident disease was resected at the initial operation and incomplete when there was residual loco-regional recurrence was defined as an intraabdominal relapse localized to a single site. Multiple or peritoneal implants (sarcomatosis) were classified as distant metastatic disease as were recurrence at other intra- or extra-abdominal sites (e.g., liver, lung, or bone).

Clinical and pathologic data were analyzed. Descriptive statistics were calculated using frequencies, means and medians as appropriate to the type of data.

Sectioned tissue in H&E glass slides are evaluated for specific histologic cell types including epithelioid, spindle cell, and mixed cell types. For immunohistochemical study, all representative formalin fixed and paraffin-embedded tumor tissue were cut to 2-3 micron thickness. All antigens used here included CD117 (c-kit), smooth muscle actin (SMA) and S-100 protein.

Result

Patient and tumor characteristics

The H&E glass-slides in Department of Pathology of Ramathibodi Hospital were reviewed from 17 February 1998 through 17 July 2006 (Fig. 1, 2). The total reviewed cases were 53 cases (Table 1). The range of age was between 25 and 79.There were males 20 (37.7%) in 53 cases. There were females 33 (62.2%) in 53 cases. The 53 cases of tumors came from the stomach 24 (45.2%) cases, small intestine 12 (22.6%) cases, colon 6 (11.3%) cases, mesentery 3 (5.6%) cases,

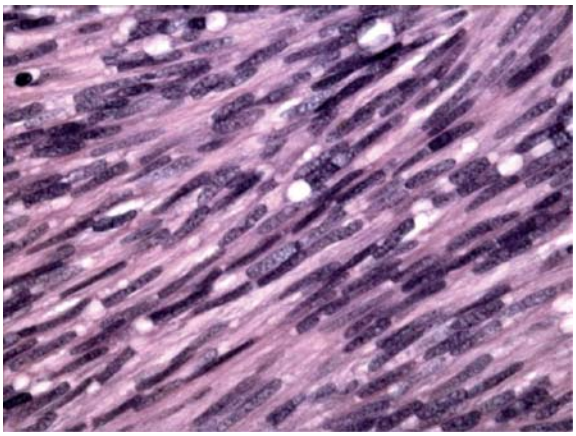

Fig. 1 The histology of spindle cell type of GIST

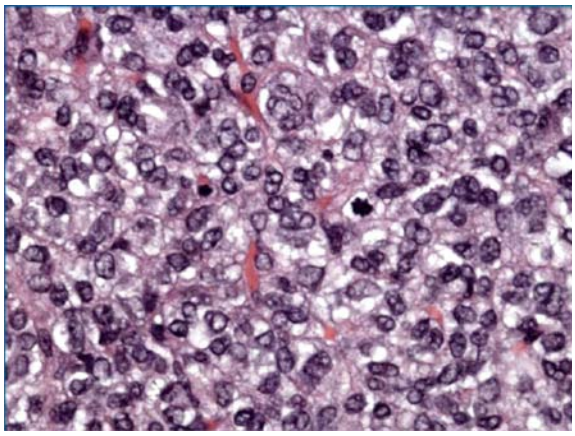

Fig. 2 The histology of epithelioid type of GIST

retroperitoneum 4 (7.5%) cases, omentum 3 (5.6%) cases, and liver 1 (1.8%) case.

The revision found 42 cases of GISTs with CD117 positivity. All of them had 26 cases (61.9%) of spindle cell type and 16 cases (38.1%) of mixed cell type. None of them had solely epithelioid type. Only GISTs in the colon and omentum had predominant mixed cell type (mixed cell type/spindle cell type = 4/2 and 2/1 respectively).

There were CD117 positive 42 cases (79.2%), SMA positive 24 cases (45.2%), and S-100 positive 18 cases (33.9%). Simultaneous positivity for CD117 and SMA was 18 (33.9%) cases, CD117 and S-100 is 8 (15.1%) cases, and CD117, SMA, and S-100 were 9 (16.9%) cases. The cases with CD117 negative had SMA positivity of 6(11.3%) cases, S-100 positivity of 1 (1.8%) case, and SMA and S-100 negativity of 4 (7.5%) cases.

There were previous diagnoses of leiomyosarcoma 33 cases, which became GIST diagnosis, due to positive of CD117, 23 cases (69.7%).

The youngest age of GIST diagnosed was 25 years old and the oldest was 79 years old. The mean age of GIST diagnosed was 55.7 years old. The GISTs (42 cases) were most often found in 46-55 [12cases (28.5%)] and 66-75 [12cases (28.5%)] years old.

