The Neurologist: Clinical & Therapeutics Journal

Funakoshi et al., Neurol Clin Therapeut J 2023, 7:3

Case Report Open Access

# A Case of Anti-AQP4 Antibody Positive Neuromyelitis Optica Spectrum Disorder Coexisting with Pre-Clinical Systemic Lupus Erythematosus Following COVID-19 mRNA BNT162b2 Vaccination

**Takumi Funakoshi[1,2]*, Ryosuke Oda[1,2], Yuichiro Toyama[1], Hirohiko Shizukawa[1] and Shin Hisahara2**

[1]*Department of Neurology, Sapporo-Kousei General Hospital, Hokkaido, Japan*
[2]*Department of Neurology, Sapporo Medical University, School of Medicine, Hokkaido, Japan*

## Introduction

The spread of COVID-19 led to rapid global administration of vaccines. The risk of exacerbation, recurrence, and new-onset autoimmune diseases due to the COVID-19 vaccine has been suggested. There are also scattered reports of neurological complications. Among the neurological complications, there have been reports of new-onset neuromyelitis optica spectrum disorder (NMOSD), a central nervous system inflammatory disease.

## Case Report

We present the case of a 28-year-old healthy woman who developed refractory nausea, vomiting, headache, and hiccups five days after COVID-19 vaccination. No neurological symptoms were observed. Blood tests were positive for anti-aquaporin-4 antibody (AQP4-Ab), and positive serological abnormalities suggestive of pre-clinical Systemic lupus erythematosus (SLE). Brain magnetic resonance imaging (MRI) showed FLAIR hyperintense lesions in the right medial occipital lobe. The patient was diagnosed with coexisting NMOSD and pre-clinical SLE. She was treated with corticosteroids, and her symptoms resolved, the hyperintense lesions observed on brain MRI also improved.

## Conclusion

To our knowledge, this is first case of AQP4-Ab positive NMOSD coexisting with pre-clinical SLE following COVID-19 vaccination. We also believe that this is the first report in which neurological examinations showed only cortical lesions without acute myelitis or optic neuritis in AQP4-Ab positive NMOSD after COVID-19 vaccination. Our case suggests that NMOSD after COVID-19 vaccination has various onset patterns. The COVID-19 pandemic is trending downward, but we believe that the association between autoimmune diseases such as NMOSD and COVID-19 vaccination should continue to be studied.

## Background

During the 2019 coronavirus disease (COVID-19) pandemic, COVID-19 vaccines were rapidly administered worldwide to prevent infection. From the beginning of the pandemic, COVID-19 vaccination was reported to cause various autoimmune diseases. New-onset central nervous system (CNS) inflammatory diseases, such as neuromyelitis optica spectrum disorder (NMOSD), multiple sclerosis (MS), acute disseminated encephalomyelitis (ADEM) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) have been reported in a few cases [1]. Although rare, there are reports on the development of seropositive NMOSD, suggesting an association with COVID-19 vaccination. Here, we report a case of seropositive NMOSD with serological abnormalities suggestive of pre-clinical SLE following COVID-19 vaccination.

## Case presentation

A 28-year-old healthy female was admitted to our hospital with severe refractory headache, nausea, vomiting and hiccups. Twenty-one days before admission, she had received a third dose of the COVID-19 mRNA BNT162b2 Pfizer-BioNTech vaccine. She received the first and second dose of the COVID-19 mRNA BNT162b2 Pfizer-BioNTech vaccine without any complications. Five days after receiving the third dose of the vaccine, mild headaches, nausea, vomiting, and hiccups occurred. She was referred to our hospital on Day 21 because the symptoms had worsened. She has no family history of autonomic diseases. On admission, physical and neurological examinations revealed severe refractory headache, nausea, vomiting and hiccups. The cranial nerve examination results were normal, including decreased vision. Muscle weakness or sensory disturbances in the limbs and trunk were not observed. Deep tendon reflexes were normal. Photosensitivity and Raynaud's phenomenon were observed; however, it was unclear when they appeared. Blood tests revealed normal blood counts and biochemistry. The coagulability and protein C, and S were normal. The rapid plasma region test was positive, but the Treponema pallidum hemagglutination assay (TPHA) was negative; therefore, we concluded that it was a biological false-positive.

Autoantibody testing revealed positive antinuclear antibodies (ANA) with a titer of 1:80 and anti-double-stranded DNA antibodies (ds-DNA-Ab, 73 IU/mL). Antiphospholipid antibodies and lupus anticoagulant test results were negative additionally, the anti-aquaporin-4 antibody (AQP4-Ab; cell-based assay) test was positive. Tests for anti-myelin oligodendrocyte protein antibodies (MOG-Ab; cell-based assay) were negative. Cerebrospinal fluid studies revealed slightly increased cell count (52/μL, 85% lymphocytes, 15% monocytes), and normal protein level. The oligoclonal IgG bands were negative, and IgG index was elevated to 0.99. Brain MRI revealed FLAIR hyperintense lesions in the gray matter of the right medial occipital lobe (Figure1 a). No lesions were observed on dorsal side of the medulla oblongata or around the third and fourth ventricles (Figure1 c). Computer tomography of the chest, abdomen, and pelvis revealed no significant findings.

