

Antiphospholipid syndrome (APS) or Hughes syndrome - pregnancy

Antiphospholipid antibody syndrome (APS), also known as Hughes Syndrome, is a disorder characterised by multiple antibodies that are associated with both arterial and venous thrombosis. There are three primary classes of antibodies associated with APS:

- anticardiolipin antibodies
- lupus anticoagulant
- antibodies directed against specific molecules including a molecule known as beta-2-glycoprotein 1.

There are two main classifications of APS. If the patient has an underlying autoimmune disorder, such as systemic lupus erythematosus, the patient is said to have secondary APS. If the patient has no known underlying autoimmune disorder, it is termed primary APS.

Mechanism of APS

APS is an autoimmune disorder in which antibodies are produced against certain phospholipids that have (among other functions) a role in the coagulation cascade. The exact mechanism by which the antiphospholipid antibodies and anticardiolipin antibodies induce a thrombophilic state is not known. A great deal of research is being done to explore the interactions these antibodies have with the components of the coagulation cascade and ultimately their role in the hypercoagulable state. There are numerous theories as to how these antibodies cause a hypercoagulable state; each of these theories has supporting evidence and evidence that calls it into question.

Epidemiology of APS

- The prevalence in the general population is around 2-4%.
- Of patients with APS, over half (50%) have primary APS.
- In people with systemic lupus erythematosus, around 30% will develop APS.
- In general, anticardiolipin antibodies are more common than the lupus anticoagulant; anticardiolipin antibodies occur approximately 5 times more often than the lupus anticoagulant in patients with APS.
- In patients with an initial presentation of primary APS, around 10% will eventually be diagnosed with an autoimmune disorder such as systemic lupus erythematosus or a mixed connective tissue disorder.

Risks of APS

The role of APS in both arterial and venous thrombotic disorders is an active area of clinical research. To date, studies examining the role of APS in thrombosis are numerous. APS is associated with both arterial and venous thrombosis but there is controversy regarding the degree of risk and studies have not shown any clear differences between patients with primary APS versus secondary APS.

APS is also associated with an increased risk of recurrent thrombi. Most studies suggest that patients who have a recurrent episode will have it in a similar blood vessel type (in other words, patients who have a stroke initially will most often have a stroke if they have a recurrence) but multiple types of thrombotic events may occur. Thrombocytopenia (low platelet count) occurs in 20-40% of patients with APS.

Pregnancy and APS

APS is also associated with recurrent miscarriage in early pregnancy and other complications of pregnancy including preterm labour, pre-eclampsia and low birth weight. Fetal death beyond the tenth week of gestation is the most typical obstetric complication of APS. It is thought that placental ischaemia due to thrombi in the placenta are the cause. For women with known APS, it is suggested that pre-pregnancy counselling is obtained. This allows the pregnancy to be monitored closely from the beginning.

Several studies have examined the use of low molecular weight heparin and low-dose aspirin at doses of 75 mg daily throughout pregnancy and have demonstrated improved fetal outcomes. Guidelines produced by the Royal College of Obstetricians and Gynaecologists (1) state that aspirin plus heparin significantly improves future live birth rates in women with a history of recurrent miscarriage and antiphospholipid antibodies.

Two studies quoted in these guidelines show that the combination of aspirin and heparin reduced pregnancy loss by 40% and 54% compared with aspirin alone.

Other regimens include aspirin plus prednisone. It appears that the risk of complications associated with prednisone outweigh the benefits in most cases and this combination is not widely used.

The available evidence of the potential benefits of aspirin plus heparin during pregnancy in women with APS has been evaluated in a Cochrane Review (2):

Two trials have shown that unfractionated heparin combined with aspirin significantly reduced pregnancy loss compared with aspirin alone. In a third, low molecular weight heparin (LMWH) plus aspirin did not significantly reduce pregnancy loss compared with aspirin alone. A fourth trial found no advantage for high-dose unfractionated heparin compared with a low-dose regimen.

Three trials of aspirin alone showed no significant reduction in pregnancy loss. Prednisone and aspirin (in three trials) conferred no benefits but was associated with a significant increase in prematurity and gestational diabetes compared with placebo, aspirin, and heparin plus aspirin.

In two trials, intravenous immunoglobulin, with or without unfractionated heparin and aspirin, was associated with increased risk of pregnancy loss or premature birth when compared with unfractionated heparin or low molecular weight heparin combined with aspirin. Another trial found no difference between intravenous immunoglobulin and prednisone plus aspirin.

It was concluded that combined unfractionated heparin and aspirin may reduce pregnancy loss by 54%.

In patients for whom the above treatments are not successful, use of intravenous immunoglobulin has been used. This may be helpful in refractory cases but is not recommended for routine use .

References:

1. Regan, L., Backos, M. J., and Rai, R. The investigation and treatment of couples

with recurrent miscarriage. RCOG Guideline No. 17. 2003. London, Royal College of Obstetricians and Gynaecologists.

http://www.rcog.org.uk/resources/Public/pdf/Recurrent_Miscarriage_No17.pdf

2. Empson, et al, Prevention of recurrent miscarriage for women with antiphospholipid antibody or lupus anticoagulant. Cochrane.Database.Syst.Rev. 2005

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