

Leader

Antiphospholipid syndrome: linking many specialties

It is now five years since the first detailed descriptions of the antiphospholipid (or anticardiolipin) syndrome first appeared.^{1–4}

The three papers in this issue of the *Annals* serve to highlight the interest this subject is now generating, not only world wide, but in medical specialties far removed from rheumatology.

The original studies were in systemic lupus erythematosus. It was apparent, however, that even in lupus, most of the patients were atypical—frequently, for example, having one or two American Rheumatism Association classification criteria only. Perhaps the majority had no evidence of systemic lupus erythematosus at all.⁵

It took very little time to realise the implications of the very strong association between antiphospholipid antibodies and thrombosis, and during the past few years series of patients with strokes, myocardial infarction, pulmonary emboli, deep vein thrombosis, etc have been collected in order to assess the overall prevalence of the syndrome in general medicine.

Similarly, in obstetrics, the presence of antiphospholipid antibodies is a clear risk factor for placental vessel thrombosis and miscarriage,⁴ and anticardiolipin and lupus anticoagulant estimations are important investigations in women suffering recurrent miscarriages.

Clinically, there is a 'grey area' between the diagnosis of 'atypical lupus' and the primary antiphospholipid syndrome. In general, the latter term is kept for those patients who have had no history of synovitis, serositis, rashes, etc, and who have no other lupus associated—for example, anti-DNA—antibodies.⁶

The series of 20 patients with the antiphospholipid syndrome described by Mackworth-Young *et al* in this issue conforms to the earlier descriptions.⁷ Nine out of 19 had positive antinuclear antibody tests, but none fulfilled the criteria for the classification of systemic lupus erythematosus. Seven had venous and five arterial thrombosis. Of the 15 female patients with pregnancy, 12 suffered abortions—up to eight in some patients. Their series reaffirmed some of the other features of the syndrome—livedo reticularis, migraine, and thrombocytopenia. Of interest was the inclusion of heart abnormalities—

valvular disease is being increasingly recognised in association with the antiphospholipid syndrome.^{8,9} The serological features of their group are typical: high levels of IgG anticardiolipin antibodies are associated with thrombosis. Low to moderate levels of IgM antibodies are less significant.

Perhaps most interesting of all are the occasional patients who have all the features of the antiphospholipid syndrome and yet who do not have anticardiolipin antibodies. Some of these patients do have lupus anticoagulants—highlighting the need in our present state of knowledge to carry out both tests routinely.¹⁰

There may be many explanations. The antibodies may fail to recognise phospholipids if their stoical arrangement is altered. One monoclonal antibody, for example, was shown to bind hexagonal but not lamellar phospholipid.¹¹ Or, possibly, some patients may have antibodies recognising individual phospholipids—such as the patient described by Staub *et al* with several venous thromboses and myocardial infarction, whose serum contained antibodies against the zwitterionic phospholipid phosphatidylethanolamine.¹²

Clinically, apart from the risk of placental thrombosis, the most prominent as well as the most grave feature of the syndrome is cerebral thrombosis.^{3,13} Transient ischaemic attacks as well as transient visual loss are common. In the series reported in this issue from St Thomas's Hospital seven out of 84 consecutive patients with raised levels of anticardiolipin antibodies had occlusive ocular vascular disease.¹⁴ A recent study reported that 38% of their patients with lupus retinopathy had the lupus anticoagulant.¹⁵ It is still not known how large a proportion of all patients with ocular occlusive vascular disease the antiphospholipid syndrome represents, though it is probably not high.¹⁶

The paper in this journal reporting acute adrenal insufficiency (possibly due to adrenal infarction) in association with anticardiolipin antibodies demonstrates the diversity of the syndrome.¹⁷ Case reports do not, themselves, stand up to close scrutiny, but do serve to suggest lines of study. Others have also reported an association between Addison's disease and anticardiolipin antibodies¹⁸ and the lupus

anticoagulant.^{19 20} One day, the strength or otherwise of this association will become clear.

So, five years on, what lessons have been learnt? Firstly, it seems that there is a clearly definable mechanism for thrombosis, possibly genetically determined. Secondly, subgroups of patients with systemic lupus erythematosus and, for example, with recurrent abortion, have been identified in whom anticoagulation is probably the most appropriate treatment. Thirdly, these clinical and laboratory observations have linked rheumatology with a broad sweep of other medical disciplines and have unearthed a clinically common syndrome. Where were all these patients before?

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