Biochemical background of Lupus Anticoagulant

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The antiphospholipid syndrome (APS) is defined as the association of antiphospholipid antibodies (aPL) in plasma of patients with arterial or venous thrombosis or recurrent fetal loss. The clinical manifestations, thrombosis and fetal loss, are (relatively) common and in most patients not due to the presence of aPL antibodies. The diagnosis of the anti-phospholipid syndrome relies on laboratory assays. None of the clinical criteria are specific for this syndrome and in the majority of individuals not due to the presence of these auto-antibodies. The results of the laboratory tests are essential to make the diagnosis. According to an international consensus meeting, the use of three different assays are permitted to detect the presence of these antibodies, one clotting assay, the lupus anticoagulant (LA), and two ELISAs with cardiolipin or β_2-Glycoprotein I (β_2GPI) as antigen, respectively. These three assays measure overlapping but not the same population of auto-antibodies and numerous studies have shown that LA correlates the strongest with the clinical manifestations that define the syndrome. LA measures auto-antibodies against prothrombin and β_2GPI, with the restriction that only a subpopulation of auto-antibodies directed to β_2GPI or prothrombin is able to induce a prolongation of a clotting assay.
Lupus anticoagulant is a surrogate biomarker; it correlates strongly with thrombotic complications and fetal loss but its in vitro activity, prolongation of clotting times, cannot explain the clinical observations. Thus LA is an epiphenomenon, its mode of action will not help to understand the pathophysiology of the syndrome. Nevertheless, understanding of how the mutual interaction between the auto-antibodies, plasma proteins and anionic phospholipid causes a prolongation of a clotting assay is very important for the development of a reliable diagnostic test. In this presentation I will review the biochemical background of lupus anticoagulant, how these auto-antibodies can compete with clotting factors for the available catalytic anionic phospholipids, the relative importance of anti-β_2GPI and anti-prothrombin antibodies, the characteristics of the proteins involved and the influence cations can have on the results.