ABSTRACT FORM ECAT SYMPOSIUM 8 – 9 NOVEMBER 2018

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Title:

Thrombotic APS pathophysiology: consequences for laboratory diagnosis

Abstract:

In the current classification criteria for antiphospholipid syndrome (APS), only thrombosis and pregnancy morbidity are included. The less frequent clinical manifestations, the so-called non-criteria manifestations (thrombocytopenia, livedo reticularis,…) are often non-thrombotic and not included in the clinical criteria. The diversity of clinical symptoms associated with APS indicate that the pathophysiology of the syndrome cannot be reduced to one mechanism.

A key player in the origin of thrombosis is certainly cell activation (platelets, endothelial cells, monocytes) with signal transduction induced by antiphospholipid antibodies (aPL) resulting in activation of proinflammatory and procoagulant cellular pathways. Influence of aPL on the hemostatic balance may contribute to the hypercoagulable state and upregulation of coagulation systems by aPL is described at multiple levels. Another mechanism is interferences of aPL with complement activation.

It is certain that antibodies against β2GPI, especially those against domain I, can be responsible for the increased thrombogenicity, whereas the role of other antibodies is less clear. Direct evidence for the pathogenicity of these antibodies comes from animal models and cell culture models. Data concerning the clinical relevance of co-factor independent aPL are limited in humans. Recently, anti-prothrombin antibodies get more attention since several studies have indicated their clinical relevance in thrombosis. However, animal models are lacking and we do not know the epitope on prothrombin to which these autoantibodies are directed.

According to the current classification criteria anticardiolipin antibodies (aCL), anti-β2-glycoprotein 1 antibodies (aβ2GPI) and lupus anticoagulant (LAC) are accepted as laboratory criteria. After the discovery of the role of β2GPI, the anti-β2GPI antibodies were added as separate criterion apart from the β2GPI-dependent aCL. LAC persists as a well-established thrombotic risk factor, illustrated in many studies. Although, when isolated LAC only is considered, the risk for thrombosis is low. Evidence has shown that patients with more than one test positive, and particularly those patients with triple positivity show the strongest association with thrombotic APS. So far, antibodies against domain I of β2GPI, should be rather considered as a confirmation of the higher thrombotic risk, rather than a candidate for replacement of the aβ2GPI. Mainly associated with LAC, the additional value of phosphatidylserine/prothrombin antibodies in APS diagnosis needs to be confirmed.

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