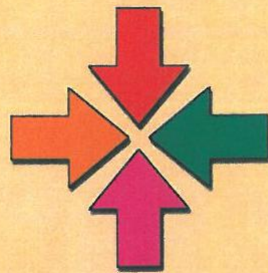


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"Suspect Immune clue until proven otherwise"

REVIEW

Antiphospholipid Syndrome: Pathogenic Mechanisms

Lyudmil Terziev, Petrunka Petrova

Centre of Clinical Immunology, University School of Medicine, Pleven, Bulgaria

SUMMARY: The review presents characteristics of the main antiphospholipid antibodies (cardiolipin and lupus anticoagulant), some factors binding them to the anion phospholipids (β 2-glycoprotein I, prothrombin, annexin V, etc.), as well as their participation in the development of APS. Possible pathogenic mechanisms such as disorders of various anticoagulant systems, synthesis of mediators, activation of platelets and endothelial cells, involvement of endothelin-1 and tissue factor, apoptosis, etc. are discussed.

Key words: antiphospholipid syndrome, antiphospholipid antibodies, cardiolipin, β 2-glycoprotein I, prothrombin, annexin V, apoptosis, tissue factor, lupus anticoagulant, prekallikrein, protein C, protein S, antithrombin III, endothelial cells, platelet

Abbreviations:

APS - antiphospholipid syndrome;	aPL - antiphospholipid antibodies;	aCL - anticardiolipin antibodies;
β 2-GPI - β 2- glycoprotein I;	LA - lupus anticoagulant;	EC - endothelial cells;
P - platelets;	ET-1 - endothelin-1;	TF - tissue factor;
PS - phosphatidylserine;	PE - phosphatidylethanolamine	

The antiphospholipid syndrome (APS) represents a clinicolaboratory complex characterized by venous and/or arterial thrombosis, often multiple, recurrent abortions, usually accompanied by moderate thrombocytopenia and the presence of antiphospholipid antibodies (aPL) such as lupus anticoagulant (LA) and anticardiolipin antibodies (aCL), or both [8]. The pathogenesis of this autoimmune disease is a complex combination of coagulant disorders, presenting on different levels and affecting anticoagulant systems. G. R. W. Hugges was the first to formulate the concept of APS in 1986. During the last 15 years, a great number of pathogenic mechanisms have been found, the clinical aspects have been extended, and efforts made to set up strict criteria in diagnosing APS.

The **antiphospholipid antibodies (aPL)** present a heterogeneous group of antibodies, and N. Harris was the first to find their main property. Through in vitro tests, he found their increased reactivity to the

negatively charged phospholipids in hard-phase immune trials [47]. A year later, T. Exner and D. A. Triplett reported their most important property: the prolongation of the phospholipid-dependent-coagulating test [34, 35]. The concept initially accepted, i.e. that the antibodies act directly against the phospholipid structures, has been revised today, and it is agreed that it can be referred to the syndrome of aPL/cofactor, and not the syndrome of aPL. The role of a cofactor is performed by many plasma proteins such as β 2 glycoprotein 1 (β 2GPI), prothrombin, protein C, annexin V, and low-density kininogens [91, 107].

The phospholipid structures themselves, that are part of this complex, are the negatively charged phosphatidic acid, phosphatidylinositol, phosphatidylserine, cardiolipin, as well as the neutral phosphatidylethanolamine and phosphatidylcholine. These phospholipids are, generally speaking, polar lipids, composed of a phosphate moiety, one or more fatty acid molecules and different chemical head groups, and they possess a non-polar hydrocarbon hydrophobic tail, and a polar hydrophilic head group. Regardless of the variety of their chemical structure, they perform one major function in the cells - structural maintenance.

Correspondence:

Dr. Ljudmil Georgiev Terziev
Centre of Clinical Immunology, University School of Medicine
5800 Pleven, Bulgaria
e-mail: immunelab@abv.bg