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FACTOR VIII RELATED ANTIGEN, COAGULATION TESTS AND ACUTE RENAL FAILURE

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Summary

Coagulation factors were measured in 50 patients presenting with acute renal failure on the day of their admission (D1) and seven days later (D7). A number of changes were observed, particularly in those patients with a poor prognosis (decreased platelet counts and plasminogen concentrations and increased factor VIII related antigen concentrations). In the majority of cases it would appear that disseminated intravascular coagulation remains sub-clinical.

Introduction

It has long been recognised that patients with acute renal failure (ARF) may have disordered haemostasis. Such disorders of coagulation may be partially responsible for the ARF and have been implicated in the pathogenesis [1, 2].

In view of the low incidence of haemorrhagic and thrombotic complications in patients with acute renal failure [3, 4] we have studied the main coagulation factors in 50 patients. We have determined the specific defects in coagulation in these patients and analysed the particular patterns observed.

Patients and methods

Fifty patients with acute renal failure (33 men, 17 women) were studied. The causes of the acute renal failure were as follows: obstruction 12, post-surgical 10, toxic eight, septic eight and undetermined aetiology five.

The coagulation parameters studied were platelet counts (plat), fibrinogen concentrations (F), activated partial thromboplastin time (APTT), prothrombin time (PT), factor VIII related antigen concentrations (FVIII R:AG), factor VIII coagulant (FVIIIc), plasminogen (PLG), antithrombin III (ATIII), α_2 antiplasmin (α_2AP), α_2 macroglobulin (α_2M), α_1 antitrypsin (α_1AT) and the antitrypsin inhibitor C_1 (C_1I).

All patients were examined within 24 hours of hospitalisation (D1). On the basis of outcome the patients were divided into two groups, group A 22 patients

TABLE I. Average values (average + SEM) of parameters studied in the different groups of patients

Group		Day		Plat Gi/L	F g/L	APTT sec	PT U.Fr†	α_2AP U.Fr†	α_2MA mg/dl	α_1AT mg/dl	C_1I mg/dl	ATIII U.Fr†	PLG U.Fr†	FVIIIc U.Fr†	FVIII R:Ag U.Fr†
Normal values				140 400	2 4	28 33	0.85 1	0.8 1	120 300	130 250	13 29	0.8 1	0.8 1	0.8 1.2	0.8 1.2
	n = 50	Day 1	Mean	226	5.6	32	0.75	0.8	165	314	21	0.7	0.8	1.3	3.29
			SEM	23	0.3	1.1	0.05	0.04	20	20	1	0.03	0.02	0.1	0.2
	n = 22	Day 7	Mean	397	5.8	32	0.83	0.9	249	302	20.6	0.8	0.8	1.3	3.24
			SEM	44	0.5	1.3	0.07	0.05	24	26	1.8	0.04	0.03	0.1	0.3
A	n = 22	Day 1	Mean	272	5.9	34	0.7	0.8	265	333	19	0.8	0.9	1.3	3.35
			SEM	35	0.4	1.8	0.03	0.06	30	35	1	0.04	0.04	0.09	0.3
B	n = 28	Day 1	Mean	204	5	35	0.7	0.7	236	300	23	0.7	0.7	1.4	3.37
			SEM	29	0.4	1.3	0.03	0.05	33	23	1.7	0.04	0.02	0.08	0.2
A	n = 14	Day 7	Mean	513	6.1	30	0.9	0.9	274	276	20	0.8	0.9	1.3	2.41
			SEM	41	0.5	1.4	0.02	0.06	35	16	1.6	0.03	0.03	0.09	0.2
B	n = 8	Day 7	Mean	193**	5.3	34	0.7**	1	205	347	21	0.8	0.7**	1.3	4.65***
			SEM	33	0.9	2.3	0.05	0.05	21	66	4.3	0.06	0.03	0.1	0.2
C	n = 42	Day 1	Mean	238	5.6	35	0.7	0.8	256	324	20	0.8	0.8	1.3	3.29
			SEM	19	0.3	1	0.03	0.04	24	23	1	0.03	0.03	0.06	0.2
D	n = 8	Day 1	Mean	211	4.6	36	0.7	0.8	208	264	22	0.7	0.7*	1.3	3.68
			SEM	14	0.4	4	0.06	0.1	63	29	4	0.07	0.04	0.1	0.5
C	n = 13	Day 7	Mean	480	5.8	30	0.9	0.9	262	270	19	0.9	0.9	1.3	2.4
			SEM	38	0.5	1.4	0.03	0.06	31	16	2	0.03	0.04	0.1	0.3
D	n = 8	Day 7	Mean	290**	5.8	33	0.7**	0.9	229	347	22	0.8	0.7**	1.3	4.4***
			SEM	83	0.9	2.2	0.05	0.06	38	58	3	0.06	0.04	0.1	0.3

