

Making the Difference

By: Dr. Munther Khamashta

For years patients with antiphospholipid syndrome (APS) went undiagnosed and untreated. Now, once the condition is diagnosed through a simple blood test, treatment can make an enormous difference.

Patients with APS have “sticky blood” which leads to an increased risk of thrombosis clotting – in the veins and arteries. In pregnant women, the syndrome can also lead to frequent miscarriage. It is often associated with systemic lupus erythematosus (SLE).

In 1983 Dr. Graham Hughes, the head of the Lupus Unit at St. Thomas’s, first identified the association of antiphospholipid antibodies (aPL) with an unusual combination of clinical features of vein and arterial thrombosis, miscarriage, and reduction in the number of platelets (thrombocytopenia) in the absence of classical SLE.

Thrombosis

Deep vein thrombosis (DVT) in the legs is the most frequently reported symptom. This may be a one off, or be recurrent. In some women, it happens soon after they start taking the oral contraceptive pill. The major concern in DVT patients is the risk of it spreading to the lungs (pulmonary embolism). Internal organs may also clot such as the kidney, liver, brain and eye.

Major artery thrombosis is less common than in the veins. However, thrombosis in the arteries has more severe consequences, particularly in small arteries in the brain, when it can lead to stroke. Other arterial thrombosis may also occur, e.g. eye, renal, coronary and peripheral arteries.

Other Symptoms

As already mentioned, the most dramatic and serious neurological symptom is a stroke, but also includes seizures, movement disorders (including chorea), memory loss, visual disturbances, spinal cord problems and migraine. Our most recent experience on a group of 345 SLE patients showed that aPL was significantly more frequent in patients with chronic headache than in those without. Interestingly, in some of our patients with severe and chronic headache resistant to conventional treatment, it often reduced or went completely when treatment with heparin or warfarin was started to treat thrombosis.

Some patients with APS can exhibit symptoms that very often mimic multiple sclerosis (MS). In our experience, a careful medical history, a previous history of thrombosis and/or recurrent miscarriage, an abnormal brain scan and response to anticoagulant therapy all contribute to reaching a correct diagnosis. We believe that testing for aPL should become routine in patients with “atypical” MS. Although the threat of the development of a stroke is the biggest fear, one wonders how many individuals with more subtle forms of brain involvement are either being misdiagnosed, or not being diagnosed at all.

Heart symptoms are frequent in APS patients. There are two areas of the heart which can be affected, the heart valves and the coronary arteries. Early myocardial infarction (heart attack) has been documented both in patients with APS associated with SLE and in primary APS. Valve involvement affects up to 35% of patients, mitral valve involvement being the most frequent and can be confirmed by a process called echocardiography, which is now a part of the routine screen in our APS clinic. Renal disease, in particular thrombosis of the kidney artery with restricted blood supply to the kidney and raised blood pressure, is also a risk in patients with APS.

Renal vein thrombosis may also occur. In a small percent of patients, the platelet numbers are affected and, rarely, platelet counts may fall to dangerously low levels. Thus, patients who have been diagnosed as having low platelet counts (thrombocytopenia) should also be checked for the syndrome.

Blotchy skin is also common, and some patients develop a purplish vein coloration on the back of the wrists and others on the knees. Skin ulcers are also a common complication in APS. They normally appear in the legs although they can be elsewhere on the body.

Treatment

Recurrent thrombosis can be prevented by a long-term oral anticoagulation treatment, warfarin, which thins the blood. In APS patients we try to keep the blood two to four times thinner. Patients on warfarin treatment undergo regular blood testing. The most serious side effect is internal bleeding, so the optimal dose of warfarin needs to be balanced according to the therapeutic effect required and the risk of bleeding for each individual.

Patients with positivity for aPL but without history of thrombosis generally do well with low dose aspirin (75-100 mgs) daily in order to reduce platelet stickiness and prevent clots. Aspirin is the safest form of prophylaxis, or prevention, of thrombosis; the most common side effect being limited to indigestion and the most serious, but rare, to allergic reactions. Though aspirin is the logical first line treatment, aspirin alone is often not enough and some aPL positive patients develop thrombosis despite treatment.

We wondered whether a possible therapeutic alternative to aspirin in selected patients might be a low dose of warfarin. In order to provide evidence we have designed a five-year study which is funded by the ARC. An international collaborative clinical trial comparing aspirin alone versus aspirin plus low dosage of warfarin has been started.

Antiphospholipid antibody testing

There are two main types of aPL tests that are used for the diagnosis: the first is the anticardiolipin antibody (aCL), which is an immunological test and the second one is the lupus anticoagulant (LA), which is a coagulation-based test. Although they measure broadly the same thing, in a sizeable number of cases (around 20%) one or other test may prove negative. In other words, one test alone could miss the diagnosis. These tests are available in most major hospitals throughout the world, and clinicians now recognize that these simple tests can make a great difference to treating patients with this condition.

One of the gains from the recognition of APS Syndrome is that it is a significant cause of recurrent miscarriage. Thankfully, this is now treatable. The simple theory as to the cause is that the “sticky blood” is unable to reach the smallest blood vessels in the placenta.

Treatment in pregnancy: Pregnancy complicated by APS requires expert care and a multidisciplinary team approach. In our pregnancy clinic, patients with APS undergo assessment and counselling before they conceive. Close monitoring of pregnancy is essential.

For women with recurrent miscarriages, but without a history of clotting, the traditional treatment is low dose aspirin. Heparin is also increasingly being used in these patients especially if they had previous miscarriages during the second or third trimester, or other pregnancy complications such as pre-eclampsia. For those women with previous thrombosis we use aspirin together with subcutaneous heparin injections. Heparin is the anticoagulant treatment of choice during pregnancy, as warfarin is toxic to the developing fetus. The success rate in APS pregnancy has risen from 20% to over 70%.

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