Females were GIST in 28 out of 42 cases (66.6%) and males were 14 out of 42 cases (33.3%).

The stomach was the most primary site of GIST 18 out of 42 cases (42.8%), small intestine 10 (23.8%), colon 6 (14.3%), mesentery 2 (4.8%), retroperitoneum 2 (4.8%), omentum 3 (7.1%), and liver 1 (2.4%).

All patients in the present review had one or more signs or symptoms, most commonly abdominal pain (77%), abdominal mass (74%), GI bleeding (43%) and partial small bowel obstruction (30%). Other patients developed weight loss (14%) and urinary symptoms (9%).

Both mean and median tumor size were 7.7 cm (range, 0.5-20 cm).

Both mean and median mitosis which CD117 positive were 50/50HPFs (range, 3 to > 200).

The most consistent histopathologic features used to predict aggressiveness were tumor size and mitotic index. Fletcher categorized GISTs into very low, low, intermediate, and high-risk tumors based on an estimation of their potential for recurrence and metastasis (Fig. 3)[22].

Extent of disease classification

In 34 cases (80.9%) the tumor was confined to the site of origin; the authors classified this as localized disease. In four cases (9.5%) the tumor invaded into adjacent organs or peritoneum; the authors classified this as locally advanced disease. The most common sites of direct local extension were adjacent peritoneum or omentum, a noncontiguous segment of small bowel, bladder/ureter, colon, and abdominal wall. In two patients (4%), multiple primary lesions within small bowel (without distant metastases) were seen in four case of locally advanced disease. Four patients (9.5%) presented with distant metastatic disease. The patients with multiple peritoneal implants (sarcomatosis) were also included in this category. In these eight patients, the sites of distant metastases were as follows: liver only in three cases; omentum or peritoneum only in four cases; and liver plus omentum in one case.

Table 1. Patient and tumor characteristics

No.	Sex	Age	Location	Size (cm)	Previously diagnosis	Mitotic count	Cell type	CD 117	SMA	S-100
1	F	64	stomach	9	leiomyosarcoma	10	spindle	-	+	-
2	F	29	jejunum	8	leiomyosarcoma	15	spindle	+	+	+
3	F	68	stomach	9	leiomyosarcoma	>100	mixed	-	+	-
4	F	61	ileum	10	leiomyosarcoma	20	spindle	+	+	+
5	F	66	rectum	10	leiomyosarcoma	3	spindle	+	-	+
6	F	49	jejunum	6	leiomyosarcoma	>100	spindle	-	+	-
7	M	36	stomach	3	leiomyosarcoma	>50	spindle	-	-	-
8	M	53	stomach	6	leiomyosarcoma	20	spindle	+	+	-
9	F	47	stomach	6	leiomyosarcoma	<2	spindle	+	-	+
10	F	68	stomach	13	leiomyosarcoma	50	mixed	+	-	+
11	M	44	stomach	10.5	leiomyosarcoma	0-1	mixed	-	-	-
12	F	64	retroperitoneum	15	leiomyosarcoma	12	mixed	-	+	-
13	M	30	jejunum	15	leiomyosarcoma	8	mixed	+	+	+
14	F	50	stomach	15	leiomyosarcoma	>100	spindle	-	+	-
15	F	66	retroperitoneum	5	leiomyoma	25	spindle	+	-	-
16	F	42	retroperitoneum	7	leiomyosarcoma	<5	spindle	+	-	-
17	F	74	stomach	20	leiomyosarcoma	8	mixed	+	-	+
18	F	44	jejunum	11	leiomyosarcoma	>50	mixed	+	-	-
19	M	72	rectosigmoid	11	leiomyosarcoma	20	mixed	+	+	-
20	M	70	stomach	9	leiomyosarcoma	0-1	spindle	+	-	-
21	M	34	duodenum	15	leiomyosarcoma	>50	mixed	+	+	-
22	F	50	duodenum	6.5	leiomyosarcoma	3	spindle	+	-	+
23	F	56	stomach	4	leiomyosarcoma	0-1	spindle	+	-	-
24	F	55	stomach	4	leiomyosarcoma	0-1	mixed	+	-	-
25	F	39	stomach	12	leiomyosarcoma	7	spindle	+	-	-
26	M	39	mesentery	12	leiomyosarcoma	3	mixed	-	-	-
27	F	42	retroperitoneum	6	leiomyosarcoma	150	spindle	-	-	-
28	M	36	stomach	6	GIST	5	spindle	+	+	+
29	F	25	cecum	8	GIST	100	mixed	+	+	+
30	M	70	stomach	2	leiomyosarcoma	>200	mixed	+	+	-
31	M	72	jejunum	17	leiomyosarcoma	50	spindle	+	+	-
32	M	55	mesentery	1.5	leiomyosarcoma	20	spindle	+	+	-
33	F	51	omentum	3.5	leiomyosarcoma	100	mixed	+	+	+
34	F	46	omentum	7	GIST	10	spindle	+	-	+
35	F	78	stomach	3	GIST	50	mixed	-	-	+
36	F	75	stomach	5	GIST	50	mixed	+	-	-
37	F	77	stomach	5	leiomyosarcoma	>100	spindle	+	+	+
38	M	64	ileum	10	leiomyosarcoma	50	mixed	-	+	-
39	F	44	liver	3	GIST	20	spindle	+	+	-
40	F	45	mesentery	4	GIST	20	spindle	+	-	-
41	F	64	stomach	13	GIST	25	spindle	+	+	-
42	M	56	stomach	6	GIST	100	spindle	+	+	+
43	M	55	stomach	8	GIST	50	spindle	+	-	-
44	F	56	rectum	9	GIST	1-2	spindle	+	-	+
45	F	67	jejunum	5.5	GIST	2	spindle	+	-	+
46	M	53	stomach	4.5	GIST	6	mixed	+	-	-
47	F	67	stomach	0.5	GIST	2	spindle	+	-	-
48	F	68	stomach	5	GIST	15	spindle	+	-	-
49	M	79	omentum	4	GIST	40	mixed	+	-	-
50	F	53	ileum	12	GIST	3	spindle	+	+	-
51	F	63	jejunum	13	GIST	6	mixed	+	-	-
52	M	55	rectum	14	GIST	15	mixed	+	+	+
53	F	55	colon	3	GIST	>100	mixed	+	-	-

