ASK THE EXPERT

Antiphospholipid Syndrome

BY GRAHAM R.V. HUGHES, M.D.

By far the most challenging aspect of managing patients with antiphospholipid syndrome (APS) is recognizing them. It's an off-the-radar-screen diagnosis and "if doctors do not look for it, they can't find it," said Dr. Graham R.V. Hughes, head of the lupus research unit at St. Thomas' Hospital in London. Yet as physicians start identifying more APS patients, it could become one of the most frequently diagnosed autoimmune disorders of this century, he predicted.

Dr. Hughes and his colleagues first described APS, also called Hughes Syndrome, in 1983. Characterized by a persistent elevation of antiphospholipid antibodies, the condition is associated with a tendency to form venous and arterial blood clots throughout the body. APS can occur in the presence of lupus or another autoimmune or rheumatic disorder, known as secondary APS, but also is present with no definable associated disease.

Estimated to affect millions of people worldwide, APS often goes undetected because the wide spectrum of signs and symptoms, ranging from headache to chronic leg ulcers and pregnancy loss, can mimic those of other conditions.

In this month's column, Dr. Hughes emphasizes the importance of raising awareness of APS, as well as the impact that such efforts have already had on diagnosis and treatment.

Rheumatology News: How significant a role does APS play in some of the more common prothrombotic health problems?

Dr. Hughes: As awareness of the syndrome grows, it is recognized to be a significant contributor to a number of conditions. A 1-in-5 rule seems to apply. That is, it's estimated that APS is associated with 1 in 5 deep vein thromboses, 1 in 5 strokes occurring in people aged 55 years and younger, and 1 in 5 recurrent miscarriages. It is also increasingly recognized as a differential diagnosis in a variety of other conditions. Although I am somewhat prejudiced, I do think that APS is one of the three major connective tissue diseases seen by rheumatologists.

RN: Physicians are probably more aware of the condition than they were a decade ago. What has been the impact of that awareness?

Dr. Hughes: It has translated very palpably into diagnostic and treatment gains. Many patients who had been misdiagnosed with neurologic disease, including multiple sclerosis, have been recognized as having APS and have received successful treatment. When treated for APS, many of the associated neurologic events, including headaches, confusion, and stroke, subside. Similarly, because APS is more readily recognized as a cause of repeated miscarriages, obstetricians are more likely to test for it and the outlook for successful pregnancy in these women is much improved. As awareness continues to grow, so will detection and treatment.

RN: What are some of the challenges of diagnosing APS?

Dr. Hughes: As in all biologic assays, there are significant and well-documented pitfalls. It is commonly recognized that the routine screening tests—the anticardiolipin and lupus anticoagulant—may miss some cases. And increasingly, the term "seronegative APS" is being used to describe the patient with migraine, stroke, several previous miscarriages, thrombocytopenia, and livedo reticularis, whose aPL tests are doggedly negative. Three possibilities spring to mind: The diagnosis may be wrong, conventional testing may fail to pick up cases with antibodies directed against different phospholipids or protein cofactors, or previously positive aPL tests have converted to negative. Clinical observation should still lead the way when it comes to defining disease groups, whatever the shortfalls of the laboratory support.

RN: What are the treatment options?

Dr. Hughes: Once diagnosed, the therapeutic options for anticoagulation are considerable. Aspirin is the most commonly used drug, but there is a very strong role for warfarin, especially in the presence of neurologic manifestations. Also, we use intravenous immunoglobulin quite frequently, especially in an acute situation. Treatment options in pregnancy include starting low-dose aspirin prior to pregnancy, heparin for anticoagulation, and prednisone or intravenous immunoglobulin for immunosuppression.

RN: What advances are in the pipeline?

Dr. Hughes: There is a role for self-testing kits, especially for managing the risk of recurrent miscarriage. Some women suffer multiple miscarriages before the diagnosis is made and others are incorrectly diagnosed with infertility. Even among patients with lupus, it is now recognized that most of the excess fetal loss occurs in association with aPL antibodies. Also, newer forms of anticoagulation are on the way that will possibly dispense with international normalized ratio measurement. Trials underway are assessing the use of heparin in APS headache and the use of immunoglobulin. ■

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