A6 ANTI-ARGONAUTE 2 (AGO2/SU) AND -RO ANTIBODIES ARE THE COMMON AUTOANTIBODY SPECIFICITIES IN PRIMARY ANTI-PHOSPHOLIPID SYNDROME (PAPS)

A Ceribelli, I Cavazzana, F Franceschini, A Tincani, B A Pauley, J Y F Chan, E K L Chan, M Satoh *Rheumatology Unit and Chair, Università degli Studi, Spedali Civili, Brescia, Italy*

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Purpose Primary antiphospholipid syndrome (PAPS) is defined as patients with anti-phospholipid antibodies and thrombotic or obstetric symptoms, without systemic lupus erythematous (SLE) or other systemic rheumatic diseases. PAPS patients can have incomplete SLE-like features and some can evolve into SLE during follow-up. However, few studies systematically examined lupus autoantibodies and their clinical significance in PAPS. The aim of our study is to characterise lupus autoantibodies in PAPS to analyse their clinical and laboratory correlations and their predictive role for the evolution of PAPS into SLE.

Methods Sera from 52 PAPS patients were screened by indirect immunofluorescence (IIF) antinuclear antibodies (ANA), immunoprecipitation (IP) of 35S-labeled K562 cell extract and ELISA (anti-argonaute 2 (Ago2, Su), 60kRo, 52kRo, La, dsDNA)). Anti-Ago2/Su positive sera were also tested for anti-GW body (GWBs) by IIF double staining using rabbit anti-GWBs serum.

Results ANA were positive in 56% of PAPS patients. Anti-Ago2/Su antibodies were found in 13% (7/52) and anti-Ro/SSA in 10% (5/52) by IP. Interestingly, 79% (41/52) were negative by IP, thus anti-Ago2/Su and anti-Ro/SSA were the only identifiable specificities by IP in PAPS patients. No other lupus-related autoantibody was detected. Positive samples had a single specificity except one case that had both. No particular association with clinical features of anti-phospholipid syndrome was found, except that IgG anti-β2glycoproteinI (β2GPI) antibodies were less frequent in anti-Ago2/Su positive patients ($p=0.02$). Although 2/7 anti-Ago2/Su positive patients had malar rash, there was no significant association between the presence of anti-Ago2/Su or Ro/SSA and SLE-like features in PAPS. None of anti-Ago2/Su or –Ro positive patients developed SLE during follow-up. Although Ago2 is a key component of GWBs and IIF staining of Ago2 localises to GWBs, only 1/7 anti-Ago2/Su serum showed a typical cytoplasmic GWBs staining.

Conclusions Anti-Ago2/Su (13%) and –Ro (10%) antibodies were found in sera from PAPS, but no other lupus-related autoantibodies were identified by IP. Ago2, a microRNA binding protein, is a key component in RNA silencing complex but the link with PAPS remains to be clarified. A recent report on specific interaction of Ro60 and β2GPI in apoptotic cells may be relevant to our finding. Clarifying why Ago2/Su and Ro are specific targets of autoimmune response in PAPS may help to understand the mechanisms of autoantibody production.