Total 53 cases; range age 25-79; M:F = 20:33
Abbreviations: M: male; F: female; size: maximum diameter in cm; MC: mitotic count (mitoses/50 HPFs); histomorphology, histomorphological subtype according to Fletcher et al[22]

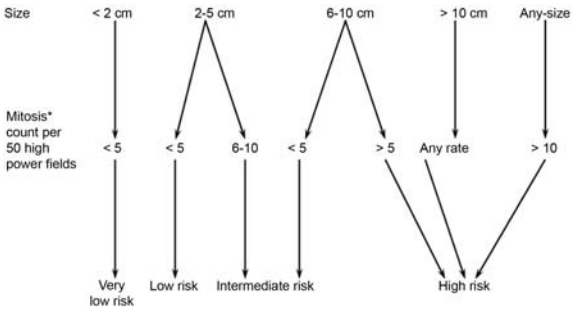

Fig. 3 Algorithm based on the consensus approach for assessing the risk of malignancy of GIST reached at a National Institutes of Health workshop held in April 2001

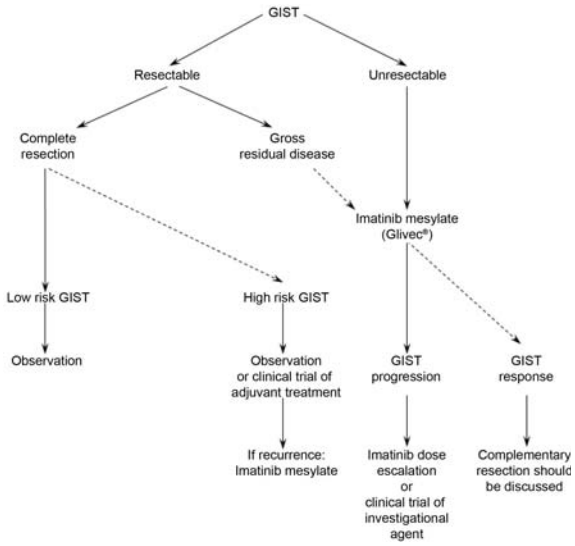

Fig. 4 Treatment algorithm for patient with primary presentation of GIST[23]

Surgical management

All patients underwent surgical resection. Complete gross resection was achieved in 70% of cases, with 30% of patients having gross residual local or distant metastatic disease. Of the 34 patients who underwent complete resection, microscopic margins were recorded as negative in 22 patients (52.3%) and positive in nine patients (21.4%); they were not recorded in the other four patients (9.5%). However, most of the margins examined were axial on the small bowel or resected adjacent organs, and very few comments were made regarding the circumferential margin. All 11 patients presenting with localized primary tumors had complete resection, as did 19 of 24 patients with locally advanced disease.

