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Stage-related Correlations between Immunoglobulins and Complement Components in Preoperative Sera from Patients with Gastric Carcinoma*

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Abstract—*Immunoglobulins A, G and M and complement components C3, C4 and C1-INH were quantitated in sera taken preoperatively from 168 patients with gastric carcinoma. The values were grouped according to stages (pTNM). The concentrations of C4 and C1-INH increased with advancing stage of disease and were above normal mean values in all stages. The concentration of IgG was below the normal mean value among all the patients and with the lowest concentration in stage III. Concentrations of IgA and C3 were above normal means but without significant relation to stages. There was a positive correlation between the concentrations of IgG and C1-INH in sera from patients with stage IV carcinoma, while the same correlation was negative in stages I–III. Although the results varied among the patients within each stage, the profiles of immunoglobulin and complement concentrations are of value in the preoperative staging of the disease.*

INTRODUCTION

IN RECENT years several reports have dealt with the concentrations of immunoglobulins in sera from patients with various malignancies. Preoperatively, both increased [1–4], normal [5] and decreased [6] concentrations of immunoglobulins have been described. These discrepancies can be due to differences in the selection of patients, staging of the disease and collection of sera.

Alsabti [7] found a positive correlation between the extent of metastatic breast cancer and increased concentration of serum IgA, and Moertel *et al.* [1] found a negative correlation between both IgG and IgA and the time of survival in patients with unresectable gastrointestinal carcinoma.

The results of complement investigations are, however, more consistent. Complement activity (CH_{50}) and concentrations of components (mostly C3, C4 and C1-INH) are elevated in many tumour-bearing hosts [8–11], and particularly in patients with advanced disease [12–14]. Special interest has been focused on the C1-inactivator (C1-INH) since the serum concentration seems to parallel disease activity [15–18].

We have conducted a longitudinal study of patients with gastric carcinoma to obtain an immunological profile of these patients. In this report we present the preoperative serum concentrations of immunoglobulins and complement components related to the stages of the carcinoma.

MATERIALS AND METHODS

Patients with newly detected gastric carcinoma admitted to the Department of Surgery during the years 1977–1981 were studied. Patients with additional tumours or other diseases were excluded. In total 168 patients fulfilled the criteria and entered the study. They were divided into stages I–IV (see Table 1) according to the TNM post-surgical histopathological classification [19]. The patients were between 27 and 86 yr old. Mean age was 66.1 ± 11.8 yr and median age was 67.0 yr,

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and 41.1% of the patients were women. The age and sex distribution is shown in Table 1.

The immunoglobulins G, A and M and the complement components C3, C4 and Cl-INH were quantitated in sera prior to surgery. Single radial immunodiffusion using commercial plates purchased from Behringwerke AG, Marburg-Lahn, F.R.G. were employed.

The mean values were compared by Students' t test. In grouped samples the regression coefficient (b) was tested against zero. The correlation of pairs of variables in ungrouped samples was tested by the coefficient of correlation (r). Statistical methods and formulas were taken from the 'Documenta Geigy' [20].

RESULTS

The serum concentrations (mean ± 1 S.D.) of immunoglobulins and complement components are presented in Table 1. The concentrations of C4 and Cl-INH in each stage were significantly higher than the mean concentration among healthy individuals. In the entire series the concentrations of IgA and C3 were also significantly above the mean of healthy individuals, whereas the concentration of IgG was significantly below this mean. The concentration of IgM was not different from that of healthy individuals.

The concentrations of C4 and Cl-INH increased with advancing stage of disease, the increase through the stages being highly significant ($P < 0.001$ for both C4 and Cl-INH). The stage-related increase in C3 was not significant ($0.1 > P > 0.05$).

The concentration of IgG in stage III was significantly lower than that in stages I–II ($0.05 > P > 0.025$) and in stage IV ($P > 0.001$).

There were only slight differences in the mean concentrations of IgG, C4 and Cl-INH between the sexes in the whole material. Furthermore, there were no systematic differences in these parameters between the sexes in each of the four stages. The mean age variation between the stages was slight. There was no consistent correlation within or between the various immunoglobulin classes and complement components (Table 2).

There was a highly significant negative correlation between the concentrations of IgG and Cl-INH in stages I–III (Fig.1). In stage IV the same correlation was positive ($r = 0.2323, P < 0.05$).

DISCUSSION

Patients with advanced gastric carcinoma had the highest serum concentrations of the complement components C3, C4 and Cl-INH, particularly the last two. These results are in accordance with the results reported previously by others from studying patients with various malignancies (see Introduction).

The increased concentrations of complement in patients with malignant diseases are supposed to reflect an increased production rate because of the inflammatory process in and around the tumour mass [12–14, 21, 22].

The increasing concentrations of C4 and Cl-INH were probably not due to dehydration or the nutritional state of the patients because there was no consistent correlation between various immunoglobulins and the complement components. Furthermore, the change in immunoglobulin and complement profile cannot depend on age or sex, as there were no significant differences between the patients in the various stages.

The concentration of IgG also had a significant relation to stages, but different from that of the complement components. Notably, the lowest mean concentration of IgG was found in stage III.

Our results further extend previous observations on immunoglobulins and complement components in sera from patients with malignant diseases, as we found significant correlations between the concentrations of IgG and Cl-INH.

