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## SSA Positivity as Predictor of Relapse in Patients with Neuromyelitis Optica Spectrum Disorder

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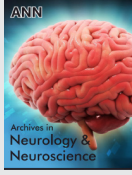
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## Opinion

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# SSA Positivity as Predictor of Relapse in Patients with Neuromyelitis Optica Spectrum Disorder

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## Opinion

Neuromyelitis Optica Spectrum Disorder (NMOSD) is an autoimmune astrocytopathy that is associated with serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG) [1]. This central nervous system (CNS) inflammatory syndrome has specific core clinical characteristics, three common presentations include optic neuritis that can be bilateral with more severe visual impairment as compared with patients with multiple sclerosis, longitudinal extensive transverse myelitis (LETM) typically involving three or more vertebral segments, and area postrema syndrome characterized by intractable hiccups and intractable nausea & vomiting.

The association of NMOSD with other autoimmune entities is well recognized. The latest diagnostic criteria by the international panel of NMO diagnosis include the coexistence of systemic lupus erythematosus (SLE) and Sjögren syndrome (SS) in the spectrum of this condition [2]. Several mechanisms for the co-association of AQP4 and SSA have been proposed such as common genetic or environmental factors that could predispose the patient for autoimmunity. Moreover, the presence of autoantibodies and other inflammatory pathways may contribute to the disruption and loss of integrity of the blood brain barrier, which could then facilitate the CNS manifestations of NMOSD [3]. The clinical implications of the association between AQP4 and SSA are poorly understood and have not been investigated in a large cohort.

Our objective was to determine if anti-Ro (SSA) positivity (+) is a predictor of relapses and disability among patients with NMOSD. Using an ICD-9/ICD-10 diagnosis for NMOSD, after obtaining institutional IRB approval, we conducted a retrospective chart review at three different medical centers in New Orleans between the period of July of 2018 and July 2010. Data extracted included age, gender, race, SSA, AQP4-IgG, expanded disability status scale (EDSS), disease modifying therapy (DMT), and time since initial presentation for each relapse. We used a repeated events Cox proportional-hazard model to determine the predictors of relapse risk. Furthermore, we also determined the predictors for time to sustained EDSS  $\geq 7$ .

We identified 29 patients with NMOSD, of these we found 11 with SSA antibody. From our 29 patients with NMOSD, mean age was  $\pm$  SD =  $45 \pm 13$  years, 79% were female. SSA positivity was determined by serological testing and patients were included regardless of a clinical diagnosis of Sicca syndrome. As far as race, 72% were African American (AA), and 18% were Caucasian. All of our patients met diagnostic criteria for NMOSD2, 69% were AQP4+ (cell-based assay). 30% of patients were SSA+ and all of these patients were African American (AA) females. 24% patients were AQP4+ and SSA+.

Patients with NMOSD that were positive for SSA+ were at higher risk of relapse (HR 1.95(1.10,3.44)),  $p=0.0017$ . AQP4+ patients

showed a trend for higher relapse risk (HR 1.23(0.65,2.33)),  $p=0.3$ ). After controlling for gender and age, SSA+ remained a significant predictor of relapse risk in patients with NMOSD (HR 1.70(1.10,2.65)),  $p=0.03$ ).

Restricting the analysis to women with NMOSD also showed that SSA+ was a significant predictor of relapse risk. (HR 1.79(1.19,2.69)),  $p=0.03$ ).

Moreover, there was a trend in SSA patients for higher risk of sustained severe disability (EDSS $\geq$ 7) (HR 5.0(0.9-27),  $p=0.06$ ). Another observation was that the use of Rituximab reduced the risk of relapse (HR 0.27 (0.10, 0.77),  $p=0.003$  compared to no DMT.

Our study is limited due to its retrospective design; however, our results suggest that patients with NMOSD and SSA+ have almost twice the risk of relapse, and a trend toward greater disability. These findings may support the previously proposed mechanism of co-association between AQP4 and SSA where the presence of several autoantibodies could disrupt the BBB and therefore lead to more devastating clinical syndrome<sup>3</sup>.

These findings may help guide clinicians when approaching patients presenting with NMOSD and SSA positivity. It would be

reasonable for one to more cautiously monitor these patients and consider using more aggressive therapies in this subset of patients with NMOSD. These results need to be validated in a larger cohort.

### Statistical Analysis

Our statistical analysis was conducted by senior author, Dr. Jesus F. Lovera, MD, MsPH. Louisiana Healthcare Science Center, at New Orleans.

### Acknowledgement

None.

### Conflict of Interest

No conflict of interest.

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