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CLINICAL STUDY

Serum bFGF Concentrations in gastric cancer patients

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Abstract: *Background:* Angiogenetic factors play an important role in the formation of new blood vessels involved in the growth and metastatic spread of solid tumors, but there is limited information regarding the clinical significance of serum bFGF levels in gastric cancer patients.
Patients and methods: Serum bFGF concentrations were measured by quantitative sandwich enzyme immunoassay technique in 30 controls and in 30 gastric cancer patients before surgery. The association between preoperative serum bFGF levels and clinical pathological features were evaluated.
Results: Preoperative serum bFGF levels in patients with gastric cancer were significantly higher than those in control patients (p=0.027). On the other hand; there is no relationship between serum bFGF levels and clinical-pathologic parameters in gastric cancer patients.
Conclusion: Circulating bFGF might not be a marker suitable for assessing tumor progression *(Tab. 1, Ref. 7).*
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Key words: gastric cancer, basic fibroblast growth factor, angiogenesis.

Abbreviations: bFGF – basic fibroblast growth factor.

Advances in diagnosis and treatment have offered excellent long-term survival for early gastric cancer patients; however, the prognosis of advanced disease remains poor (1). Cancer morbidity results in large part from metastases, and majority of patients with advanced cancer die due to complications of metastases, not the primary tumor. The metastatic process consists of tumor cell detachment, local invasion, motility, angiogenesis, vessel invasion, survival in the circulation, adhesion to endothelial cells, extravasations, and regrowth in different organs (1). In each step, causative molecules that have been identified can be regarded prognostic factors.

The human bFGF gene family consists of at least 23 different genes encoding related polypeptides. The bFGFs are mitogenic for many cell types, both epithelial and mesenchymal. Some bFGFs, like bFGF2, have potent angiogenic activity and have been implicated as promoters of tumor angiogenesis. bFGFs have also been shown to increase the motility and invasiveness of a variety of cell types (2, 3).

There is little known about the clinical significance of serum bFGF levels in gastric cancer patients (4).

In this study, we measured bFGF levels in the serum of patients with gastric cancer and evaluated the clinical significance they might have.

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Materials and methods

This study is a retrospective case-control study.

We examined 30 patients aged between 34–83 years with gastric cancer treated in the Ankara Numune Hospital 5th Surgery Clinic, between December 2003 and April 2004. There were 20 men and 10 women. Patients who had received chemotherapy, radiotherapy or blood transfusion were excluded. Thirty patients without malignant pathology operated for benign pathologies, in age range from 18–69 were studied as the control group (Tab. 1).

Signed informed consent was obtained from all patients. The regional research board approved the project.

Patients enrolled in the study were diagnosed with gastric cancer by endoscopic biopsy and all patients underwent operation for curative or palliative reasons. The information about the patients was recorded into a standard study form. This form includes the presence of distant metastases (detected by preoperative radiological investigations), liver function tests, tumor markers (CEA, AFP, Ca19-9), metastases and local invasion found in peroperative exploration, histological type(Lauren classification), differentiation (differentiated, undifferentiated) of the tumor and tumor staging (based on TNM of the International Union Against Cancer) (Tab. 1).

In the preoperative period, 5cc. venous blood was obtained from all patients in the study and the control group and the samples were kept at -20 degree of Celsius after centrifugation. Total serum bFGF levels were measured by quantitative sandwich enzyme immunoassay technique, using an ELISA kit for bFGF (ACCUCYTE; CytImmune Sciences, Inc., College Park, MD).

All data were analyzed using ,SPSS for Windows 11.0 program. Data were tested for normality and were found to be not normally distributed. Accordingly, all data are presented as median value with nonparametric analyses being employed to as-

Tab. 1. Demographic distrubition of patients included in the study.

	Gastric cancer patients n=30	Control patients n=30
Sex (male/female)	10/20	11/19
Age (median)	64.5	56.5
Histological type		
Differentiated	4	
Undifferntiated	26	
Lymph node metastases		
Negative	7	
Positive	23	
Peritoneal metastases		
Negative	5	
Positive	25	
Liver metastases		
Negative	24	
Positive	6	
Stage Ia	1	
Ib	2	
II	2	
IIIa	7	
IIIb	7	
IV	11	
Lauren		
Intestinal	13	
Diffuse	17	

sess differences. Kruskal–Wallis analysis of variance (ANOVA), the Mann–Whitney U test, and the Wilcoxon rank test were used to evaluate differences between multiple groups, unpaired and paired observations, respectively. ANOVA (F) test was used for those with more than two groups. Correlations were evaluated using the Spearman rank test. In these tests, p values lower than 0.05 were considered significant.

Results

Serum bFGF levels were detectable in all control patients. Their median serum bFGF level was 0.4 (0.4–65.2) ng/ml. Correlation was found between serum bFGF levels and age(r=-0.556; p=0.001) in control patients.

Preoperative serum bFGF levels (45.3[40–542.1]ng/mL) in patients with gastric cancer were significantly higher than those in control patients (p=0.027). There was no significant difference between males and females regarding serum bFGF levels (p=0.948), nor there was any correlation between serum bFGF levels and age (r=0.189; p=0.318). Subgroup analyses were performed for bFGF levels based on site, stage and grade but the differences were not significant.

Conclusion

Growth of solid tumors depends upon the occurrence of neovascularization. So far, many angiogenic peptides have been identified and their locoregional expression, effects on tumor vascularity, relations with tumor aggressiveness, and clinical significance as a poor prognosticator, have been suggested (3).

Both VEGF and bFGF were detected in the circulation of patients with solid tumors. If those angiogenic peptides can be measured in the circulation and their values are quantitatively related with progression of tumor, they will serve as a useful tool for planning a stage-specific treatment (3, 5).

Levels of circulating VEGF and bFGF correlate with tumor progression or survival in a variety of cancers including breast, lung, colorectal, prostate, soft tissue sarcomas. Moreover; bFGF levels were inversely correlated with recurrence-free survival in patients with breast, lung and ovarian carcinomas. It is possible that tumors which utilize bFGF-driven angiogenesis are less aggressive and thus less likely to recur. Alternatively, tumors that secrete low levels of bFGF may utilize alternative angiogenic pathways that make them more aggressive (6).

On the other hand, there is little known about the clinical significance of serum bFGF levels in gastric cancer patients (3, 4). Yoshikawa et al. demonstrated that plasma bFGF was not associated with either clinical pathologic factors or survival (4). On the contrary; Hao et al demonstrated that higher expression of bFGF in carcinoma tissues than in the control gastric mucosa correlated with the pathological parameters of the tumor. Positive correlation was observed between high expression of bFGF and short survival in this study. Also, the positive correlation was found between bFGF expression and MVD (7).

Our present study revealed higher serum levels of bFGF in carcinoma patients than in control patients; but there was no correlation between serum bFGF levels and clinical-pathologic parameters of gastric cancer patients.

In conclusion, circulating bFGF might not be a marker suitable for assessing gastric cancer progression.

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