Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

J Rheumatol. Author manuscript; available in PMC 2018 June 01.

Published in final edited form as:

J Rheumatol. 2017 June ; 44(6): 959–960. doi:10.3899/jrheum.160978.

Pediatric Neuromyelitis Optica Spectrum Disorder and Sjögren Syndrome: More Common Than Previously Thought?

Sabrina Gmuca, MD,

Department of Pediatrics, Division of Rheumatology, The Children's Hospital of Philadelphia, Philadelphia, PA

Scott M. Lieberman, MD, PhD, and

Stead Family Department of Pediatrics, Division of Rheumatology, Carver College of Medicine, University of Iowa, Iowa City, IA

Jay Mehta, MD, MS

Department of Pediatrics, Division of Rheumatology, The Children's Hospital of Philadelphia, Philadelphia, PA

Key Indexing Terms

Pediatric Sjögren's syndrome; Neurologic manifestations; Autoimmunity

To the Editor

We read with interest the report by Kornitzer *et al* in Volume 43 and agree that increased awareness and a better understanding of the association between pediatric systemic autoimmunity and neuromyelitis optica spectrum disorder (NMOSD) is warranted. In their report, Kornitzer *et al* refer to cases previously published by our group as unconfirmed cases of NMOSD due to a lack of NMO-IgG results(1). Here, we provide additional information regarding these cases as well as to report two new cases to highlight the co-occurrence of childhood Sjögren syndrome (SS) and NMOSD.

Case 1 is an 11 year old African American girl initially hospitalized for acute transverse myelitis and bilateral optic neuritis in the setting of sicca symptoms. ANA, SS-A and SS-B antibodies were positive. Lip biopsy was consistent with SS (Table 1). As the patient was diagnosed in 2003, one year prior to the discovery of the aquaporin-4 antibody (2), NMO-IgG testing was unavailable at that time. She was re-admitted 5 years later with jerking upper extremity movements and altered cognitive speed. Brain magnetic resonance imaging (MRI) revealed interval progression of disease with an enlarged expansile T2 hyper-intense lesion extending from T3-T5. Serum NMO-IgG testing was positive. She was treated with intravenous methylprednisolone, rituximab, cyclophosphamide and apheresis. Initial report of this case (3) was prior to her subsequent NMO-IgG testing, and details of her positive

Address correspondence to: Dr. Sabrina Gmuca, Department of Pediatric Rheumatology, The Children's Hospital of Philadelphia, 34th Street and Civic Center Boulevard, Wood Building, Fourth Floor, Philadelphia, PA 19104, gmucas@email.chop.edu, 215-590-2547.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

NMO-IgG status were not included in subsequent studies that were focused more on childhood SS than on NMOSD (4, 5). Thus, Case 1 clearly meets diagnostic criteria for NMOSD (6).

Case 2 is a 13 year old African American girl diagnosed with concomitant SS and NMOSD after presenting with acute visual changes due to left optic neuritis. This case was previously reported in research focused on childhood SS and therefore did not include full details regarding her neurologic course (4, 5), which we outline here. She developed blurry vision in her left eye accompanied by pain with left lateral gaze and supraorbital headache. Vision improved after 3 days of methylprednisolone. MRI of the brain and spine showed hyper-intensities in the posterior internal capsules on fluid attenuation inversion recovery (FLAIR) images. MRI of the cervical and thoracic spine showed expansion and T2 prolongation with a patchy lesion involving the cervical and thoracic spine. Spinal fluid examination showed 600 WBCs with 59% lymphocytes, 370 RBCs, glucose of 51 mg/dL and protein of 220 mg/dL. Cerebrospinal anti-neuronal antibodies were negative and serum NMO-IgG was positive. She had a high titer ANA and positive SS-A and SS-B antibodies, along with a lip biopsy demonstrating histopathology characteristic of SS (Table 1). She was initially treated with hydroxychloroquine, glucocorticoids and cyclophosphamide and transitioned to mycophenolate; however due to worsening visual symptoms she received apheresis and rituximab.

To identify additional cases of NMOSD and SS, we performed an IRB-approved retrospective chart review at The Children's Hospital *of* Philadelphia from May 1, 2001 until January 1, 2016. All patients with ICD-9-CM code for NMO were included. In addition to the two aforementioned cases, we identified two children with NMOSD who were diagnosed with SS by a pediatric rheumatologist. Case 3 is a 15 year old African American boy with a history of Autism with intractable emesis and hiccups that resolved after empiric treatment with methylprednisolone. He was found to have positive NMO-IgG and demyelinating brain and spinal lesions along with positive ANA, SS-A, SS-B and RNP antibodies (Table 1). A lip biopsy was deferred given need for general anesthesia. He was initiated on mycophenolate and rituximab for NMOSD and probable SS. Case 4 is an 11 year old Caucasian boy with a history of encephalitis presenting with blurry vision. NMO-IgG was positive and imaging demonstrated left optic nerve enhancement resulting in a diagnosis of NMOSD. He had positive SS-A and ANA antibodies. He had sicca symptoms and mildly reduced salivary pooling. Salivary gland cysts were visualized on ultrasound and a lip biopsy demonstrated chronic sialadenitis and focus score > 0 foci/4 mm^2 (4).

