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ANTIBODIES TO BOTH RO52 AND RO60 DEFINE A SUBSET OF SJÖGREN’S MOST SUITABLE FOR CLINICAL TRIALS OF AGENTS TARGETING LYMPHOPROLIFERATIONS

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Background: Anti-SSA antibodies comprise reactivity to two distinct proteins, Ro52 and Ro60, encoded by separate genes and found on separate ribonucleoprotein particles. Specific testing for Ro52 and Ro60 antibodies is now clinically available, yet the phenotypic correlates of Ro52 and Ro60 reactivity profiles have not been well defined.

Objectives: To determine the phenotypic correlates of antibody reactivity to Ro52 alone, Ro52 + Ro60, and Ro60 alone in patients being evaluated for Sjögren’s syndrome (SS).

Methods: We initially studied 840 patients seen at the Hopkins Sjögren’s Syndrome Center with suspected or established SS. Each had serum tested for antibodies to recombinant Ro52 (Inova Quanta Lite ELISA) and Ro60 (IVTT immunoprecipitation). We then validated our findings in a second cohort consisting of 194 patients, each with testing for antibodies to recombinant anti-Ro52 and anti-Ro60 by a chemiluminescent assay (Inova Bioflash). Statistical analyses were performed using JMP pro 13.

Results: The discovery cohort of 840 patients included 751 (89%) women, with a mean age of 58±13.5 years. 371 (44%) patients met the ACR/EULAR classification criteria. There were 311 with anti-Ro52 +Ro60, 108 with anti-Ro60 alone, 95 with anti-Ro52 alone, and 326 with neither antibody. The 311 patients with anti-Ro52+Ro60 reactivity had a distinctive phenotype, with a markedly increased prevalence of ANA>1:320, RF, IgG>1560 mg/dL, and SS-B positivity (p<0.008 for all inter-group comparisons) and an increased prevalence of focus score ≥1 and hypechoic lesions on parotid gland ultrasonography which trended toward statistical significance. These differences were also validated in the second cohort, with the exception of focus score and parotid gland hypechoic lesions, possibly as a result of smaller group numbers. The Ro52 and Ro60 alone groups were equivalent to each other in their phenotypic associations, except for RF, which was higher in the Ro52 alone group. Measures of lacrimal and salivary gland function and the prevalences of extraglandular manifestations did not show consistent differences between the groups or the two cohorts.

Conclusion: Testing anti-Ro52 and anti-Ro60 in patients with suspected or established SS identifies a unique subset, namely those with both Ro52 and Ro60 antibodies, distinguished by a much higher prevalence of B-cell activation markers and glandular inflammation as measured by focus score and hypechoic lesions. This subset may be most suitable for inclusion in clinical trials where the therapeutic agent targets glandular lymphoproliferation.

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