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Thrombosis and Antiphospholipid Antibodies in Non-SLE Patients: Predictive Value of Antiphosphatidylserine Antibodies

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Dear Sir,

The clinical relevance of antiphospholipid antibodies (aPL) in patients with thromboembolic events but without systemic lupus erythematosus (SLE) is still a matter of debate. From previous data, it has been suggested that lupus anticoagulants (LA), rather than anticardiolipin antibodies (aCL), are associated with a high risk of venous thrombosis [1–4]. To improve aPL detection, assays against phospholipids other than cardiolipin have been proposed. Phosphatidylserine (PS) can be considered an important physiological phospholipid antigen since PS exposure on the outer surface of activated platelets is critical to initiate the blood coagulation cascade. Little is known about the association between anti-PS antibodies (aPS) and thrombosis in non-SLE patients [5, 6]. To address this issue, we compared the results of classical tests including LA, aCL, and anti- β_2 -glycoprotein I antibodies (a β_2 -GP I) to detect aPL associated with thrombosis with those of aPS.

From December 1999 to June 2000, we studied 221 consecutive non-SLE patients (167 females, 54 males, mean age 45 years, range 9–86 years) referred to the hemostasis unit for aPL detection. The inclusion criteria were: previous LA or aCL positivity, increased activated partial thromboplastin time or clinical suspicion of antiphospholipid syndrome. As controls, we studied 71 healthy subjects (48 females, 23 males; mean age 42.6 years, range 10–82 years) from a regional health center.

LA were assessed according to the ISTH recommendations [7]. aCL, a β_2 -GP I and aPS were determined by quantitative ELISAs (QuantaLite anticardiolipin, anti- β_2 -GP I IgG/IgM, Inova Diagnostics, San Diego, Calif., and Coaliza antiphosphatidylserine IgG/M Reads, Westminster, Colo., USA). The standards and controls were obtained from the Antiphospholipid Standardization Laboratory (Louisville, USA). The aPL levels in healthy controls (mean + 3 SD) were taken as normal cut-off points in this study. The values were: 13.5 GPL/ml or 11 MPL/ml for IgG or IgM aCA, respectively, 18 SGU/ml for both IgG or IgM anti- β_2 -GP I, 14.5 GPS or 20 MPS for IgG or IgM aPS, respectively.

The subjects were divided into two groups. Group 1 included 85/221 (38.5%) patients with a history of thrombosis. Among them, 79 had venous thromboembolic events and 6 had arterial thrombosis. Group 2 included 136/221 (61.5%) subjects without any thromboembolic history. The frequency of LA was 24.7% (21/85) in group 1 vs. 6.6% (9/136) in group 2 ($p = 0.001$, odds ratio 4.63; 95% CI 2.1–10.2). The frequency of aPS positivity was 20% (17/85) and

8.8% (12/136) in groups 1 and 2, respectively ($p = 0.017$, odds ratio 2.58; 95% CI 1.19–5.63). The frequency of aPS IgM was 15.3% (13/85) and 6.6% (9/136) in groups 1 and 2, respectively ($p = 0.036$, odds ratio 2.55; 95% CI 1.06–6.12). Similar results for specificity were found for LA and aPS IgM (93%). There were no significant differences in aCL (15.9% in group 1 vs. 13.6% in group 2) and anti- β_2 -GP I (7.0% in group 1 vs. 4.4% in group 2) levels between the two groups. In a multivariate analysis, LA exhibited the strongest association with thrombosis ($p = 0.008$, odds ratio 3.3; 95% CI 1.4–8.2). For aPS, the results indicated a trend towards an independent risk factor of thrombosis ($p = 0.15$, odds ratio 2; 95% CI 0.8–5.4).

Our study shows that the frequency of LA is high in patients with thrombosis and that thrombosis is strongly associated with LA. On the other hand, no correlation was found between aCL and thrombosis. These results are consistent with previous findings [1–4]. It has been suggested that the use of a panel of negatively charged phospholipids offers no advantage [8]. Previously, Triplett et al. [5] found a trend towards an increased rate of vascular complications in patients with both LA and aPS. From our results, aPS appears to have more clinical relevance than aCL. More definitive conclusions such as the proposition to include initial testing of aPS in non-SLE thrombotic patients justifies large-scale prospective studies.

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