THE ANTIPHOSPHOLIPID SYNDROME: A LABORATORY PHENOMENON ?

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The Antiphospholipid Syndrome (APS) is defined by thrombotic and/or obstetric events together with the presence of one or more of the three most common antiphospholipid antibodies (aPL), i.e. lupus anticoagulants (LAC), IgG/IgM anticardiolipin (aCL) and IgG/IgM antiβ2-glycoprotein I (aβ2-GPI) antibodies. Since the clinical events are relatively common in the general population and they do not have peculiar features, the presence of aPL is the necessary requirement to reach a proper diagnosis of APS. In this respect, APS may be considered a laboratory phenomenon, which explains the enormous work performed in the last decades to establish clear and reproducible diagnostic criteria.

The original clinical and laboratory criteria for APS were set by a group of experts in 1998 and updated in 2006. From a laboratory viewpoint, diagnosis of aCL and aβ2-GPI relies on the persistent presence of IgG or IgM at medium or high titers measured by ELISA and that of LAC on the coagulation tests originally proposed in 1995. The update of LAC diagnosis has been presented and discussed during the 54th annual meeting of the ISTH Subcommittee held in Vienna in July 2008. Clear and easy recommendations regarding which patients should be investigated, how to handle blood samples, which coagulation tests should be used, how to express, interpret and transmit the results and how to detect LAC in patients under oral anticoagulation will soon be available.

The correct diagnosis of the various aPL is strictly linked with the issue of their clinical relevance, i.e. their ability to establish the risk profile of the individual patient in order to guide his/her primary or secondary thromboprophylaxis. LAC consistently shows the highest strength of association with the arterial and venous thrombotic complications both in adults and in children. aCL and aβ2-GPI are less strongly associated, even though the former antibodies represent a possible risk factor for arterial thrombosis when present at high titre and the latter ones for venous thrombosis. In recent years, some groups have shown a stronger association between thrombosis and the presence of multiple positive aPL tests when compared to a single positive test. LAC is a laboratory phenomenon caused by the anticoagulant effect of aβ2-GPI and anti-prothrombin antibodies (aPT), which may be present alone or in combination. In other words, LAC is essentially a measure of the functional activity of subgroups of aβ2-GPI and aPT, which explains the partial overlap between LAC, aCL and aβ2-GPI on the one side and between LAC and aPT on the other. In the last years, tests developed to distinguish between β2-GPI-dependent and aPT-dependent LAC showed that only the former antibodies are consistently associated with thrombosis. Finally, most data dealing with the diagnosis and treatment of obstetric APS regard LAC and aCL, and less information is available about aβ2-GPI.