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Evaluation of preoperative elevation of serum c-reactive protein as an indicator for prognosis of colorectal cancer

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Abstract

Background: Cancer has not been elucidated in colerectal site. C-reactive protein (CRP) is a product synthesized in hepatocytes and has been reported to be up-regulated by such proinflammatory cytokines as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF). The significance of a preoperative serum elevation was evaluated using CRP as a predictive indicator for the malignant potential and prognosis.

Methods: Forty consecutive patient with colorectal cancer whose local lesions were resected in our department, plus forty healthy volunteers, were selected. Any patient with inflammatory diseases such as infection or collagen disease was excluded from the current study. The preoperative serum CRP level and the control group were measured. The relationships between the serum elevation of CRP and both the clinicopathologic factors and prognosis of the patients was investigated.

Results: The rate of patients with elevated serum CRP level was significantly higher in the colorectal cancer patients in comparison to the control group (55% versus 2.5%). Furthermores the incidence of liver metastasis, peritoneal carcinomatosis, histopathologic lymph nodes metastasis, and tumor invasion in colorectal cancer patients with a preoperatively elevated serum CRP level were significantly more frequent than in those with a negative serum CRP level. The survival rates of the colorectal cancer patients without a preoperative elevation of the serum CRP proved to be significantly more favorable than that of the colorectal cancer patients with such an elevation (94.4% versus 59.1% ; $P<0.001$).

Conclusion: A preoperative serum elevation of CRP was thus found to be an indicator of the malignant potential of the tumor as well as prognostic factor for patients with colorectal cancer.

Keywords: C-reactive protein,colorectal cancer.

Introduction

The colorectal cancer is the second most prevalent cancer and the third leading cause of cancer deaths world-wide [5,21] and is often diagnosed at a late stage [5].

Accurate prediction of prognosis is important in the management of colorectal cancer as it may assist in determining the type, timing, and appropriateness of therapy. Inflammatory status are a relatively new prognostic factor that appear to be worth investigating in colorectal cancer patients [5,22].

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The acute phase reaction occures in response to damage to the body tissues due to inflammation, trauma, and malignant disease [47, 13, 5, 22, 35]. It is characterized by the alteration in production and secretion of more than 30 different plasma proteins19,29,38. These proteins are termed the acute phase proteins19,29,38. The functions of these different proteins are variable, such as modulation of the immune response and mediation of the inflammatory response [38,43,53]. C-reactive protein (CRP) is an acute phase protein and a sensitive marker of inflammation19,29,38,43,53. It is synthesized in the hepatocytes and up-regulated by cytokines such as interleukin-1, interleukin-6 and tumor necrosis factor-a (TNF-a) [38,6,15,5,19, 29]. Preoperative CRP levels have been found to be prognostic test for various cancer [5,12,13,22, 29]. In this study we want to assess the value of CRP level in colorectal cancer patients in comparison to healthy persons, and the value of increased CRP level in prognosis of colorectal cancer patients due to clinicopathological finding, were assessed.

Methods

In this investigation 80 cases were studied. Forty consecutive patients (21 men, 19 women; age range 21-80 years) who underwent resection for colorectal cancer in our department (four university medical centers) from January 1998 to January 2001 were selected and compared with forty volunteer healthy person (20 men, 20 women; age range 20-80 years). Patients with inflammatory disease, including infections and collagen diseases, as well as primary cancers in other organs were excluded from the study.

All the patients were followed up until 5 years or death.The study was performed through an analytical method. The serum CRP value was measured by latex agglutination test. Five milliliters of blood samples were withdrawn from all the patients preoperatively and also from the control group by peripheral venupuncture and after centrifuging blood samples, the serums were mixed with a drop of latex agglutination test. After completion of the test, presence or absence of percipitation, grossly and microscopically. The chi-squared test, Fisher's exact test, and t-student test were used to compare the clinicopathological data of the patients and control group, with or without elevation of serum CRP levels. A P.value of less than 0.05 was regarded as significant.

