HOW TO MANAGE ASYMPTOMATIC CARRIERS OF ANTIPHOSPHOLIPID ANTIBODIES

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Individuals who do not display the classical features of the Antiphospholipid Syndrome (APS) (vascular and obstetric disease) are referred to as “aPL carriers”. They can be patients affected by systemic autoimmune diseases who are screened for antiphospholipid antibodies (aPL). aPL may be found in patients with “non-criteria” manifestations or in women undergoing investigations for infertility. The presence of aPL can be serendipitously discovered before a surgical procedure because of a prolonged thromboplastin time. Are these subjects at increased risk for thrombosis and adverse pregnancy outcomes (APO)? Since aPL are pathogenic autoantibodies, the answer should be “yes”. However, the magnitude of the risk can be variable from patient to patient, accordingly to the multifactorial nature of the disease.

According to international consensus,1 the thrombosis risk stratification should consider: 1) the aPL profile (type, titer, persistence), 2) the coexistence of other thrombotic risk factors, and 3) the presence of an underlying autoimmune disease. Mainly systemic lupus erythematosus (SLE), the definition of “high-risk” aPL profile comprises positivity for Lupus Anticoagulant (LA), or triple positivity, i.e. LA and aCL or anti-β2GPI antibodies. Conversely, patients with isolated, intermittently positive aCL or IgG anti-β2GPI, which was at low-medium titers, could be considered at low risk for thrombosis.

According to the literature, aPL carriers seem to have a low annual incidence of acute thrombosis, ranging from 0% to 3.8%.4 These figures are not much different from the estimated incidence of thrombosis in unselected cases (about 1% patient-years), which is also equivalent to that of major bleeding associated with the use of low dose aspirin (LDA), the most frequently used drug for primary prophylaxis.5 Therefore, the dilemma in clinical practice is to correctly select those aPL carriers for whom the expected benefit of therapy outweigh the risk.

Over years, the management of aPL carriers has been investigated in several studies enrolling different patient groups (SLE, pure obstetric APS, asymptomatic aPL carriers) and evaluating the efficacy of various interventions: LDA,6 low intensity warfarin,7 low molecular weight heparin (LMWH) in high risk situations such as surgery, prolonged immobilisation, and puerperium.8,9

Aside from drugs acting on platelets and on the coagulation system, there is evidence that immunomodulatory agents may be beneficial in primary prophylaxis of aPL carriers. Hydroxychloroquine (HCQ) is a well-recognised key-drug in the management of SLE patients and has an anti-thrombotic effect.10 The use of HCQ as primary prophylaxis has been proposed also for non-SLE patients.11 Statins may be useful in aPL carriers not only for the correction of a proatherogenic lipid profile, but also for reducing proinflammatory and prothrombotic biomarkers.12

Turning to the obstetric field, the detection of aPL antibodies has been increasingly performed in asymptomatic women, mainly for obstetrical reasons (e.g. before assisted reproductive techniques, after APO that are not included in APS classification criteria). Therefore, it is not infrequent to take the responsibility to recommend or not a treatment in “healthy” pregnant women carrying aPL. General obstetric risk should be assessed (age, hypertension, obesity, etc.). It is currently under discussion whether different aPL profiles confer the same degree of obstetric risk. LA and triple aPL positivity seem to be the major predictors of APO, although APO have been described also in patients with a “low-risk” aPL profile (e.g., IgM isotype or medium to low aPL titers).13,14 A key drug for primary obstetric prophylaxis is LDA and many physicians prescribe it to pregnant aPL carriers.15

The immunomodulatory properties of HCQ have been advocated to be beneficial in pregnant patients with aPL16 and clinical retrospective studies supported its effectiveness in refractory obstetric APS.17,18 Puerperium is considered a high-risk period for thrombosis for all women. Women who carry aPL should be considered for LMWH for 4–6 weeks after delivery.19

REFERENCES:
15. Lockshin MD. 2012.

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THE COMPLEX INTERPLAY BETWEEN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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The antiphospholipid syndrome (APS) was first described in the 1980’s. It is diagnosed when antiphospholipid antibodies (aPL) i.e. anti-cardiolipin (aCL), anti-β2Glycoprotein-I (anti-β2GPI), or medium-high titers of IgG aCL or IgG anti-β2GPI, are present. Conversely, patients with isolated, intermittently positive aCL or low anti-β2GPI, which was at low-medium titers, could be considered at low risk for thrombosis.

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The antiphospholipid syndrome (APS) was first described in the 1980’s. It is diagnosed when antiphospholipid antibodies (aPL) i.e. anti-cardiolipin (aCL), anti-β2Glycoprotein-I (anti-β2GPI) or positivity in the functional lupus anticoagulant test (LA) occurs together with any type of thrombosis (e.g. myocardial infarction, MI), stroke, venous or microvascular (thromboses) or obstetric complications.1,2 aPL recognise protein co-factors, most importantly the scavenger protein α2-Macroglobulin (α2M), that bind to membrane phospholipids. It is not fully understood how the complexes of β2GPI and anti-β2GPI antibodies initiate a pro-thrombotic state, but activation of platelets, endothelial cells and the complement cascade are associated features. Approximately 80% of APS patients are women, many are young and severely ill. There is a considerable overlap between APS and SLE. Approximately 30%–40% of SLE patients are aPL positive but only about half of them develop clinical symptoms fulfilling the APS classification criteria.