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ARTICLE

Analysis of clinicopathological characteristics of gastrointestinal stromal tumors

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Abstract: Objective: To assess clinicopathological characteristics of gastrointestinal stromal tumor (GIST) and the relationship between tumor necrosis factors and patient prognosis. Methods: Data of 60 patients with gastric cancer (GC) admitted from September 2018 to April 2019 at the Hunan Provincial People's Hospital were collected. Clinicopathological characteristics were analyzed to assess the correlation between tumor necrosis factor and clinicopathological characteristics, immunohistochemical expression, and prognosis. Results: A difference was noted between tumor necrosis and tumor size, nucleosis imaging, NIH risk grade, and desmin in GC patients ($P < 0.05$), and between tumor necrosis and sex, age, site, and levels and immunohistochemical index of DOG-1, CD117, CD34, and SMA ($P > 0.05$). Conclusion: There is a correlation between tumor necrosis and tumor size, nuclear division image, NIH risk grade, and desmin, and patients with GC have tumor necrosis and patient prognosis.
Key words: gastrointestinal stromal tumor; clinicopathological characteristics; tumor necrosis.

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***Abbreviations*:** GIST, gastrointestinal stromal tumor; GC, gastric cancer.

***Authors' Contributions*:** Ling-Ling Zhang proposed the idea of the paper and wrote the manuscript.

***Competing interests*:** The authors declare that they have no actual or potential conflicts of interest to declare.

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Introduction

gastrointestinal stromal tumor (GIST) is one of the most common middle lobe derived tumors, including spindle cell subtype, epithelioid cell subtype and mixed type [1]. Immunophenotypic expression and clinicopathological features of gastrointestinal tumors have been studied in detail in many articles. In recent years, the correlation between clinicopathology and prognosis and survival is not clear [2-5]. Therefore, based on the study of the clinicopathological characteristics of patients with gastrointestinal tumors, this paper further studies the relationship between tumor necrosis and prognosis, so as to provide basis for guiding clinical diagnosis and treatment.

Methods

Collection of general information

A total of 60 patients with confirmed gastrointestinal stromal tumor (GIST) were admitted to the Hunan Provincial People's Hospital from September 2018 to April 2019. Among the patients, 44 had gastric origin GIST and 16 had non-gastric origin GIST. The diagnosis of all selected patients were confirmed based on pathological H&E morphology and either immunohistochemical staining or genetic testing. In this study, 44 patients with gastric cancer (GC) were selected as the primary study subjects, including 24 males (54.55%) and 20 females (45.45%). All selected patients underwent surgical or puncture biopsies, among which two were preoperative pathology, 12 were intraoperative rapid pathology, and 30 were general pathology. Patients provided written informed consent.

H&E morphology of disease test tissue

Tissues were sent for pathological examination, where specimens were fixed with 4% neutral formalin solution. Then, the specimens were routinely dehydrated, embedded with paraffin, sectioned into 4-μm-thick and H&E-stained sections, and visualized using light microscopy. The samples were examined by immunohistochemical staining for immune markers such as CD117, DOG-1, CD34, and SMA.

Follow-up and statistical analysis

All patients in this study were enrolled by telephone or outpatient visits, and the last follow-up was conducted in May 2021. Overall survival was determined from the date of diagnosis to the date of the final follow-up or death. Statistical analysis was performed using SPSS19.0 software, and P values < 0.05 were considered statistically significant.

Results

Tumor morphology based on H&E staining

Pathological examination found that GIST cells mostly presented as spindle cells (Figure 1) that were arranged in a bundle with a woven or fence structure. Furthermore, they had medium cell density, rich cytoplasm, weak eosinophilia, unclear cell boundaries, visible paracucleolar vacuoles, and nuclear polymorphism. A few cells presented as epithelioids (Figure 1), with clear cell boundaries, and others presented as mixed cell types.