Table 1. Preoperative concentrations (g/l, as mean ± 1 S.D.) of immunoglobulins and complement components in sera from patients with different stages of gastric carcinoma; the number of patients, mean age and women/men ratio in each stage are given

Stage	No.	Mean age (yr)	Women/men	IgG	IgA	IgM	C3	C4	Cl-INH
I	11	65.2	0.22	10.00 ± 3.96	2.35 ± 1.34	1.17 ± 0.41	0.896 ± 0.158	0.396 ± 0.113	0.324 ± 0.050
II	36	69.7	0.57	10.60 ± 2.45	2.34 ± 0.89	1.41 ± 1.59	0.927 ± 0.204	0.368 ± 0.102	0.355 ± 0.076
III	37	63.5	1.06	8.99 ± 3.42	2.14 ± 1.18	1.22 ± 0.65	0.947 ± 0.265	0.442 ± 0.159	0.398 ± 0.069
IV	84	65.9	0.71	11.35 ± 3.54	2.42 ± 1.16	1.30 ± 0.80	0.991 ± 0.243	0.459 ± 0.126	0.404 ± 0.080
Healthy individuals	100	62.3	1.0	12.50 ± 2.75	1.90 ± 0.70	1.40 ± 0.55	0.91 ± 0.16	0.28 ± 0.07	0.27 ± 0.07

Table 2. Coefficients of correlation between preoperative concentrations of immunoglobulins and complement components in sera from patients with different stages of gastric carcinoma

	IgG	IgA	IgM	C3	C4
Stage I ($n = 11$)					
IgA	0.733*				
IgM	0.421	0.503			
C3	-0.065	0.180	0.037		
C4	-0.084	0.197	0.037	0.786**	
C1-INH	-0.608*	-0.523	-0.720*	0.182	0.283
Stage II ($n = 36$)					
IgA	0.167				
IgM	0.291	0.378*			
C3	-0.082	0.215	-0.033		
C4	0.014	0.278	0.021	0.396*	
C1-INH	-0.495**	0.147	0.187	0.344*	0.248
Stage III ($n = 37$)					
IgA	0.028				
IgM	0.016	-0.120			
C3	-0.068	-0.077	0.194		
C4	0.033	0.124	0.028	0.389*	
C1-INH	-0.576***	-0.213	0.195	0.313	0.257
Stage IV ($n = 84$)					
IgA	0.308**				
IgM	0.292**	0.205			
C3	0.097	0.126	0.090		
C4	0.091	-0.044	-0.114	0.242*	
C1-INH	0.232*	0.023	-0.010	0.357**	0.217

*$0.05 > P > 0.01$; **$0.01 > P > 0.001$; ***$P < 0.001$.
†$n = 79$ for C1-INH in stage IV.

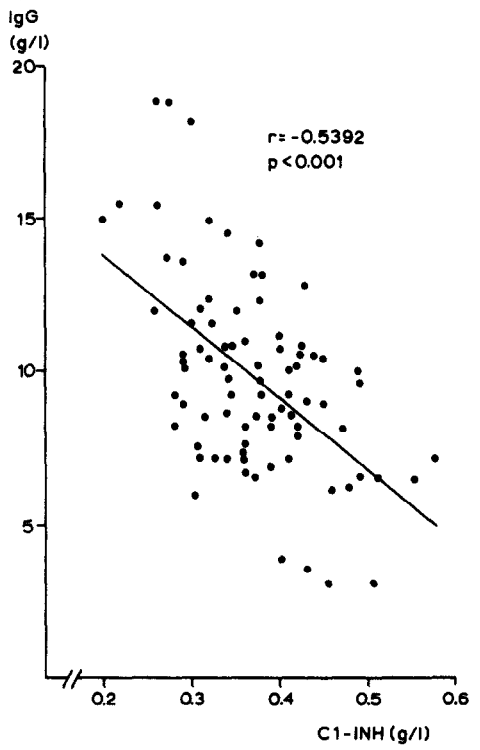

Fig. 1. Relation between concentrations of IgG and C1-INH in preoperative sera from 84 patients with gastric carcinoma, stages I–III (r = coefficient of correlation).

The correlation was negative in stages I–III and positive in stage IV.

It is tempting to explain the negative correlation between IgG and C1-INH in stages I–III as a result of absorption of IgG to tumour tissue. Most tumour tissues have previously been shown to be rich in IgG [23, 24], which may be a consequence of the high content of Fcγ-receptor in tumour [25].

That IgG is bound in gastric carcinoma is probable, and is supported by the results reported by MacSween and Eastwood [26]. They measured the amount of IgG in the eluates of tumours from resected carcinoma of the colon and found that the amount of IgG in tumour tissue was significantly higher in Dukes' stage C than in Dukes' stage A tumour. This is of particular interest in relation to our findings. The histo-pathological counterpart of Dukes' stage C colonic carcinoma is stage III (pTNM) gastric carcinoma, which had the lowest concentration of IgG in serum. Further studies are needed to elucidate the correlation between IgG and C1-INH.

The elevated IgA concentration among all the patients can be explained by the stimulation of the secretory IgA system.

The preoperative staging of gastric carcinoma relies at present upon poorly defined criteria, except in patients with histologically verified metastasis. Determination of immunoglobulins and complement components apparently gives additional information for the staging of the disease in the individual patient.

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