COAGULATION PROFILE IN SYSTEMIC LUPUS ERYTHEMATOSUS STUDIES IN 20 PATIENTS

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SYNOPSIS

Coagulation studies were performed in 20 patients with systemic lupus erythematosus (SLE). Abnormalities of haemostatic function occurred in 19 (95%) patients. Seven patients had thrombocytopenia, 9 had the circulating lupus anticoagulant and 13 had abnormal fibrinolysis. Qualitative platelet defect was found in 11 patients. The haemostatic abnormalities were not invariably associated with disease activity.

INTRODUCTION

Clinical and laboratory abnormalities of haemostasis have long been known to be part of systemic lupus erythematosus (SLE) (1). Significant deviations from normal maybe more common than previously suspected and may occur in the absence of overt symptoms of coagulation abnormalities (2). This present study presents the analysis in 20 patients with SLE to determine the clinical relevance of laboratory haemostatic abnormalities and the relationship between the haemostatic disorders and activity of the underlying SLE.

MATERIALS AND METHODS

20 patients fulfilling the revised criteria of the American Rheumatism Association (3) for systemic lupus erythematosus were examined for their coagulation profile. There were 18 females and 2 males with mean age of 26.1 years (range 14-37). The mean duration of disease from diagnosis was 1.7 years (range 3 months-10 years). 19 patients were receiving steroid medication. Dosages of prednisolone range from 5-30mg a day. One patient was on cyclophosphamide. All denied ingestion of aspirin or salicylates. Assessments included complete history and physical examination. Controls included 20 healthy volunteers who had no haemostatic abnormality. Detailed clinical data of the 20 patients are given in Table 1.

Table 1 Detailed clinical data of 20 LE patients

Patient	Age	Sex	S.complement	Clinical activity
1	26	F	28	Cutaneous vasculitis
2	22	F	43	Rash, arthritis
3	31	F	13	Hypertension, bruising
4	20	F	<10	Rash, psychosis, leucopenia
5	23	M	11	Photosensitive rash
6	22	F	11	Pleuritis, psychosis
7	28	F	10	Rash, pleuritis, psychosis
8	29	F	10	Proteinuria
9	37	F	43	Thrombocytopenia, bruising
10	27	F	<10	Proteinuria, psychosis
11	26	F	10	Deep vein thrombosis right leg
12	20	F	14	Rash, arthritis, thrombocytopenia
13	28	F	10	Haemolytic anaemia
14	19	F	12	None
15	14	M	<10	Pleuritis
16	35	F	30	None
17	36	F	13	None
18	30	F	28	Myositis
19	29	F	28	Pulmonary hypertension
20	21	F	<10	Thrombocytopenia, leucopenia

Haemostatic Studies

Platelet count, prothrombin time, and activated partial thromboplastin time were assayed by standard techniques. Platelet aggregation studies were done in an aggregometer by the method of Born and Cross (4). Fibrinolytic activity was determind as euglobulin clot lysis time (5). Fibrinogen degradation products were measured by the method of Merskey, Kleiner and Johnson (6). Fibrinogen levels were estimated according to the technique of Ratnoff and Menzies (7). Coagulation factors II (8), V (9), VIII (10), X (11) were measured by methods using deficient plasma as substrate in the prothrombin time or partial thromboplastin time test. Factor VIII:Ag was assayed by immunoelectrophoresis technique (12).

The concentration of antithrombin III antigen was measured by immunodiffusion (12) and the antithrombin activity by a clotting assay (13).

The presence of the circulating lupus anticoagulant was detected by kaolin partial thromboplastin time with modifications by Boey et al (14).

RESULTS

Thrombocytopenia, abnormal platelet function

Seven patients had platelet counts less than 100,000/mm^3. None had any bleeding episodes. 3 of the 7 patients had the circulating lupus anticoagulant. Impaired platelet function was found in 11 patients. Striking defect was noted in the aggregation induced by collagen. Anti-platelet antibody was not assayed. The in-vitro abnormalities appeared to correlate with the clinical activity of the SLE.

Coagulation profile

The circulating lupus anticoagulant was present in 9 patients (45%). One patient had recurrent deep vein thrombosis. In another patient with popliteal vein thrombosis, the lupus anticoagulant was not detected. This patient was heavily immunosuppressed with steroids and cyclophosphamide when the assay was done. 4 patients with the inhibitor had histories of recurrent abortions. The patient with the highest titre of the lupus inhibitor had five abortions. The other associations with the circulating lupus anticoagulant were thrombocytopenia in 3 patients and a positive sero-reaction for syphills in another 3 patients.

None of the patientss in this study had low levels of Factors I, II, V, VIII or X. Antithrombin III levels were also normal.

Impaired fibrinolysis was observed in 12 patients. 6 patients had prolonged euglobulin clot lysis time. Fibrin degradation products were abnormal in 12 patients. No patients. No patient had signs of clinical disseminated intravascular coagulation at the time of study.

DISCUSSION

Abnormalities of haemostasis, especially thrombocytopenia are not uncommon in SLE (1). In our study of 20 patients, despite multiple laboratory abnormalities, no spontaneous life-threatening bleeding was encountered. Alarcon-Segovia found that patients with thrombocytopenia, even with an associated haemolytic anaemia, had a less severe course (15). Thrombocytopenia in our patients was not associated with a particularly malignant course.

Bleeding was not encountered in the 11 patients with impaired platelet function. The cause of the defect in our patients has not been ascertained. No patient gave a history of aspirin ingestion. A possible cause is anti-platelet antibody damage. The presence of serum anti-platelet factors contribute to poor platelet function (16).

The circulating lupus anticoagulant was detected in 9 patients (45%). This inhibitor appears to have a specific anti-phospholipid activity against the phospholipid portion of the prothrombin activator complex (17). We confirm the association of the lupus anticoagulant with thrombocytopenia and another antibody with phosphlipid specificity, the biological false positive reaction for syphilis (18). The presence of the lupus anticoagulant appear to define a subset of patients with recurrent abortions (19). Lubbe et al (20) showed maternal suppression of the lupus anticoagulant with corticosteriods in 6 patients with recurrent abortions. 5 of their 6 patients subsequently had successful live pregnancies. It is noteworthy that in our study, the patient with the highest titre of the inhibitor had had 5 intrauterine deaths.

The most important association of the lupus anticoagulant is with thrombosis (14). In our study one patient with repeated deep vein thrombosis had the circulating inhibitor. The cause of thrombosis appear to be due to the cross-reaction of the lupus anticoagulant with phospholipids in platelets. This cellular damage at endothelial cell surface results in lowered prostacyclin concentration and a predisposition to thrombosis (19).

Endothelial cell dsyfunction was also manifested by the finding of elevated levels of von Willebrand factor (VIII:Ag) in 17 patients (21,22).

Abnormal fibrinolysis as part of the haemostatic picture of SLE was observed in 13 patients. The significance of this is uncertain.

In general, the haemostatic abnormalities in our patients were not invariably related to lupus disease activity or to any clinical manifestations such as bleeding. In most instances, they appear to be an independent aspect of the disease. It is suggested that the haemostatic abnormalities could be part of vasculitis and enhance the effects of endothelial damage, resulting in thrombosis rather than haemorrhage.

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