P.O.Box 2345, Beijing 100023,China
Fax: +86-10-85381893
E-mail: wcjd@public.bta.net.cn www.wjgnet.com

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• GASTRIC CANCER •

Mast cell density and the context of clinicopathological parameters and expression of p185, estrogen receptor, and proliferating cell nuclear antigen in gastric carcinoma

Ying-An Jiang, You-Yuan Zhang, He-Sheng Luo, Shou-Fu Xing

Ying-An Jiang, He-Sheng Luo, Department of Gastroenterology, Renming Hospital of Wuhan University, Wuhan 430060, Hubei Province, China
You-Yuan Zhang, Department of Pathology, Central Hospital of Huangshi City, Huangshi 435000, Hubei Province, China
Shou-Fu Xing, Department of Pathology, Medical College of Wuhan University, Wuhan 430071, Hubei Province,China
Correspondence to: Ying-An Jiang, Central Hospital of Huangshi City, 43 Wuhan Road, Huangshi 435000, Hubei Province, China. hszxyy@public.hs.hb.cn
Telephone: +86-714-6283783 **Fax:** +86-714-6233931
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Abstract

AIM: To investigate the relationship between the mast cell density (MCD) and the context of clinicopathological parameters and expression of p185, estrogen receptor (ER), and proliferating cell nuclear antigen (PCNA) in gastric carcinoma.

METHODS: Mast cell, p185, ER, and PCNA were detected using immunohistochemical S-P labeling method. Mast cell was counted in tissue of gastric carcinoma and regional lymph nodes respectively, and involved lymph nodes (ILN) were examined as usual.

RESULTS: MCD was significantly related to both age and depth of penetration (χ^2=4.688,P<0.05 for age and χ^2=9.350, P<0.01 for depth of penetration) between MCD>21/0.03 mm^2 and MCD≤21/0.03 mm^2 in 100 patients; MCD in 1-6 ILN group patients was significantly higher than that in 7-15 ILN or >15 ILN group patients (u=6.881, 8.055, P<0.01); There were significant differences intergroup in positive expression rate of p185, ER and PCNA between MCD >21/ 0.03 mm^2 and MCD≤21/0.03 mm^2 in 100 patients.

CONCLUSION: Mast cell may have effect on inhibiting invasive growth of tumor, especially in the aged patients; The number of mast cells, in certain degree, may predicate the number of involved lymph nodes, which is valuable for assessment of prognosis; MCD was related to the expression of p185, ER, and PCNA in gastric carcinoma. It suggests that mast cell accumulation may inhibit the proliferation and the dissemination of the gastric carcinoma.

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INTRODUCTION

Recently, many studies have reported on the association of mast cell with various tumors[1-9]. In several malignancies, mast cell has been found to correlate with growth, penetration and prognosis of tumor[10-13]. Therefore, our study was undertaken to investigate the relationship between the mast cell density (MCD) and the context of clinicopathological parameters and expression of p185, estrogen receptor (ER), and proliferating cell nuclear antigen (PCNA) in gastric carcinoma.

MATERIALS AND METHODS

Materials

The specimens of gastric carcinoma, histologically confirmed, were surgically obtained from 421 patients. The patients had undergone curative tumor resection at our hospital between 1984 and 1998. And only 100 patients were chosen at random in our study. Among 100 patients, 41 patients had lymph node metastases. All resected tissue specimens were fixed in formalin, embedded in paraffin, and cut into 3-4 μm serial sections. 459 lymph nodes were collected from 41 patients (range, 8-26 per patient).

Methods

Mast cell, p185, ER, and PCNA were detected using immunohistochemical method (agents from Maixin-Bio Corp. Fuzhou, China).The count of mast cells in the tissue of gastric carcinoma was as described by Takanami *et al*[10]. A grid (0.15 mm by 0.2 mm) which was defined an area of 0.03 mm^2 per field was used for to count mast cells. Similarly, that of mast cells in regional lymph nodes was described by Bowers *et al*[14].A grid which defined an area of mm^2 per field was used. ILN was examined using routine pathological method. The results were expressed as the means ±SD. Statistical analyses were performed using the Chi-square and u test. A P value less than or equal to 0.05 was considered significant.

RESULTS

Table 1 showed the clincopathologic parameters for two groups (high MCD group, MCD was more than 21/0.03 mm^2, and low MCD group, MCD was equal to 21/0.03 mm^2 or less). There were no significant differences between two groups regarding both degree of differentiation and largest dimension of tumor. However, MCD was significantly related to both age and depth of penetration (P<0.05 for age and P<0.01 for depth of penetration) (Figure 1).

Table 2 showed correlation between MCD and cancerous metastases in regional lymph nodes. MCD in 1-6 ILN group patients (n=21) was 12±3.11, 7-15 ILN (n=14), 6±2.06, >15 ILN (n=6), 5±1.33, respectively. MCD in 1-6 ILN group patients was significantly higher than that in 7-15 ILN or >15 ILN group patients (P<0.01), but, MCD in 7-15 ILN group patients was not significantly higher than that in >15 ILN group patients (P>0.05) (Figure 2).

