Publication of the Month

November 11/10: IgA anti-ß2-Glycoprotein I Autoantibodies

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IgA Anti-β2-Glycoprotein I Autoantibodies Are Associated with an Increased Risk of Thromboembolic Events in Patients with Systemic Lupus Erythematosus

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Background: According to the international consensus statement on antiphospholipid syndrome (APS), antiphospholipid antbodies (aPL) of the IgG or the IgM isotype have to be positive for the classification of APS. The IgA isotype (either anticardiolipin antibodies [aCL] or anti-β2-glycoprotein I antibodies [anti-β2GPI]) do not fulfil laboratory criteria for APS classification. However, they are discussed in the consensus paper. They were not considered as diagnostic marker because of a lack of specificity of this marker and because of a lack of data showing their role in APS. It is unclear whether ethnicity may play a role in the prevalence of IgA anti-β2GPI antibody. However, there are hints that anti-IgA occur more often in Africans, Afro-Americans and Hispanic populations than in Caucasians. However, in certain cohorts, many individuals test positive for IgA aPL without other aPL. Therefore, the role of IgA antibodies against anti-β2GPI is controversially discussed.

Summary: Sweiss et al. reasoned that if IgA aPL contribute to the clinical manifestations of the antiphospholipid syndrome, then an association with thromboembolic events should manifest in patients whose only aPL is of IgA isotype. They performed a retrospective chart review of 56 patients (31 with systemic lupus erythematosus [SLE] and 25 without SLE) whose only positive aPL was IgA anti-β2GPI and compared their clinical features with 56 individually matched control patients without any aPL. Patients with isolated IgA anti-β2GPI had a significantly increased number of thromboembolic events, as compared to controls. When patients were stratified into those with and without SLE, the association between isolated IgA anti-β2GPI and thromboembolic events persisted for patients with SLE, but was lost for those without SLE. Titers of IgA anti-β2GPI were significantly higher in SLE patients who suffered a thromboembolic event. Among patients with isolated IgA anti-β2GPI, there was an increased prevalence of diseases or morbidities involving organs of mucosal immunity (i.e. gastrointestinal system, pulmonary system, and skin).

Conclusions: 23 of the 56 patients with isolated IgA anti-β2GPI had repeated aPL testing, and, of these, 21 had persistently positive IgA anti-β2GPI. Thromboembolism occurred in 13 (62%) of the patients with persistently elevated IgA anti-β2GPI.
The presence of isolated IgA anti-β2GPI is associated with an increased risk of thromboembolic events, especially among patients with SLE. IgA anti-β2GPI is associated with an increased prevalence of morbidities involving organs of mucosal immunity.

Comment: Although the patient cohort in this study is rather small, it still can serve as a clear hint for the relevance of IgA anti-β2GPI in the diagnosis of APS.