Based on the International Panel for NMO Diagnosis [2], the patient was diagnosed with seropositive NMOSD because of AQP4-

***Corresponding author:** Takumi Funakoshi, Department of Neurology, Sapporo-Kousei General Hospital, Hokkaido, Japan, E-mail: hisahara@sapmed.ac.jp

**Received:** 01-May-2023, Manuscript No: nctj-23-100326; **Editor assigned:** 03-May-2023, Pre-QC No: nctj-23-100326 (PQ); **Reviewed:** 18-May-2023, QC No: nctj-23-100326; **Revised:** 24-May-2023, Manuscript No: nctj-23-100326 (R); **Published:** 31-May-2023, DOI: 10.4172/nctj.1000143

**Citation:** Funakoshi T, Oda R, Toyama Y, Shizukawa H, Hisahara S (2023) A Case of Anti-AQP4 Antibody Positive Neuromyelitis Optica Spectrum Disorder Coexisting with Pre-Clinical Systemic Lupus Erythematosus Following COVID-19 mRNA BNT162b2 Vaccination. Neurol Clin Therapeut J 7: 143.

**Copyright:** © 2023 Funakoshi T. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Ab positivity and area postrema syndromes (APS). Although she exhibited characteristics of systemic lupus erythematosus (SLE), such as photosensitivity, Raynaud's phenomenon, false-positive syphilis, positive ANA, and ds-DNA-Ab, she did not meet the EULAR/ACR 2019 SLE classification criteria. Ds-DNA-Ab has a very high specificity for SLE, and simultaneously, the SLE symptoms and other serological abnormalities were observed. Therefore, we diagnosed pre-clinical SLE. The patient received intravenous methylprednisolone (IVMP 1000mg, 3days) on Day 25. She experienced remarkable improvement in APS, and the symptoms disappeared immediately after IVMP. She was maintained on prednisone 45mg daily (1mg/kg) from Day 8 and was slowly weaned. Brain MRI revealed improvement in the gray matter legions (Figure1 b). The patient was discharged on Day 34 with no apparent recurrence.

## Discussion

During the COVID-19 pandemic, COVID-19 vaccines were distributed worldwide. The mRNA BNT162b2 vaccine demonstrated 95% efficacy in preventing COVID-19 in the phase three trial of the Food and Drug Administration [3]. However, COVID-19 vaccines, including the mRNA BNT162b2 vaccination, are associated adverse events, including new-onset neurological and rheumatic autoimmune diseases. Autoimmune diseases induced by mRNA vaccines are currently being actively researched. It is believed that peptide sharing between the SARS-CoV-2 spike protein and human protein is significant at the heptapeptide level [4]. Therefore, the most likely mechanism is that the antibodies produced against the SARS-CoV2-spike protein in response to vaccination, may lead an autoimmune reactions. Neuroimmune diseases after COVID-19 vaccination, including CNS inflammatory disease, such as NMOSD, MS, ADEM and MOGAD, have rarely been reported [1]. There is limited evidence linking COVID-19 vaccines to disease onset. The factors that trigger CNS inflammatory diseases, including NMOSD, are not well understood. However, some reports suggest that infections by bacteria, or viruses, and vaccinations may be implicated in the onset of CNS inflammatory diseases [5].

Both AQP4-Ab positive and AQP4-Ab negative NMOSD have been reported after COVID-19 vaccination. We identified six cases of AQP4-Ab positive NMOSD by reviewing previous reports [6-10]. Based on these reports, the different types of vaccines, mRNA vaccines, virus vector vaccines, and inactivated vaccines exhibit almost the same frequency of onset. The number of days from vaccination to disease onset ranged from 2 to 31. The vaccination frequency was 1 -2 times. Myelitis occurred most commonly, followed by optic neuritis, area postrema syndrome, and multiple brain lesions. Only patient was positive for oligoclonal IgG bands.

NMOSD is an antibody-mediated central nervous system disease. AQP4-Ab is the specific antibody identified in patients [11]. Typical presentations of NMOSD include optic neuritis, transverse myelitis, area postrema syndrome, and other brainstem, diencephalic, and cerebral presentations. This report presents a case of young, previously healthy female patient with new-onset central nervous system inflammatory disease following COVID-19 vaccination. There are two novelties for postvaccination AQP4-Ab positive NMOSD in our case: gray matter lesions on brain MRI, and serological features suggestive of pre-clinical SLE.

Our patient exhibited area postrema syndrome without any neurological symptoms. Although she had area postrema syndrome, there were no lesions on the dorsal side of the medulla oblongata or around the third and fourth ventricles in brain MRI. Our case showed FLAIR hyperintense lesions in the gray matter of the right medial occipital lobe. We could not confirm a relationship between the patient's clinical symptoms and the lesions. NMOSD rarely present with cerebral cortical lesions [12]. To our knowledge, this is the first case of AQP4-Ab positive NMOSD that occurred after COVID-19 vaccination.