Table 1 Correlation between MCD and Clinicopathologic finding of gastric carcinoma (n=100)

Variable	MCD>21/0.03 mm²	MCD≤21/0.03 mm²	*P* Value
Age (yrs)			
<60	16	25	<0.05
≥60	36	23	
Degree of differentiation			
Well	18	14	>0.05
Moderately	23	21	
Poorly	11	13	
Largest dimension of tumor (in mm)			
≤30	30	36	>0.05
>30	22	12	
Depth of penetration			
Involved serosa	21	34	<0.01
Not involved serosa	31	14	

Table 2 Correlation between MCD and cancerous metastases in regional lymph nodes (n=41)

Variable	*n*	MCD ($\bar{x}\pm s$, /mm²)
1-6 ILN	21	12±3.11
7-15 ILN	14	6±2.06
> 15 ILN	6	5±1.33

ILN: involved lymph nodes

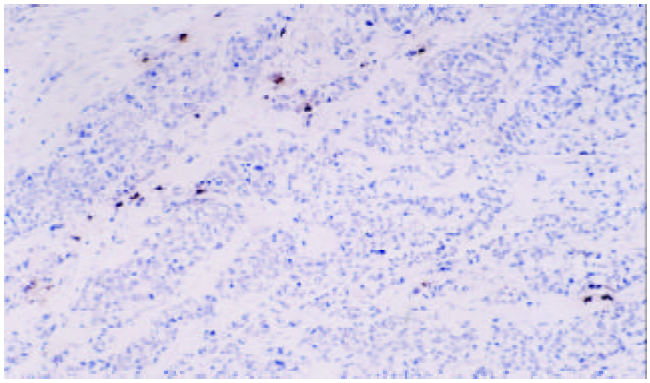

Figure 1 Mast cells of gastric carcinoma (Tryptase labeling, DAB staining, original magnification, ×100)

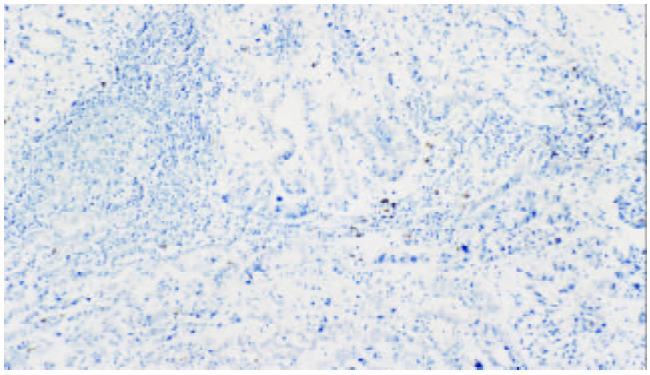

Figure 2 Mast cells of regional lymph nodes of gastric carcinoma (Tryptase labeling, original magnification, ×100)

There were significant differences intergroup in positive expression rate of p185, ER and PCNA between high MCD group (the MCD was more than 21/0.03 mm²) and low MCD group (the MCD was equal to 21/0.03 mm² or less) (P<0.01). As was shown in Table 3 (Figure 3,4,5).

Table 3 Correlation between MCD and the positive expression rate of p185, ER, and PCNA in the gastric carcinoma tissues

MCD	*n*	Positive expression rate (%)		
		p185	ER	PCNA
>21/0.03 mm²	52	22(42.31)	11(21.15)	12(23.08)
≤21/0.03 mm²	48	31(59.62)	28(53.84)	27(51.92)
P Value		<0.01	<0.001	<0.01

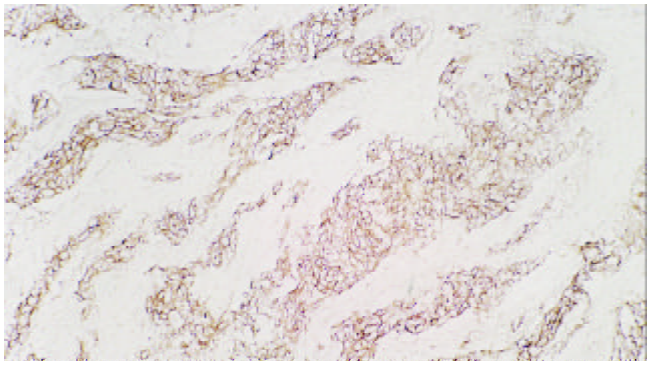

Figure 3 p185 of gastric carcinoma (Original magnification,×100)

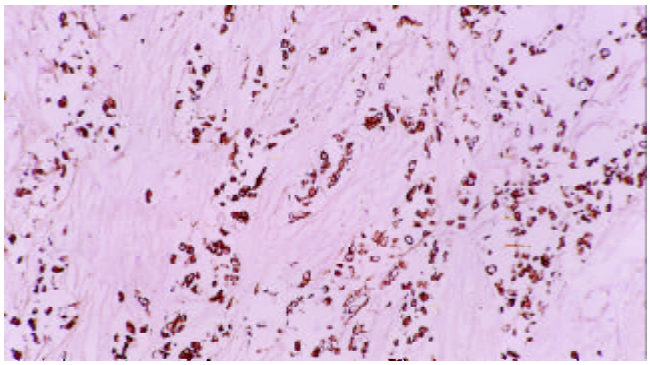

Figure 4 Estrogen receptor of gastric carcinoma (Original magnification, ×100)