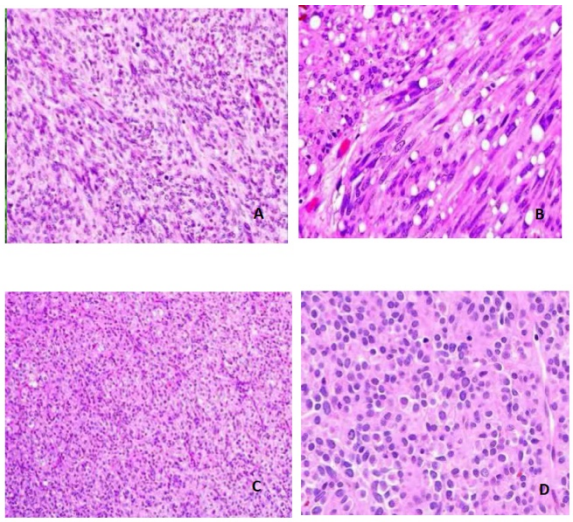

Figure 1. Disease detection based on tissue morphology using H&E (A-B shows ×10 and ×20 for spindle cell subforms, respectively, and C-D show epithelioid cell subforms at ×10 and ×20, respectively).

Correlation analysis of tumor necrosis and clinicopathological characteristics in patients with GIST

Clinicopathological features of patients with GISTs

There were a total of 60 patients with primary GISTs. Among them, the origin of GIST was as follows: 44, stomach (73.33%); eight, small intestine (13.33%); two, colon (3.33%); three, esophagus (5%); two (3.33%); and one, mesentery (1.67%). Among the patients, 44 had gastric-derived GIST, which was our primary focus. There were 24 males and 20 females, with a ratio of six : five. The oldest patient was aged 80 years, while the youngest was aged 30 years, leading to a median age of 56 years. The tumor had minimum and maximum diameters of 0.5 cm and 36 cm, respectively, with the average diameter being seven cm. Tumor locations were observed, and 30 tumors were located under the plasma membrane, 11 in the submucosa, and three in the gastric wall muscle layer. Tumor monogenesis occurred in 41 elderly patients and three more cases of the elderly have occurred. Nuclear division images were at least 2/50 HPFs, of which the highest nuclear division images was 20/50 HPFs. Among the patients, 24 presented

with tumor necrosis (54.5%) and 20 presented without tumor necrosis (45.5%). The extremely low, low, medium, and high risk groups included 6, 12, 16, and 10 patients, respectively. Based on immunohistochemical staining, 36 patients (81.8%) were positive for DOG-1, 39 (88.6%) were positive for CD117, 32 (72.7%) were positive for CD34, 21 (47.7%) were positive for SMA, and 9 (20.5%) were positive for desmin.

Correlation of tumor necrosis and clinicopathological characteristics (Table 1)

Fourteen male and 10 female patients presented with tumor necrosis, and 10 male and 10 female patients did not have tumor necrosis. Eighteen and six patients aged over 60 years presented with and without tumor necrosis, respectively. There were 12 and eight patients with and without tumor necrosis, respectively, among people aged under 60 years. In the lower plasma membrane group, there were six and 24 patients with and without tumor necrosis, respectively. In the submucosa group, there were four and seven cases with and without tumor necrosis, respectively. In the gastric wall group, there were two and one patient with

Table 1. Correlation between tumor necrosis and clinicopathological factors of patients with gastrointestinal stromal tumors

