CASE REPORT

DOI: 10.5336/caserep.2022-94634

Combination of Neuromyelitis Optica Spectrum Disorder with Myasthenia Gravis, Systemic Lupus Erythematosus and Hashimoto's Thyroiditis: A Case of Multiple Autoimmune Syndrome

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ABSTRACT Autoimmunity reflects an altered immune status. The coexistence of three or more autoimmune diseases in a patient constitutes multiple autoimmune syndrome. Here, an interesting case with a history of Hashimoto's thyroiditis and got the diagnosis of systemic lupus erythematosus during her evaluation, in which the clinical signs of neuromyelitis optica spectrum disorder (NMOSD) and miyasthenia gravis co-occurred will be discussed. In addition to high-dose pulse steroid, plasmapheresis and intravenous immunoglobulin treatments, rituximab treatment was started and the patient is followed up without clinical worsening and disability in the three-year follow-up. Patients with diagnosis of NMOSD need special attention as multiple immune-mediated disorders may be present simultaneously or sequentially during the course of the disease process. This case report emphasizes the importance of a multidisciplinary team approach for a better understanding of disorders related to the breakdown of immune tolerance.

Keywords: Neuromyelitis optica; miyasthenia gravis; systemic lupus erythematosis; autoimmune diseases; Hashimoto's thyroiditis

Neuromyelitis optica spectrum disorder (NMOSD) is a rare disease associated with the development of antibodies to the central nervous system. Long segment spinal cord demyelination and inflammation (myelitis), severe optic nerve involvement and/or persistent vomiting and hiccups (area postrema syndrome) are the clinical forms that are important for the diagnosis of the disease.[1] Approximately 20-30% of the patients with NMOSD have a coexisting organ-specific or systemic autoimmune disease.[2] It is critical to know that there may be another autoimmune disease or diseases accompanying NMOSD and to consider it in the differential diagnosis. Here, we present a case of NMOSD with concurrent multiple autoimmune diseases, we aimed to highlight unique clinical features and the challenges encountered in diagnostic and treatment management.

CASE REPORT

A 31-year-old right-handed female patient was admitted with complaints of double vision, severe nausea and vomiting, balance difficulties, dizziness, fever, and widespread aches. In her medical history within a month, she was hospitalized with the diagnosis of posterior circulation stroke with diffusion restriction in the left thalamic and right bulbus, and was discharged with antiaggregant treatment. However, her symptoms aggravated after discharging from the hospital. Widespread pain was evaluated as chest pain coronary angiography was performed and it was evaluated as normal. In history, she described an arthritis attack, and got diagnosed with Hashimoto's thyroiditis. She had a history of 2 healthy births and cigarette use. On admission, neurological examination revealed bilateral ptosis prominent on the left,

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Peer review under responsibility of Turkiye Klinikleri Journal of Case Reports.

Received: 30 Nov 2022 ***Received in revised form:*** 01 Feb 2023 ***Accepted:*** 01 Feb 2023 ***Available online:*** 08 Feb 2023

exotropia in the right eye, conjugate gaze paralysis and bilateral horizontal nystagmus with the fast phase to the direction of gaze. The speech was dysarthric, the elevation of the uvula was decreased bilaterally, and she reported hypoesthesia in the right V3 dermatome. Motor examination was normal. The cerebellar examination showed left sided ataxia with a positive Romberg sign. There was urinary retention.

In blood examinations, sodium, chlorine, and potassium levels were low. Thyroid-stimulating hormone level was high, and fT4 was low, anti-thyroid peroxidase and anti-thyroglobulin levels were high. A complete blood count revealed a low white blood cell with a low lymphocyte count. Hypochromic microcytic anemia was detected. In autoantibody examinations, the anti-nuclear antibody (ANA) was 4+, anti-dsDNA was 2+, the anti-histone antibody was 2+, anticardiolipin immunoglobulin (Ig)-M was positive, and the anti-acetylcholine receptor (AChR) antibody was positive with high titer (2.65 nmol/L). The opening pressure of the cerebrospinal fluid (CSF) was 80 mmH_2O and the appearance was clear. There were 120 cells per cubic millimeter, predominantly leukocytes with polymorphonuclear leukocytes. The protein level was 180.7 mg/dL, and the albumin level was 93.7 mg/dL. The CSF meningitis/encephalitis panel (bacterial and viral), and CSF cultures were negative. The CSF IgG index was 1.23 mg/dL, and the oligoclonal band was Type 4 positive. Myelin oligodendrocyte glycoprotein-IgG antibody tested in serum was negative and anti-aquaporin-4 (AQP4) IgG was positive in serum.

