To the Editor:

Ginsberg et al. have reported that in patients with systemic lupus erythematosus (SLE) the presence of high circulating levels of antiphospholipid antibodies (ACA) is associated with an ongoing prothrombotic state. This was documented by finding significantly higher values of F1+2, a marker of thrombin generation, in ACA(+) patients than in ACA(−) ones. We have data supporting the association between antiphospholipid antibodies (APLA) and an ongoing prothrombotic state, but we do not confirm that this is closely related to ACA positivity.

We studied 45 patients (39 women, 6 men, ages 20 to 58 years) having SLE according to ARA criteria. Fifteen (33%) (12 women, 3 men, ages 21 to 58 years) had a history of thromboembolism: 7 venous thrombosis, 2 arterial thrombosis, 2 venous and arterial thrombosis, 3 recurrent fetal loss, and 1 recurrent fetal loss and venous thrombosis. All but 9 were under treatment with prednisone (5 to 25 mg/d) or methyl prednisolone (4 to 24 mg/d).

Patients were not treated by anticoagulants in the month preceding the study. No patients had active infection, surgery, or trauma in the previous 3 months.

Between 8 AM and 9 AM a blood sample was taken from each patient fasting from at least 12 hours to evaluate lupus anticoagulant (LA), ACA, and F1+2.

LA was defined by the prolongation of at least two coagulation tests and by the positivity of confirmatory test with phosphatidylinerine-phosphatidylcholine liposomes. ACA levels were measured by an enzyme-linked immunosorbent assay (ELISA method, validated in an international workshop, with the upper limit of 10 GPL (antiphospholipid IgG) U/mL, as being 3 SD above the mean of 40 healthy volunteers. Patients were considered LA(+) or ACA(+) if positivity persisted on two separate occasions at least 2 months apart. Plasma F1+2 levels were assayed by an ELISA method (ENZIGOST F1+2; Behringwerke, Marburg, Germany); 30 healthy subjects matched for sex and age (25 women, 5 men, ages 23 to 56 years) were used as control (ref val 0.6 ± 0.2 nmol/L, range 0.3 to 1.2 nmol/L). Statistical analysis was performed by Mann-Whitney U-test and Fisher exact test.

Sixteen (35%) and 20 (44%) were LA(+) or ACA(+) respectively. Twelve (27%) were both LA(+) and ACA(+). The disease activity, defined as previously described, was similar in LA(+) and LA(−), or ACA(+) and ACA(−) subgroups. The Odds ratio for the association between LA positivity, ACA positivity, and the occurrence of previous thrombosis were 26 (95% confidence interval 4.01 to 190.9; P < .0001) and 4.0 (95% confidence interval 0.9 to 18.8; P < .071) for LA and ACA, respectively. F1+2 was higher in LA(+) than in LA(−) (1.83 ± 0.58 vs 0.64 ± 0.27 nmol/L; P = .0001) and in ACA(+) than in ACA(−) patients (1.38 ± 0.81 vs 0.81 ± 0.49 nmol/L; P < .04). F1+2 levels of LA(+) and ACA(+) were greater than controls (P < .0001). By excluding patients with previous thrombosis, only LA(+) still have F1+2 values significantly higher than LA(−) (P < .03) and controls (P < .001).

To further assess the relation between APLA and F1+2, we divided SLE patients in four subgroups, ie, LA(+)ACA(+), LA(+) ACA(−), LA(−) ACA(+), and LA(−) ACA(−); F1+2 was higher in LA(+) ACA(+) (P < .001) and LA(+) ACA(−) (P = .006) than in LA(−) ACA(−). This latter group had F1+2 similar to LA(−) ACA(−) (Fig 1).

Our data confirm the association between APLA and increased thrombin generation in SLE patients. However, this study shows that only the presence of LA is strictly related to an ongoing prothrombotic state, thus confirming the heterogeneity of APLA. The presence of distinct LA-related ACA subgroups could perhaps account for F1+2 differences observed between LA(+) ACA(+) and LA(−) ACA(−) patients.

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REFERENCES


Fig 1. Plasma F1+2 levels in SLE patients with (+) and without (−) LA and ACA.

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Lupus anticoagulant and increased thrombin generation in patients with systemic lupus erythematosus [letter; comment]

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