Clinicopathological factors	Necrosis (+)	Necrosis (-)	χ^2	*P*
Sex				
Male	14	10	0.447	0.081
Female	10	10		
Age(years)				
≧ 60	18	6	2.655	0.119
< 60	12	8		
Site				
Under the plasma membrane	6	24	6.385	0.602
Submucosal membranes	4	7		
Inside the stomach wall	2	1		
Number of tumors				
Single hair	16	25	11.209	0.305
Multiple	2	1		
Tumor size				
≦ 1 cm	3	2	2.338	< 0.001
≦ 2 cm	5	3		
2.1 cm ~ 5 cm	8	2		
5.1 cm ~ 10 cm	9	4		
> 10 cm	6	2		
Nuclear division image (individual /50 HPF)				
< 5	7	5	18.296	< 0.001
6 ~ 10	10	8		
> 10	8	6		
Risk grading				
Very low	3	3	22.741	< 0.001
Low level	5	7		
Medium size	8	8		
High-level	7	3		

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and without tumor necrosis, respectively. The single-of tumors with and without tumor necrosis were 16 and 25, respectively, Tumor tumors were two and one, respectively. Among patients with tumor size ≤ one cm, there were three and two patients with and without tumor necrosis, respectively, tumor size ≤ two cm, five and three patients, respectively; tumor sizes of 2.1–5 cm, eight and two patients, respectively; tumor sizes of 5.1–10 cm, nine and four patients, respectively; and tumor size > 10 cm, six and two patients, respectively. The 5/50 HPFs < cases in patients with tumor necrosis and without tumor necrosis were seven and five patients, respectively; nucleodivision images 6–10/50 HPFs were ten and eight, respectively; 10/50 HPF > 10 were eight and six, respectively.

A chi-square test for tumor necrosis was used to analyze the difference between tumor size, nuclear division image, and NIH risk grade ($P < 0.05$). No difference between tumor necrosis and sex, age, site, or number was established statistically ($P > 0.05$).

Correlation between tumor necrosis and immunohistochemical indicators in GC patients

The negative CD117 cases in groups with and without tumor necrosis were three and two, respectively. The positives cases were 21 and 18 cases, respectively. Four cases were negative for DOG-1 those with and without tumor necrosis, respectively, The positives were 20 and 16 cases, respectively. CD34 negative individuals were seven and five in those with tumor necrosis and without tumor necrosis and the positive cases were 17 and 15 cases, respectively. SMA negative individuals in groups with and without tumor necrosis were 11 and 12, respectively. Positive cases were 13 and 8 cases, respectively. The negative CD117 in groups with and without tumor necrosis were three and two and the positive cases were 21 and 18 cases, respectively. Individuals negative for Desmin with and without tumor necrosis were 18 and 17, and positives were found in six and three cases, respectively.

A chi-square test was used to analyze the difference between tumor necrosis and positivity for CD117 ($P = 0.186$), DOG-1 ($P = 0.214$), CD34 ($P = 5.339$), SMA ($P = 3.318$) ($P > 0.05$), and desmin ($P < 0.001$) ($P > 0.05$) (Table 2).

Survival prognosis

As of May 2021, 44 postoperative follow-up appointments was 0 – 10 – 10,40 patients, 90.9%,10,5 years, 75%, seven and three, and 65.3% and 88.4%, respectively, which were statistically significant ($\chi^2 = 10.359$, $P < 0.01$) (Figure 2).

Dicussion

GISTs are one of the most common meso-derived tumors and are potentially derived from Cajal cells from the primitive gut or (interstitial cells of Cajal, ICCs) of the plexus [1]. It is reported to be a non-neural but closely related stromal cell in the intestinal wall. ICCs are pacemaker cells with gastrointestinal motility that produce rhythmic slow-wave electrical activity, conduct neural signals, regulate the transmission of neurotransmitter, and are

Table 2 Correlation between tumor necrosis and immunohistochemical index in patients with gastric cancer

Immunohistochemical index	Necrosis (+)	Necrosis (-)	χ^2	*P*
CD117				
Positive	21	18	0.745	0.186
Negative	3	2		
DOG-1				
Positive	20	16	0.952	0.214
Negative	4	4		
CD34				
Positive	17	15	5.339	0.974
Negative	7	5		
SMA				
Positive	13	8	3.318	0.772
Negative	11	12		
Desmin				
Positive	6	3	12.564	< 0.001
Negative	18	17		