Results

The rate of patients with elevated serum CRP level was significantly higher in colorectal cancer patients in comparison to control group (55% versus 2.5%). In colorectal cancer patients, the primary lesions were located in the cecum and ascending colon 6(15%), the transverse colon 1(2.5%), the descending colon 4(10%), the sigmoid colon 5(12.5%), and the rectum 25(60%). In 5(12.5%) patients, liver metastases were detected preoperatively by both abdominal computed tomography and ultrasonography. The preoperative elevation of the serum CRP value in colorectal cancer group was recognized in 22(55%) patients (group A), whereas this elevation was recognized in 18(45%) patients (group B). The clinicopathological factors are shown in the Table 1. No significant differences was observed regarding age or gender between groups A and B. The maximal size of the tumor in group A (5.8±2.1 cm) was significantly larger than those in group B (4.1±1.5 cm; $P<0.01$). The incidence of peritoneal dissemination in group A (22.7%; 5 of 22) was significantly higher than those in group B (5.5%; 1 of 18; $P<0.05$), and the incidence of liver metastases in group A (18.2%; 4 of 22) was also significantly more frequent than that in group B (5.5%; 1 of 18; $P<0.05$). Moreover, a significant difference was seen between the proportion of histopathologically detected lymph node metastases in group A and B (54.5%; 12 of 22, versus 16.7%; 3 of 18; $P<0.05$).

Clinicopathologic Backgrounds (Serum elevation of CRP)			
Clinicopathologic factors	Positive n=22	Negative n=18	P Value
Male/female	14/8	11/7	NS
Age, years (Range)	51.5 (21-80)	51.7 (29-71	NS
Location of tumors			
Cecum and ascending colon	2	3	<0.01
Transverse colon	-	1	
Descending colon	3	1	
Sigmoid colon	1	4	
Rectum	16	9	
Maximal size of tumor (cm)	5.8±2.1	4.1±1.5	<0.01
Differentiation			
Well	12	13	<0.05
Moderately	3	1	
Poorly	7	4	
Liver metastases			
Positive	4	1	<0.01
Negative	18	17	
Lymph nodes metastases			
Positive	12	3	<0.01
Negative	10	15	
Peritoneal carcinomatosa			
Positive	5	1	<0.01
Negative	17	17	
Stage (dukes classification)			
A	1	5	<0.05
B	5	4	
C	9	7	
D	7	2	

Table 1.The clinicopathological factors and elevated serum CRP level.

The ratio of stage D cases by Dukes' classification, for which the surgical treatment was an absolute noncurative resection for either liver metastase or peritoneal dissemination, was significantly higher in group A than in group B (31.8% versus 11.1%).

The 5 year survival rate in group A were 59.1%; and significantly more unfavorable than those in group B which were 94.4% (P<0.01). Also poorly differentiated tumors were higher in group A than in group B (31.8% versus 22.2%).

Discussion

In patients with chronic malignant disease, changes in protein metabolism will result in muscle wasting, oedema, cachexia, or the production of acute-phase proteins, such as CRP [19,44,51]. The acute phase synthesis of CRP is upregulated by such proinflammatory cytokines as interleukin-1, interleukin-6, and tumor necrosis factor [29,46], which act as autocrine growth factors for neoplasms [29,45, 47]. It has also been reported that following tumor recurrence and progression, a proportion of patients will develop an acute-phase protein response [29,54]. Moreover, the serum CRP can be measured more easily and promptly compared with other oncogenic markers. Thus the hypothesis that the serum concentration of CRP may be an indicator of the malignant potential of the colorectal cancers is proved to be valid.

In 3 case-control studies reported that serum

CRP level in patients with colorectal cancer was higher than those in controls [11,17,25,34].

Shumin [11] reported that there were no significant positive associations between CRP levels and stage of colorectal cancer. Some previous studies have noted independently the apparent association between CRP and poor prognosis [29,19,39,44]. Our results indicate that increased CRP in cancer patients is significantly higher than the control groups, and generally associated with the larger tumor size, lymph node or liver metastases, peritoneal carcinomatosis, and advanced Dukes' stage. Also the CRP expression correlated inversely with overall survival. These results suggested that the serum CRP level could thus be an indicator of the malignant potential and a marker of metastases in colorectal cancer.

The prognosis of patients without a preoperative elevation of serum CRP level proved to be significantly better than that of patients with such an elevation. These results indicated that the serum CRP level may be used as a prognostic factor in colorectal cancer, and therefore can also provide valuable information when determining the treatment strategies for such patients.

In order to elucidate relationship between the serum CRP and alterations in the oncogens concerned with metastases in colorectal cancer, further investigations are thus required.

In conclusion, an elevation in the serum CRP level is considered to be an indicator of the malignant potential in the tumor as well as an appropriate prognostic factor for patients with colorectal cancer.

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