Antiphospholipid antibody syndrome

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Antiphospholipid antibody syndrome ("Hughes' syndrome") is a systemic autoimmune disease, characterised by the association between antiphospholipid antibodies and venous and arterial thrombosis, pregnancy morbidity, or thrombocytopenia.
Antiphospholipid antibodies are a heterogeneous group of auto-antibodies directed against phospholipid-binding proteins.
Antiphospholipid antibodies can be categorised broadly into those that prolong phospholipid-dependent coagulation assays, known as lupus anticoagulants (LAs), and anticardiolipin (aCL) antibodies which target a molecular congener of cardiolipin.
Diagnosis of antiphospholipid antibody syndrome (APS) is based on (1):

Clinical criteria

– **Vascular thrombosis** - One or more clinical episodes of arterial, venous, or small vessel thrombosis in any tissue or organ confirmed by imaging studies, Doppler studies, or histopathology (without significant vessel wall inflammation)
– **Pregnancy morbidity** (normal morphology on ultrasonography or direct examination findings)
  - One or more unexplained foetal deaths at more than 10 weeks' gestation
  - One or more premature births at less than 34 weeks' gestation due to severe pre-eclampsia, eclampsia, or placental insufficiency
  - Three or more unexplained consecutive spontaneous abortions at less than 10 weeks' gestation, excluding maternal anatomical or hormonal abnormalities and paternal and maternal chromosomal causes.
– **Thrombocytopenia**

Laboratory criteria

– Detection of beta 2-glycoprotein-I dependent aCL antibodies of the immunoglobulin G (IgG)/immunoglobulin M (IgM) isotype in medium/high titer (>40 IgG phospholipid units [GPL], >40 IgM phospholipid units (MPL), or >99th percentile) on two or more occasions at least 12 weeks apart (measured by a b 2-GPI-dependent enzyme-linked immunosorbent assay [ELISA]).
– Detection of lupus anticoagulant on two or more occasions at least 12 weeks apart, according to the guidelines set forth by the International Society of Thrombosis and Haemostasis.
  - Prolonged phospholipid-dependent coagulation (e.g., aPTT, Kaolin clotting time [KCT], dilute Russell viper venom test, dilute PT)
  - Failure to correct the prolonged coagulation time by a mix with platelet poor plasma (PPP)
  - Shortening or correction of the prolonged coagulation time with excess phospholipid
  - Exclusion of other coagulopathies (e.g., factor VIII inhibitor, heparin).

This syndrome is referred to as primary APS when it occurs alone and secondary APS when it occurs in association with other conditions such as systemic lupus erythematosus, during therapy with medications such as chlorpromazine, or during infection, neoplasm and haemolymphopathy. The main clinical pictures depend on thrombotic events that can involve both the arterial and the venous system, and affect any vas-

cular bed. Obliterative thrombotic microangiopathy determining perivascular infiltration is the dominant lesion. Antiphospholipid antibodies from patients with the syndrome have been shown to play a direct role in the development of thrombotic manifestations in experimental animal models. Several hypotheses have been proposed to explain the molecular basis of the prothrombotic state associated with these antibodies. Antiphospholipid antibodies have been reported to bind to and activate endothelial cells, interfere with natural anticoagulant pathways, disrupt annexin V binding to anionic phospholipids, and interfere with fibrinolysis. However, the clinical significance of any one (or more) of these pathways remains unclear. Venous thromboembolism is the most common initial clinical manifestation among patients with APS; neurological, renal, cutaneous, myocardial, gastrointestinal and endocrine involvement is also described. Arterial events in APS most commonly involve the cerebral circulation, with stroke being the initial clinical manifestation in 13% and transient ischaemic attack in 7% of patients with APS (2,3). Other neurological symptoms include chronic headaches, dementia (similar to the dementia of Alzheimer's disease), and seizures. Infrequently, individuals will develop chorea (a movement disorder in which the body and limbs writhe uncontrollably), or cognitive dysfunction (such as poor memory). Although it is difficult to predict which patients with antiphospholipid antibodies will develop thrombosis, once a thrombotic event has taken place, secondary prevention is mandatory. Recommendations for treatment of APS have long been based on studies with a retrospective design. Recently, three prospective studies (two controlled and one uncontrolled small series) have addressed the role of anti-aggregant and anticoagulant therapy in patients with stroke and antiphospholipid antibodies. However, results from prospective and retrospective studies are not in full agreement. In addition to the obvious differences in design, other factors such as the considerable variability in the study groups account for the discrepancy. While future investigations must better define homogeneous subsets of patients with APS, current secondary prophylaxis of thrombosis in these patients must be tailored according to individual estimated risk of recurrences, risk of haemorrhage and severity of potential recurrent events. According to APASS (Antiphosphpolipid Antibodies and Stroke Study) data, patients with a first ischaemic stroke and a single positive antiphospholipid antibody test result, who do not have another indication for anticoagulation, may be treated with aspirin (325 mg/day) or moderate-intensity warfarin (INR, 1,4-2,8). Aspirin is likely to be preferred because of its ease of use and lack of need for laboratory monitoring (4).

References

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