Discussion

GISTs are infrequently encountered mesenchymal tumors of the GI tract. The authors identified 42 cases of malignant GIST from the retrospective database. The immunohistochemical study especially CD117 is very important for identification of GISTs. Tae recent study reveals new cases of GISTs that were previously diagnosed with leiomyosarcoma (31 out of 33 cases or 93.9%). The present data is much different from other data such as Tzen[24] (35%) and de Schipper[25] (47.2%).

The histologic findings corresponded with other data[9,26,27] in the point of mostly spindle cell type. However, mixed cell type (concomitant epithelioid cells and spindle cells) was predominant in the colon and omentum. The author's data is relevant to Miettinen[28] for omental tumors but colonic tumors have mainly spindle cell type by Miettinen[28].

The analysis of GISTs at all sites in the GI tract suggested that the clinical behavior of the small intestinal GISTs differ from that of gastric or colorectal GISTs, the benign behavior is frequently in the stomach but the malignant behavior is frequently in the colon. This is a controversial topic, however, and some other authors have concluded that the behavior of GISTs is similar regardless of site[29]. On the other hand, there is considerable evidence in the literature that anatomic site does have prognostic implications, with small bowel GIST having a worse prognosis than gastric. A study published by Emory et al. in 1999 examined 1004 cases of GIST. Anatomic site was a highly significant independent predictor of survival in a multivariable analysis; patients with small intestinal tumors had poorer survival than those with gastric tumors. However, both benign and malignant tumors were included in their series, and the precise number of benign lesions at each site is not clear[30].

The authors have reviewed current knowledge of gastrointestinal stromal tumor (GIST) management. Surgical resection is the treatment of choice for these tumours. GIST studies have shown that after surgical resection these tumors span a wide clinical spectrum from benign to malignant tumors. Newly developed prognostic scales make it possible to distinguish low malignant (benign or low risk) from high malignant (malignant or high risk) potential GIST. While low malignant potential GIST have an excellent prognosis

after resection, high malignant potential GIST involve a high rate of recurrence with poor survival after surgical treatment alone. Imatinib mesylate is a powerful agent against metastatic or recurrent GIST. Imatinib mesylate is one of the first examples of a drug that targets an intracellular signaling molecule in clinical cancer therapy for stromal tumors.

However, experience of follow-up with imatinib mesylate therapy is short, and some questions remain. In the light of the results in CML, there is reason to believe that imatinib may be even more effective when given earlier in the management of GIST, for example as adjuvant therapy for high malignant potential GIST. This approach is under investigation.

Conclusion

GISTs, defined as a specific tumor type with distinctive immunohistochemical and genetic features, differ from true leiomyomas and schwannomas and constitute the large majority of all gastrointestinal mesenchymal tumors. C-kit expression has emerged as an important defining feature for these tumors, and their pathogenesis involves c-kit mutations at least in a subset of cases. Other genetic changes are under intensive study.

GISTs are the most common mesenchymal neoplasms of the stomach and small intestine and are relatively less frequent at other gastrointestinal sites. A lack of awareness of their broad morphological spectrum can complicate diagnosis. Nevertheless, an increasing awareness of their histologic, immunophenotypic, ultrastructural, and molecular features coupled with an evolving understanding of their histogenesis is facilitating our ability to identify these tumors.

Consequently, it should now become increasingly possible (and important) to study selected tumor populations (or subgroups), retrospectively and prospectively, in an attempt to highlight the parameters influencing their biological behavior.

Treatment of GISTs and targeted therapy using Imatinib

When possible, complete surgical excision is the treatment of choice for localized GISTs. The role of radiotherapy is limited by the potential toxicity to surrounding structures, especially the intestines[31]. There has been a 40-69% partial response of inoperable and metastatic GISTs to targeted therapy using imatinib (Glivec, Novartis)[32]. This is indeed remarkable for a tumor that was previously regarded as being generally resistant to conventional chemotherapy.

