Primary Sjögren Syndrome in a Child with a Neuromyelitis Optica Spectrum Disorder

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To the Editor:

Neuromyelitis optica spectrum disorders (NMOSD) are a group of rare autoimmune diseases typically affecting women in their 40s and 50s, as does Sjögren syndrome (SS), another autoimmune disease. We describe a 6-year-old girl who presented with clinical and laboratory findings of both an NMOSD and SS.

A 6-year-old previously healthy Korean girl presented with a 1-day history of fever, headache, progressive right-sided weakness, and altered mental status. Cerebrospinal fluid (CSF) analysis revealed an elevated protein without pleocytosis or oligoclonal bands. Magnetic resonance imaging (MRI) of the spinal cord showed contiguous T2 hyperintensity, and MRI of the brain showed extensive white matter lesions bilaterally (Figure 1), suspicious for demyelinating disease. She was treated with high-dose methylprednisolone, resulting in marked improvement, and continued treatment with tapering doses of prednisone, but flared when the prednisone was discontinued.

CSF was positive by ELISA for neuromyelitis optica autoantibody (NMO)-immunoglobulin G (IgG), as was the serum when subsequently tested. Blood was also positive for antinuclear antibody (ANA) at 1:160 (speckled) and anti-SSA (Ro) antibody. Anti-SSB (La), anti-dsDNA, anti-Sm, and anti-RNP antibodies, rheumatoid factor, and complement factor 3 (C3) and C4 were negative or normal. The patient also started receiving azathioprine (AZA) as a steroid-sparing agent.

The patient had no symptoms of SS, such as mouth or eye dryness, joint pain, or parotitis. An ophthalmological examination was normal. However, a minor salivary gland biopsy revealed > 1 lymphocytic aggregate per 4 mm², consistent with a diagnosis of SS. Based on studies showing its efficacy in treating both SS and NMOSD1,2, rituximab (RTX) was started, after which the prednisone and AZA were discontinued. Repeat MRI demonstrated improvement and no new lesions. Three years after presentation, continued treatment with RTX every 6 months and taking no other medica-

Primary SS in children, though rare, has been reported6,7. SS is characterized by plasma cell and lymphocyte infiltration of the exocrine glands, classically resulting in clinical xerostomia and xerophthalmia. In children, however, SS often presents insidiously, most commonly with recurrent parotid swelling, but also with a broad spectrum of symptoms outside of the typical sicca syndrome seen in adults6,7. CNS involvement is well documented in both pediatric and adult patients with SS8. Patients with SS usually have anti-SSA and/or anti-SSB antibodies, but the presence of these antibodies may not be of diagnostic significance and may be present in completely asymptomatic individuals. Because of the lack of typical symptoms in pediatric SS, diagnosis is often difficult.

NMOSD have a high prevalence of coexistent autoimmune disorders and markers. Over 40% of adult patients with NMOSD have comorbid autoimmune diseases and over 75% have autoantibodies aside from NMO-IgG: as many as 64% also have a positive ANA and 15%–38% have a positive SSA4. Interestingly, while there are multiple reports of coexisting SS and NMOSD in adults6,7, to our knowledge, this has not been definitively reported in pediatrics. Several patients with NMOSD have been reported to have
positive anti-SSA. While these patients may also have had SS, they either did not otherwise meet diagnostic criteria for SS (because of the lack of salivary gland biopsies)\(^{10}\) or specific details concerning SS diagnosis were not published\(^{4}\). Clinical and imaging findings possibly consistent with an NMOSD along with definitive SS have also been reported, but the diagnosis of an NMOSD was not confirmed because no NMO-IgG results were reported\(^{8,11}\).

An intrinsic link between SS and NMOSD has been suggested\(^{12}\). The human salivary glands possess aquaporin-3 and aquaporin-5 channels\(^{13}\); AQP4 channels have been found in rodent salivary glands\(^{14}\). Autoimmunity in the salivary gland, in the context of SS, may result in an immune response against AQP4\(^{12}\). Previous studies have suggested that patients with SS with neurologic deficits should have an examination for NMOSD\(^{15}\). Conversely, our case suggests that patients presenting with NMOSD should be evaluated for the possibility of SS, and in addition highlights the difficulties inherent in detecting and diagnosing SS in children.

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REFERENCES