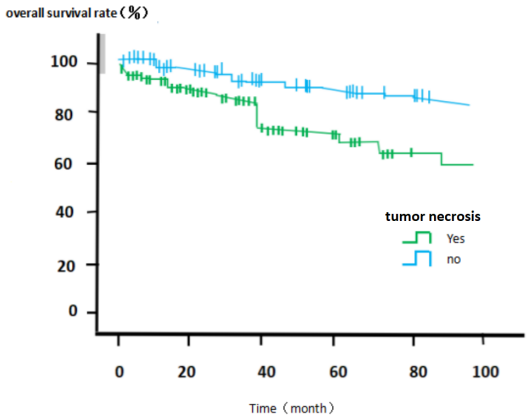

Figure 2. Survival prognosis

associated with multiple gastrointestinal motility diseases. They can be present in any part of the intestinal tract from the esophagus to the rectum; however, they are most commonly present in the stomach (over half) and second most commonly in the small intestine (about a quarter) or in the retroperitoneum, mesentery, mesenterum, etc. (collectively referred to as GIST outside the gastrointestinal tract). Patients are reported primarily around the age of 60 years [2]. The age of onset in most cases is around 56 years, which is largely consistent with our data. DOG-1 expression was detected in 61 gastrointestinal MISTs based on immunohistochemistry, and the relationship between DOG-1 and various GIST clinicopathological features was analyzed according to CD117 [3]. DOG-1 can serve as a potential reference indicator for GIST diagnosis and as a prognostic factor [4]. ICCs were prevalent in leiomyomas of the esophagus, stomach, and small intestine and could not be misdiagnosed as GIST because tumor cells express CD117 and DOG-1. However, the immunohistochemical indicators of CD117 and DOG-1 were expressed at 88.6% and 81.8%, respectively. Stone et al. [5] analyzed the expression of Ki-67 proliferation index in 139 patients with GIST, and the relationship with disease progression in patients with GIST suggested that the Ki-67 proliferation index, tumorigenesis site, and tumor size were factors affecting disease progression. Cheng et al. [6] studied clinicopathological features of 280 patients with GIST and discovered that their age, nucleosis count, and metastatic recurrence rate were risk factors for death. Another study analyzed clinicopathological data of 300 patients with GIST and found that factors related to the prognosis of patients included positive or unclear margins, tumor tissue rupture, postoperative metastatic recurrence, and active nucleosis [7]. Yu et al. [8]retrospectively analyzed 653 patients and summarized clinical characteristics and found that GISTs were mainly over 40 years old, clinical symptoms can be atypical, and the prognosis can be assessed by nuclear division image, maximum tumor maximum diameter, radical surgery and improved NIH risk grade.

Shi et al. [9] The analysis of c-kit, platelet-derived growth factor receptor A (P D GF R A) in 288 patients found a high c-kit and PDGFRA gene mutation rate and diverse mutation type loci in GIST, which was closely related to clinicopathology and prognosis in GIST patients, and could provide a reference for the whole management of GIST.

Van et al. [10]retrospectively analyzed the clinical data of 287 GIST patients treated with surgery, and the tumor size, nuclear division image, risk grade, and postoperative targeted drug treatment of GIST were independent risk factors affecting postoperative recurrence, metastasis and prognosis.

The early diagnosis rate of gastrointestinal mesostima is low, with a unique tumor cell immune phenotype and histopathology. Positive CD117, CD34 expression is an important basis for the diagnosis of disease. Clinical tumor malignancy can be further judged by tumor size, nuclear division image and tumor cell density [11].

In this study, overall survival and tumor necrosis in patients with GIST were compared. Therefore, tumor tissue necrosis appears to partly determine the prognosis of patients with GIST. The disadvantage of this study was that the statistical results were biased because of the small sample size.

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