* $p < 0.005$; ** $p < 0.001$; *** $p < 0.0001$; †U.Fr = Unit Fractions
Group A: patients who recovered; Group B: patients who died; Group C: non septic patients; Group D: septic patients
For abbreviations see text

(mean age 57.4 ± 7.4 years) who recovered and group B 28 patients (mean age 64 ± 4.5 years) died. Coagulation studies were repeated seven days after admission (D7) in the 14 patients in group A and in the eight patients in group B who survived for seven days or more.

Results

The mean (± SEM) values for all the parameters analysed are shown in Table I. In addition to the results for patients in group A and B on D1 the data has been further divided to give the results in those patients without sepsis (group C, n = 42) and those with primary sepsis (group D, n = 8). At D7 22 patients were examined (group A, n = 14 and group B, n = 8). In addition patients who developed secondary sepsis by D7 (n = 9) were compared with those without infection (n = 13).

In general on D1 increased F, longer PT, very high FVIII R:AG, lower PLG, high α_1 AT and slightly increased FVIIIc was found. Comparison between group A and group B revealed that PLG only was significantly lower in group B ($p < 0.05$). In addition PLG was significantly lower in the septic than the non-septic patients ($p < 0.005$).

On D7 the patient data were similar to that on D1, however comparing group A and group B patients showed that there was a more marked decrease in platelet counts ($p < 0.001$), a more prolonged PT ($p < 0.005$), a decrease in PLG ($p < 0.001$) and a marked increase in FVIII R:AG ($p < 0.0001$) in the group B patients.

Comparison between group C and group D patients produced similar results to those obtained in comparing group A with group B. Group D patients who had lower platelet counts ($p < 0.001$), a more prolonged PT ($p < 0.001$), a greater decrease in PLG ($p < 0.001$) and a more marked increase in FVIII R:AG ($p < 0.0001$).

In comparing the results obtained in relationship to the cause of the acute renal failure a significant elevation of FVIIIc ($p < 0.05$) was found in patients with a toxic aetiology.

Discussion

In this study a decrease in such parameters as platelet counts, PT, PLG, α_1 AP, ATIII would suggest that there is probably a consumption coagulopathy in these patients. This process is accentuated in patients with a poor prognosis as there is a significant decrease in platelet counts noted on D7 in group B and group D patients. In addition in group D patients a significant decrease in PT and PLG was observed. However the continued high fibrinogen values and the lack of marked platelet decrease in the majority of patients (only one patient developed disseminated intravascular coagulation (DIVC)) indicates that in acute renal failure DIVC remains sub-clinical in the majority of patients.

PLG appears to be of value in the follow-up of patients with ARF. We found its reduction to be significant on D1 and D7 in the group of patients who died including the subset with sepsis. The reduction could be on account of increased

rates of consumption of coagulation factors or impaired synthesis. It is difficult to give a prognostic value to this parameter in isolation, but it may prove of value if measured sequentially.

A significant increase in FVIIIc concentrations was found only in the group of patients with a toxic cause for their acute renal failure. This has been confirmed in a further series of cases.

It is interesting to note that in all patients high values of FVIII R:AG were found but very high values were obtained on D7 in patients who died and in septic patients. This very high value indicates a poor prognosis and is probably a manifestation of vascular endothelial damage [5] as similar increases were found in both groups. This is a well recognised phenomenon although the mechanism either by release from damaged endothelial cells or increased synthesis is unclear.

In conclusion although changes in coagulation factors are seen in ARF such changes are in most cases insufficient to produce specific clinical features. However, patients with disordered fibrinolytic and thrombotic processes and vascular endothelial damage require constant monitoring of their haemostatic factors including PLG and FVIII R:AG in addition to conventional studies.

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