Furthermore, our patient exhibited serological features suggestive of pre-clinical SLE. New-onset SLE after COVID-19 vaccination has been reported, and some cases have been simultaneously positive for various autoantibodies [13]. This patient had not been tested for autoantibodies before vaccination; therefore, we could not determine whether she had autoantibodies such as AQP4-Ab before the onset of symptoms. We must consider the possibilities that she could have been an asymptomatic carrier, that vaccination induced the symptoms, or that vaccination induced *de novo* antibody production. NMOSD is known to coexist with various autoimmune diseases such as rheumatoid arthritis, Sjögren's syndrome, and SLE [14]. However, they have been reported to develop simultaneously in postvaccination NMOSD. Some patients did not meet the diagnostic criteria and coexisted as pre-clinical conditions. There have been a few reports of AQP4-Ab positive NMOSD following COVID-19 vaccination, with autoantibodies suggestive of other autoimmune diseases. In one case, serum MOG-Ab was positive for AQP4-Ab positive NMOSD with myelitis [10]. In another case, ANA, anti-SS-A antibody, anti-SS-B antibody, anti-Ro-52 antibody, and proteinase 3-ANCA were positive in AQP4-Ab positive NMOSD with area postrema syndrome [9]. In our case, ANA and ds-DNA-Ab were positive, and false-positive serological results for syphilis were observed. We considered these serological findings to be suggestive of SLE. Photosensitivity and Raynaud's phenomenon were observed, but it was not clear whether they appeared after vaccination. Therefore, we concluded that the patient possibly asymptomatic SLE before vaccination.

## Conclusion

In summary, we present the case of a young, healthy female who experienced new-onset AQP4-Ab positive NMOSD following COVID-19 vaccination. The presence of gray matter lesions on brain MRI and serological abnormalities suggestive of pre-clinical SLE are novel features of AQP4-Ab positive NMOSD after COVID-19 vaccination. Although there are a few reports on the relationship between the onset of NMSOD and COIVD-19 vaccination, the underlying mechanism has not been fully established. Although the COVID-19 pandemic is trending downward, it is necessary to remain attentive to the onset of autoimmune diseases such as NMOSD after COVID-19 vaccination.

### Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images. A copy of the written consent form is available for review by the editor-in-chief of the journal.

### Competing Interest

None

#### References

1. Ibrahim I, Salama S (2022) A systematic review of cases of CNS demyelination following COVID-19 vaccination. J Neuroimmunol 362: 577-765.

2. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, et al. (2015) International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 85(2): 177-189.

3. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, et al.( 2020) Safety and Efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Eng J Med 383(27): 2603-2615.

4. Kanduc D, Shoenfeld Y (2020) Molecular mimicry between SARS-CoV-2 spike glycoprotein and mammalian preteomes:implications for the vaccine. Immunol Res 68(5): 310-313.

5. Karussis D, Petrou P (2014) The spectrum of post-vaccination inflammatory CNS demyelinating syndromes. Autoimmun Rev 13: 215-224.

6. Anamnart C, Tisavipat N, Owattanapanich W, Apiwattanakul M, Savangned P, et al. (2021) Newly diagnosed neuromyelitis optica spectrum disorders following vaccination: case report and systematic review. Mult Scler Relat Disord 103-414.

7. Badrawi N, Kumar N, Albastaki U (2021) Post COVID-19 vaccination neuromyelitis optica spectrum disorder: Case report and MRI findings. Radiol Case Rep 16(12): 3864-3867.

8. Caliskan I, Bulus E, Afsar N, Altintas A (2022) A Case With New-Onset Neuromyelitis Optica Spectrum Disorder Following COVID-19 mRNABNR162b2 Vaccination. Neurologist 27(3): 147-150.

9. Chen S, Fan XR, He S, Zhang JW, Li SJ, et al. (2021) Watch out for neuromyelitis optica spectrum disorder after inactivated virus vaccination for COVID-19. Neurol Sci 42(9): 3537-3539.

10. Kuntz S, Saab G, Schneider R (2022) Antibody-Positive Neuromyelitis Optica Spectrum Disorder after Second COVID-19 Vaccination: a Case Report. SN Compr Clin Med 4(1): 130.

11. Dutra BG, Rocha AJ, Nunes RH, Junior ACMM (2018) Neuromyelitis Optica Spectrum Disorders: Spectrum of MR Imaging Findings and Their Differential Diagnosis. Radiographics 38(1): 169-193.

12. Kim W, Lee JE, Kim S, Huh SY, Hyun JW, et al. (2016) Cerebral Cortex Involvement in Neuromyelitis Optica Spectrum Disorder. 12(2): 188-193.

13. Nelson MC, Rytting H, Greenbaum LA, Goldberg B (2022) Presentation of SLE after COVID vaccination in a pediatric patient. BMC Rheumatol 6(1): 81.

14. Shahmohammadi S, Doosti R, Shahmohammadi A, Mohammadianinejad SE, Sahraian MA, et al. (2019) Auto immune diseases associated with Neuromyelitis Optica Spectrum Disorders: A literature review. Mult Scler Relat Disord 27: 350-363.