These four cases demonstrate the common autoimmune milieu shared between pediatric NMOSD and SS (7, 8). Three of the four cases had confirmatory lip biopsy results for SS which Kornitzer *et al* cite as a distinguishing feature of their case report. However, all of our NMOSD cases had positive SS-A antibodies highlighting the relationship between NMOSD and SS. Given the lack of validated diagnostic or classification criteria for pediatric SS (9, 10), further elucidation of the association between NMOSD and SS may inform future diagnostic criteria for SS. The presence of anti-SS-A or SS-B antibodies in a child with NMOSD should prompt further evaluation for SS including a biopsy and/or imaging studies

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

to assess for salivary or lacrimal gland inflammation. Similarly, neurologic involvement in pediatric SS should prompt an evaluation for NMSOD.

Acknowledgments

Funding: Dr. Gmuca is supported by the National Institute of Health Rheumatology Research Training Grant T32-AR007442-29.

References

1. Kornitzer JM, Kimura Y, Janow GL. Primary Sjogren Syndrome in a Child with a Neuromyelitis Optica Spectrum Disorder. J Rheumatol. 2016; 43:1260–1. [PubMed: 27252507]
2. Lennon VA, Wingerchuk DM, Kryzer TJ, Pittock SJ, Lucchinetti CF, Fujihara K, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. Lancet. 2004; 364:2106–12. [PubMed: 15589308]
3. Arabshahi B, Pollock AN, Sherry DD, Albert DA, Kreiger PA, Pessler F. Devic disease in a child with primary Sjogren syndrome. J Child Neurol. 2006; 21:285–6. [PubMed: 16900921]
4. Yokogawa N, Lieberman SM, Alawi F, Bout-Tabaku S, Guttenberg M, Sherry DD, et al. Comparison of labial minor salivary gland biopsies from childhood Sjogren syndrome and age-matched controls. J Rheumatol. 2014; 41:1178–82. [PubMed: 24786923]
5. Yokogawa N, Lieberman SM, Sherry DD, Vivino FB. Features of childhood Sjogren's syndrome in comparison to adult Sjogren's syndrome: considerations in establishing child-specific diagnostic criteria. Clin Exp Rheumatol. 2016; 34:343–51. [PubMed: 26812559]
6. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015; 85:177–89. [PubMed: 26092914]
7. Carvalho DC, Tironi TS, Freitas DS, Kleinpaul R, Talim NC, Lana-Peixoto MA. Sjogren syndrome and neuromyelitis optica spectrum disorder co-exist in a common autoimmune milieu. Arq Neuropsiquiatr. 2014; 72:619–24. [PubMed: 25098478]
8. Wingerchuk DM, Weinshenker BG. The emerging relationship between neuromyelitis optica and systemic rheumatologic autoimmune disease. Mult Scler. 2012; 18:5–10.
9. Houghton K, Malleson P, Cabral D, Petty R, Tucker L. Primary Sjogren's syndrome in children and adolescents: are proposed diagnostic criteria applicable? J Rheumatol. 2005; 32:2225–32. [PubMed: 16265707]
10. Bartunkova J, Sediva A, Vencovsky J, Tesar V. Primary Sjogren's syndrome in children and adolescents: proposal for diagnostic criteria. Clin Exp Rheumatol. 1999; 17:381–6. [PubMed: 10410277]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1

Cases of Pediatric Neuromyelitis Optica Spectrum Disorder and Confirmed or Probable Sjögren Syndrome

Case	Sjögren syndrome	Race	Age (years)	Gender	SS-A (Units)*	SS-B (Units)*	ANA titer+	NMO Ig-G (serum)	Salivary Biopsy Findings	Miscellaneous
Case #1	Confirmed	African-American	11	F	108.7	35.5	1:160	Positive	Aggregates of minor salivary glands with several foci of periductal primarily lymphocytic inflammation consistent with SS.	Positive Schirmer test
Case #2	Confirmed	African-American	13	F	108.9	76.7	≥ 1:1280	Positive	Multiple sections show regional mucous gland lobules exhibiting multiple discrete foci of lymphocytes and plasma cells consistent with SS.	Normal Schirmer test
Case #3	Probable	African-American	15	M	109.6	68.5	≥ 1:1280	Positive	Deferred given history of autism and need for general anesthesia.	Anti-RNP antibody positive (113.9 Units)*
Case #4	Confirmed	Caucasian	11	M	158.3	Negative	1:160	Positive	Multiple sections show regional mucous gland lobules exhibiting duct ectasia, acinar degeneration, stromal fibrosis and an infiltrate of lymphocytes and plasma cells and focus score > 0 foci/4 mm^2.	Reduced salivary pooling. Salivary gland cysts visualized on ultrasound.

Legend. ANA=anti-nuclear antibody. NMO Ig-G= neuromyelitis optica immunoglobulin G.

*Normal range for anti-SS-A, anti-SS-B, anti-RNP antibodies based on ELISA testing: 0–19 Units.

+ANA titer reference range by immunofluorescence testing: 1:20.

J Rheumatol. Author manuscript; available in PMC 2018 June 01.