Publication of the Month

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September 09/11: Pathogenesis of the Antiphospholipid Syndrome

Key messages:

- *Antiphospholipid antibodies (aPL) are both diagnostic markers and pathogenic drivers for the antiphospholipid syndrome.*
- *β2 glycoprotein I-dependent autoantibodies seem to be the main pathogenic subpopulation of aPL.*

Meroni PL, Borghi MO, Raschi E, Tedesco F
Pathogenesis of antiphospholipid syndrome: understanding the antibodies
Nat. Rev. Rheumatol. 2011; 7: 330-339

Background:
Antiphospholipid syndrome (APS) is characterized by vascular thrombosis and/or pregnancy morbidity, in association with antiphospholipid antibodies (aPL). Detectable by anticardiolipin, anti-β2 glycoprotein I and lupus anticoagulant assays, aPL are not only diagnostic of APS but are also believed to have a pathogenic role, mediating several clinical manifestations of the syndrome.

Key points:

- Antiphospholipid antibodies (aPL) are autoantibodies that are diagnostic and pathogenic for APS.
- aPL mediate several procoagulant mechanisms that can explain their thrombogenic effect in animal models, and their epidemiological association with APS in clinical studies.
- Whereas evidence shows that a second hit (usually an inflammatory event) is required for thrombus formation in APS, this requirement is less clear for fetal loss.
- In addition to placental thrombosis, other mechanisms for direct effects of aPL on placental tissues have been proposed.
- β2 glycoprotein I (β2GPI)-dependent autoantibodies seem to be the main pathogenic subpopulation of aPL.
- More information about the epitope specificity of anti-β2GPI aPL, as well as about the tissue expression of the target molecule, might help to better understand the pathogenesis of APS.

Conclusions:
Although APS is considered as a single disease, there seem to be slightly different mechanisms for the two clinical manifestations of APS, thrombosis and pregnancy morbidity. Thrombosis does not seem to have sole responsibility for the obstetrical complications. The three aPL subtypes (anticardiolipin, anti-ß2GPI and lupus anticoagulant) detect slightly different populations. Whether different subpopulations of autoantibodies, detected by the same diagnostic assays, are responsible for the different clinical manifestations remains an open question.

Comment:
Pier Luigi Meroni et al. published this review on the pathogenesis of the antiphospholipid syndrome (APS) in Nature Reviews / Rheumatology in June this year. This article is the most comprehensive and summarizing review on this matter in the last years and is worth to read for everybody interested in autoimmunity and in particular in APS. It is available with free access online (http://www.nature.com/nrrheum/journal/v7/n6/full/nrrheum.2011.52.html).

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