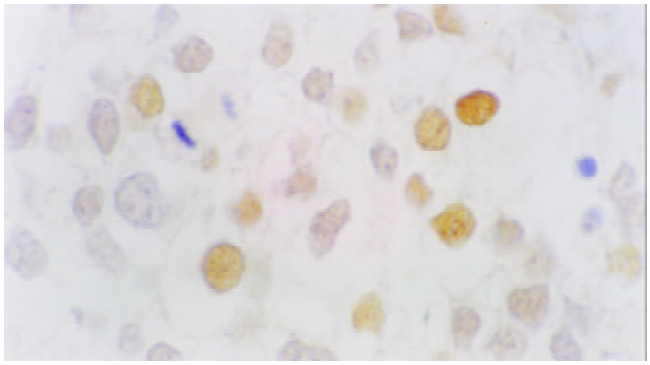

Figure 5 PCNA of gastric carcinoma (Original magnification,×400)

DISCUSSION

Numerous studies have shown that mast cell plays an important role in tumor growth. Dabbou *et al*[15,16] found that mast cells were accumulated around the periphery of the invasive and metastatic rat mammary adenocarcinoma, and they believed that interactions between mast cell and tumor cell were important for the growth and invasive properties of the tumor. Nakamura *et al*[17] found the mechanism of mast cell accumulation at sites of tumors was that tumor cells could produce a factor which might not be the already known mast cell growth factors. Wang *et al*[18] found that the anti-tumor effect of mast cell might be related to releasing of tumor necrosis factor (TNF) and non-TNF cytotoxicity. Our results revealed there were no significant differences intergroup regarding both degree of differentiation and largest dimension of tumor between MCD >21/0.03 mm^2 and MCD$\leqslant$21/0.03 mm^2. MCD was significantly related to both age and depth of penetration (P<0.05 for age and P<0.01 for depth of penetration).

The data indicate the lymph node status is associated with the patients' prognoses in many malignancies, and may be useful in assessing the outcome of this disease[19-28]. The treatment regimen was depended on not only whether involved lymph node was present or not, but also the number of involved lymph node[20,29]. Maurel *et al*[30] had examined 7.7±0.2 lymph nodes per specimen in 851 patients with resected colorectal carcinoma, the results strongly pointed out that at least eight lymph nodes must be examined and they called the number of eight as a "golden number". At least eight lymph nodes per specimen were examined in our study as done by Maurel *et al*[30]. Roder *et al*[20] followed up 477 patients with gastric carcinoma of lymph node metastasis, and they found that 5-year survival rates were as follows (1) 1-6 involved lymph nodes: 45.5 %; (2) 7-15 involved lymph nodes:29.7 %; (3) >15 involved lymph nodes: 10.4 %. There was a highly significant difference in survival (P<0.0001). Our results indicated that MCD in 1-6 ILN group patients was 12±3.11, 7-15 ILN, 6±2.06, >15 ILN, 5±1.33, respectively. MCD in 1-6 ILN group patients was significantly higher than that in 7-15 ILN or >15 ILN group patients (P<0.01), but, MCD in 7-15 ILN group patients was not significantly higher than that in >15 ILN group patients (P>0.05). In other words, the higher MCD was in regional lymph nodes, the lower number of ILN of gastric cancerous metastases was. It demonstrates that the number of mast cells, in certain degree, may predicate the number of involved lymph nodes of gastric cancerous metastases. Therefore, MCD is a valuable parameter for assessing the prognosis of patients with gastric carcinoma.

The C-erbB-2 was first identified in ethylnitosourea-induced rat neuroblastoma. It encodes a 185 kilodalton (kDa) glycoprotein. It was reported recently that overexpression and gene amplification of C-erb B-2 were frequently observed in the intestinal type gastric adenocarcinoma, and it was a prognostic indicator in tumor[31-33]. ER is commonly known to be present in the cell of the breast and endometrium, but have also been identified in diverse normal and neoplastic nonreproductive tissues. The expression of ER has been considered to be a favorable prognostic factor in breast carcinoma and endometrial carcinoma but a poor prognostic factor in gastric carcinoma[34]. PCNA is an auxiliary protein of DNA polymerase delta which plays a major role in synthesizing DNA and is expressed in the nuclei, particularly in the late phase of G_1 and S. Therefore PCNA is a useful marker for proliferative activity[35-37]. Our results showed there were significant differences intergroup in the positive expression rate of p185, ER and PCNA between MCD>21/0.03 mm^2 and MCD $\leqslant$21/0.03 mm^2. It suggests that mast cell accumulation may inhibit the proliferation and the dissemination of gastric carcinoma. This finding may provide a molecular foundation of the further study on relation between mast cell and gastric carcinoma.

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