

Antiphospholipid syndrome (APS) or Hughes syndrome and pregnancy

Key points

- Antiphospholipid antibody syndrome (APS) is an autoimmune disorder associated with an increased risk of thrombosis
- It is associated with an increase risk of foetal death and pregnancy complications
- During pregnancy, combined treatment with aspirin and low-molecular weight heparin reduces the risk of death substantially more than aspirin monotherapy

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

Pathophysiology of APS

APS is an autoimmune disorder in which antibodies are produced against certain phospholipids that have a role in the coagulation cascade. The exact mechanism by which the antiphospholipid antibodies and anticardiolipin antibodies induce thrombophilic state is not known. A great deal of research is being done to explore the interactions between these antibodies and the components of the coagulation cascade, and ultimately their role in the hypercoagulable state.

Epidemiology of APS

- The prevalence in the general population is 2 - 4%.
- Of patients with APS, over half have primary APS.
- Around 30% of people with systemic lupus erythematosus will develop APS.
- In patients with APS, anticardiolipin antibodies are approximately 5 times more frequent than the lupus anticoagulant.
- 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.

Complications of APS

APS is associated with both arterial and venous thrombosis and recurrent thrombosis. There is no apparent difference in risk between primary APS versus secondary APS. Most studies suggest that recurrence will occur in a vessel similar to that involved in the primary event (in other words, patients who have a stroke initially will most often have another stroke if they have a recurrence) but multiple types of thrombotic events have also been reported. Thrombocytopenia occurs in 20 - 40% of patients with APS.

Pregnancy and APS

APS is associated with miscarriage, preterm labour, low birth-weight and pre-eclampsia; this is probably due to ischaemia secondary to placental thrombosis. Foetal death beyond the tenth week of gestation is the most frequent obstetric complication. Pre-pregnancy counselling is recommended for women known to have APS and the pregnancy should be monitored closely.

Several studies have reported improved foetal outcomes after treatment with low molecular weight heparin plus low-dose aspirin throughout the pregnancy (doses of 75 mg/day have been used). Other regimens that have been investigated include aspirin plus prednisone but the complications associated with prednisone use outweigh the benefits for most women.

Guidelines produced by the Royal College of Obstetricians and Gynaecologists COG (1) note that the live birth rate is significantly improved when women with a history of recurrent miscarriage and APS are treated with a combination of aspirin plus heparin. One cited study

showed that this combination reduced pregnancy loss by 54% compared with aspirin alone; a second reported a live birth rate of 40% after treatment with aspirin alone but 70% with aspirin plus a low molecular weight heparin.

In patients for whom the above treatments are not successful, intravenous immunoglobulin is an alternative. Current evidence suggests that this may be helpful in refractory cases but it is not recommended for routine use.

References

1. Regan L, Backos MJ, Rai R. The investigation and treatment of couples with recurrent miscarriage. RCOG Guideline No. 17. 2003. London, Royal College of Obstetricians and Gynaecologists. (www.rcog.org.uk/resources/Public/Recurrent_Miscarriage_No17.pdf)

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