COMPLEMENT ACTIVATION IN PERIPHERAL BLOOD IN RELATION TO LUPUS, ANTIPHOSPHOLIPID AND RHEUMATOID ARTHRITIS AUTOANTIBODIES: INSIGHTS FROM CLINICAL LABORATORY EVALUATIONS

Thierry Dervieux, John Conklin, Joanne Ligayon, Rowena Lafon, Armida Sace, Tyler O’Malley, Roberta Alexander, and Claudia Ibarra
Exagen Diagnostics, Vista, CA
**ABSTRACT**

**OBJECTIVE**

Evaluate the relationships between complement activation and autoantibodies associated with SLE, APS and RA from a large diagnostic immunoLOGY database.

**RESULTS**

Of the 32,404 patients tested 12% of them presented with abnormal complement activation. The overall incidence of autoantibodies ranged from 1% (anti-Sm) to 13.1% (IgM RF). The presence of SLE and APS antibodies were all associated with abnormal complement activation with adjusted OR ranging from 1.40 for anti-C1q (C195%: 1.24-1.58) to 4.52 for anti-dsDNA (C195%: 3.95-5.17), and from 1.47 for anti-cardiolipin IgG (C195%: 1.22-1.77) to 3.2 for anti-PS/PT IgM (C195%: 3.20-2.92), respectively (p<0.02). Of the 4 RA associated antibodies, only anti-CCP (adjusted OR=1.25, C195%: 1.02-1.54) and IgM RF (adjusted OR=1.17, C195%: 1.04-1.32) were significantly associated with complement activation (p<0.05). Figure 1 illustrates the relationship between the cumulative presence of lupus, APS and RA autoantibodies and abnormal complement activation. Across the cumulative range of SLE and APS associated antibodies, a 319-fold (CI95%: 240-424), and 120-fold (C195%: 94-153) increase in the likelihood of abnormal complement was detected. In contrast, the cumulative presence of RA autoantibodies yielded minimum impact of the likelihood of abnormal complement activation (adjusted OR=2.3; C195%: 2.0-2.7).

**CONCLUSION**

These diagnostic immunoLOGY data suggest that complement activation in peripheral blood is intimately related to SLE and APS antibodies.

**METHODS**

From May 2014 to November 2016, a cohort of 32,404 patients within the United States (mean 51±15 [SD] years, 86% females) was tested. EDTA whole blood and serum were collected within 48 hours of patient examination. and processed centrally in a CLIA certified/CAP accredited clinical laboratory. Abnormal complement activation was detected using peripheral blood and C4d bound to erythrocyte or B lymphocyte levels above the 99th percentile of normal healthy group. The panel of 15 autoantibodies (all determined by immunoassays) consisted of 5 SLE associated autoantibodies (anti-dsDNA confirmed using Crithidia, anti-U1 RNP, anti-C1q, anti-ribosomal P, anti-Smith, all IgGs), 6 APS associated autoantibodies (anti-cardiolipin, anti-beta2 glycoprotein 1, anti-phosphatidylycerine/prothrombin complex antibodies, IgM and IgG) and 4 RA associated autoantibodies (anti-CCP, anti-MCV, IgM RF, IgA RF). Patient data were de-identified prior to analysis. The relationships between abnormal complement activation and the presence of the autoantibodies were analyzed using multivariate logistic regression with abnormal complement activation as the dependent variable and the presence of autoantibodies as independent predictors. Adjusted Odds ratio were calculated for each of the autoantibodies.

**CB-CAPS AND AUTOANTIBODIES**

The table highlights the incidence of abnormal CB-CAPS and autoantibodies observed in the diagnostic immunoLOGY database.