Absence of antiphospholipid antibodies in Behçet's disease

Sir: Anticardiolipin antibodies (aCLA) and lupus anticoagulant (LA), both antiphospholipid antibodies (aPLA), are associated with multiple arterial or venous thrombosis, recurrent fetal losses, and thrombocytopenia.¹ They have been investigated in Behçet's disease (BD) with conflicting results. The purpose of our work was to extend the previous search for aCLA, LA, and antibodies detected by the Venereal Disease Research Laboratory (VDRL) test in BD, to aPLA directed against several anionic and zwitterionic phospholipids.

Nineteen patients (six women, 13 men), fulfilling the international criteria for diagnosis of BD² were studied. Their mean age was 34 years. Among them, eight had had venous thrombosis, one arterial thrombosis, and two both. Neurological disease, uveitis, or retinal vasculitis were each present in six patients. Seven patients were HLA-B5 positive. Fourteen patients were treated with daily colchicine—as the sole treatment in nine, associated with corticosteroids in five. Corticosteroids were used in five other patients, associated with immunosuppressive agents in three.

For all patients IgG and IgM antibodies directed against cardiolipin alone, or a mixture of five anionic phospholipids (cardiolipin, cardiolipin-zwitterionic phosphatidylglycerol, phosphatidylserine, phosphatidylserine/ phosphatidylserine, phosphatidylserine/phosphatidylethanolamine), or phosphatidylinositol-phosphatidylinositol were investigated using a slightly modified enzyme linked immunosorbent assay (ELISA) according to Harris's recommendations.² For each phospholipid normal optical values were defined as the mean optical density of a panel of 40 adult blood donor serum samples, after subtraction of optical density obtained for each serum on wells containing no phospholipids. The threshold for positivity was defined as a value higher than the mean+three standard deviations. Ten plasma samples were screened for anti-LA with a dilute activated partial thromboplastin time and a kaolin clotting time. Lupus anticoagulant was subsequently confirmed by failure to correct the anticoagulant effect in a mixture of test and normal plasmas. A VDRL test was performed in nine patients.

Using ELISA, aPLA could not be demonstrated even with extensive investigations, including measurement of antibodies directed against phosphatidylinositolphosphatidylethanolamine (recently described in systemic lupus erythematosus with thrombosis),² aCL, and aPLA directed against phosphatidylethanolamine. Similarly, LA was not found and the VDRL test was negative. Therefore, no correlation was found between clinical manifestations and aPLA.

In a few studies aCLA have been found to be positive in BD. In 1984, using a radioimmunoassay, Hull et al⁴ detected 13 patients positive for aCL A out of 70 (19%) with BD; seven were IgG, three IgM, and three IgG-IgM positive. The control rate of aCL A was 3.5% (later reported in 20 patients with BD), but in this study the ELISA method and the threshold for positivity were not described. Bergman et al⁵ detected aCL A in 13 out of 26 (50%) patients with BD, and only the IgM isotype was significantly found in BD. Interestingly, in all these studies no correlation could be found between the presence of aPLA and either biological or clinical features, except for retinal vascular disease in the first study.⁵ Our results, however, are in agreement with other studies about aPLA in BD. In 1985 Efthimiou et al⁶ did not confirm the study of Hull et al⁴ They found only two positive IgM aCLA in 25 (8%) patients with BD, but the same results were observed in controls. Another study of aCLA in 37 patients with BD was performed in 1986,⁶ and no positive results were found. Similarly, the search for LA was negative in 69 patients with BD.¹⁰ The reason for the disparity between these studies remains unclear. It cannot be explained by clinical or ethnic differences in the groups with BD studied. Unlike Pereira et al,⁹ we do not think that the use of an immunosuppressive agent can explain the absence of aPLA as only three of our 19 patients were taking such agents. This discrepancy might rather result from different technical approaches in the measurement of aPLA as false positive results can be found in an ELISA when non-specific binding on ELISA plates devoid of phospholipids has not been substracted or when the threshold for positivity is too low.²

We conclude that aPLA, including antiphosphatidylinositolphosphatidylethanolamine antibodies, are generally absent in BD, and therefore might not explain the thrombotic manifestations of this disease.

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MATTERS ARISING

Still too early for the gold rush

Sir: In their recent editorial Taha and Sturrock suggest that in arthritic patients receiving non-steroidal anti-inflammatory drugs (NSAID) the combination of gold treatment might be useful in protecting the stomach from the development of mucosal injury.¹ As a gastroenterologist I find this hypothesis fascinating and am intrigued by the possibility that the gold treatment might be useful in protecting the stomach from the development of mucosal injury.¹