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LETTER TO THE EDITOR

Antiphospholipid antibodies negativization: time for testing for non-criteria aPL?

Sir,

While we read with interest the recent article by Comarmond and colleagues[1] about the cessation of oral anticoagulants in antiphospholipid syndrome (APS), we do feel there are some points of the study still open for discussion.

Comarmond and colleagues[1] describe 10 patients with prolonged disappearance of antiphospholipid antibodies (aPL) that were stopped anticoagulation therapy. After a median duration of follow-up of 19 months since the cessation of oral anticoagulants, one out of 10 patients relapsed developing pulmonary embolism.

Recent findings contribute to the hypothesis that a persistent negative aPL profile is not an indication to interrupt oral anticoagulant therapy.

Medina and colleagues[2] investigated aPL negativization in a retrospective study in a large cohort of 70 patients with primary APS. Patients were tested for the presence of aPL, including anti-annexin A5 antibodies and, when found negative, patients were re-tested after 5 years to confirm the disappearance of autoantibodies. Persistent negativization of aPL was detected in 24 out of 70 patients. Since aPL disappearance and after 60 months of follow-up, 11 out of 24 patients (45.8%) presented with recurrence of thrombosis despite the anticoagulant treatment.

Laboratory criteria for APS include the assay test for the presence of lupus anticoagulant, anticardiolipin antibodies (aCL) and anti-β2-glycoprotein I antibodies (anti-β2GPI).[3] However, in patients with persistent disappearance of aPL, a second level screening of non-criteria aPL should be strongly encouraged before stopping the anticoagulant treatment.

For instance, the use of IgA isotypes for both aCL and anti-β2GPI are not a part of the routine diagnostic algorithm.[4] However, some data suggested a role of isolated positivity for IgA anti-β2GPI with clinical APS symptoms that might help to identify additional patients who are at risk of developing thrombotic events, recommending these tests when other aPL are negative.[4] Furthermore, among the so-called extra-criteria aPL tests, anti-prothrombin, mainly anti-phosphatidylserine/prothrombin antibodies, and anti-β2GPI domain1 antibodies have been proposed potentially to improve the diagnostic accuracy, especially when assessing the risk for both thrombosis and pregnancy morbidities in patients with suspected APS. Other antibody specificities, such as anti-annexin A5 and anti-vimentin antibodies, might be considered for thrombotic risk assessment only in selected patients, particularly when other aPL tests are negative and in the presence of clinical APS signs and/or symptoms. Indeed, further investigations are needed to assess their role in the diagnostic algorithm for APS.[5] Moreover, it would be of great interest to establish an accurate definition of the disappearance of aPL, because it might be important to specify for how long and how many negative tests must be considered to define a patient as negativized.

Persistent aPL disappearance is a hot topic in the field of APS, and further prospective studies are needed to assess successful therapeutic strategies. However, a second level screening in patients with aPL negativization is highly suggested before interrupting oral anticoagulation. Besides, when stopping anticoagulation, a physician should consider that aPL is not the only thrombotic risk factor to develop a thrombotic event in a patient. A thorough cardiovascular risk factors evaluation should always be considered and recommended before stopping anticoagulation treatment.

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