Imatinib mesylate (Glivec) is a synthetic tyrosine kinase inhibitor, which now has an established role in the management of interferon resistant chronic myeloid leukemia (CML). CML is characterized by a translocation between chromosomes 9 and 22, which produces a chimaeric protein (BCR-ABL) with tyrosine kinase activity. Imatinib acts by occupying the kinase pocket of the BCRABL oncoprotein, preventing phosphorylation of its substrate[23].

Imatinib is also effective against a number of other tyrosine kinases including c-kit and platelet derived growth factor (PDGF). It was initially shown to have striking antitumor effect in a single Finnish patient with metastatic GIST, 18 a finding confirmed by larger trials in America and in Europe[27]. It is now considered the drug of choice for metastatic and inoperable GIST. The use of Imatinib is a classic example of a drug targeted to a specific molecular defect of a tumor and marks a new era of rational and targeted molecular inhibition of cancer. Hopefully, the development of such drugs will increase in the near future. The use of such drugs will necessitate more specific diagnosis of mesenchymal tumors, using conventional histology, immunohistochemistry, cytogenetic, and molecular biology.

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การทบทวนคำวินิจฉัยเนื้องอกของเนื้อเยื่อเกี่ยวพันในระบบทางเดินอาหาร

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***ภูมิหลัง**: Gastrointestinal stromal tumors (GISTs) เป็นเนื้องอกที่เกิดจากเนื้อเยื่อเกี่ยวพันที่พบได้บ่อยที่สุดของระบบทางเดินอาหาร การวินิจฉัยในทางพยาธิวิทยามีความสำคัญมากเพราะปัจจุบันมีการรักษาที่มีความจำเพาะต่อ GISTs ที่เรียกว่า target therapy (imatinib mesylate) ในปัจจุบันการศึกษาทางฮิสโตโลยีร่วมกับเทคนิคทางอิมมูโนฮิสโตเคมิสทรีโดยเฉพาะ CD117 ทำให้สามารถวินิจฉัย GISTs จากที่แต่เดิมเคยวินิจฉัยว่าเป็นเนื้องอกของกล้ามเนื้อ (leiomyoma หรือ leiomyosarcoma) หรือ เนื้องอกของ nerve sheath (schwannoma)*

***วัตถุประสงค์**: เพื่อหาอุบัติการณ์ของ GISTs ในผู้ป่วยที่เคยวินิจฉัยว่าเป็นเนื้องอกของกล้ามเนื้อหรือ nerve sheath รวมทั้งศึกษาทางฮิสโตโลยีและอิมมูโนฮิสโตเคมิสทรีด้วย*

***วัสดุและวิธีการ**: ศึกษาข้อมูลย้อนหลังในผู้ป่วยทุกรายระหว่างปี พ.ศ. 2541 ถึง พ.ศ. 2549 โดยคัดเลือกผู้ป่วยที่เป็นเนื้องอกที่เกิดจากเนื้อเยื่อเกี่ยวพันในทางเดินอาหารและนอกทางเดินอาหารที่อยู่ในช่องท้องได้จำนวนทั้งสิ้น 53 ราย โดยวิเคราะห์ข้อมูลทางคลินิกและพยาธิวิทยา*

***ผลการศึกษา**: หลังทบทวนคำวินิจฉัยในทางพยาธิวิทยาพบผู้ป่วย GISTs จำนวน 42 ราย ซึ่งในจำนวนนี้พบผู้ป่วยที่เคยวินิจฉัยว่าเป็นเนื้องอกของกล้ามเนื้อ 33 รายที่ภายหลังศึกษาทางอิมมูโนฮิสโตเคมิสทรีด้วย CD117 แล้วพบว่าเป็น GISTs ถึง 31 ราย (93.9%) โดยพบลักษณะทางฮิสโตโลยีส่วนใหญ่เป็นชนิด spindle cell (26 ราย, 61.9%) และมีเพียงตำแหน่งที่ลำไส้ใหญ่และ omentum เท่านั้นที่พบชนิด mixed cell มากกว่า*

***สรุป**: GISTs เป็นเนื้องอกของเนื้อเยื่อเกี่ยวพันที่พบได้บ่อยที่สุดของกระเพาะและลำไส้เล็กซึ่งในบริเวณอื่นของระบบทางเดินอาหารจะพบได้น้อยกว่า การให้ความสำคัญต่อลักษณะทางฮิสโตโลยี อิมมูโนฮิสโตเคมิสทรี และชีววิทยาโมเลกุลร่วมกับความเข้าใจในพยาธิกำเนิดจะสามารถทำให้วินิจฉัย GISTs ได้ดีขึ้น*