Brain magnetic resonance imaging (MRI) revealed a T2 hyperintense lesion extending from the medulla oblongata to the posterior part of the pons, and edematous minimal enlargement in the brainstem. The presence of parenchymal enhancements in the anterior part of the medulla and superiorly at the pontomedullary junction level in the brainstem in the post-contrast images were noted (Figure 1). Computed tomography (CT) angiography and diagnostic selective angiography tests were within normal limits in the evaluation of cerebral vascularization. Minimal effusion was observed at the level of the right hemithorax major fissure in the chest CT scan. Thymoma was not observed in the patient with AChR antibody positivity.

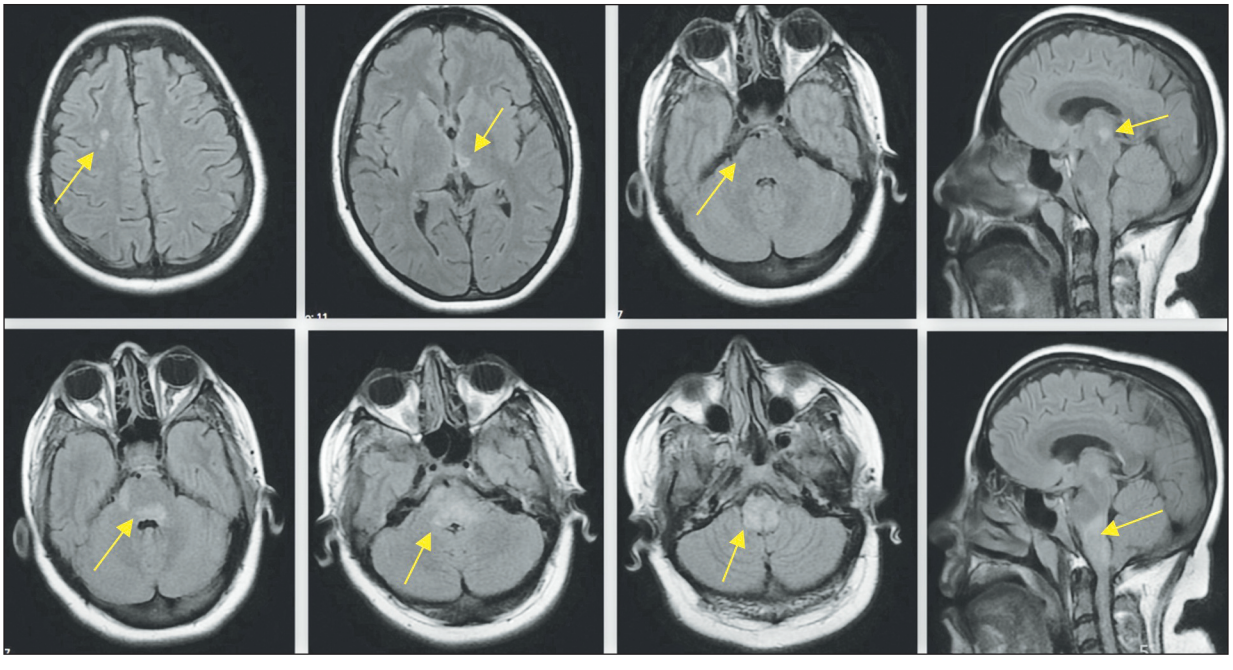

FIGURE 1: Brain MRI T2-FLAIR axial and sagittal sequences revealed hyperintense lesions (yellow arrows) in right frontotemporal cortex, left thalamus, pons, medulla oblongata, and edematous minimal enlargement in the brainstem.
MRI: Magnetic resonance imaging.

Because of the AQP4 antibody positivity, visual evoked potential examination was detected as normal. Cardiac transthoracic echocardiography revealed pericardial fluid adjacent to the right ventricle. The patient was consulted by the department of rheumatology. The patient was diagnosed with systemic lupus erythematosus (SLE) because of ANA, ds-DNA positivity, the presence of serositis, and hematological involvement. With the diagnosis of Hashimoto's thyroiditis, levothyroxine sodium 125 mcg 1x1 per oral (PO) treatment was started. Also, 1 g/day methylprednisolone treatment was started. In the clinical follow-ups, the complaints of nausea and vomiting regressed, but the bilateral lower extremity proximal muscle weakness developed. On the third day of treatment, diplopia and cerebellar findings became increasingly evident. Blurred vision and left hemihypoesthesia appeared followed by left hemiparesis. In the cervical spinal MRI, a lesion was observed between C3-C7 levels in the cervical cord, which was hyperintense on T2W images and minimally enhanced on postcontrast images (Figure 2). In thoracic MRI, an increase in intensity was observed in the T2W images in the middle part of the cord between the spinal cord T7-T12 levels. No pathological contrast enhancement was observed.

Plasmapheresis treatment was started due to worsening clinical findings under pulse steroid treatment. A significant improvement was observed in the clinic with plasmapheresis application 5 times on alternate days, pulse steroid followed by oral steroid treatment, and pyridostigmine 4x60 mg PO treatment. Rituximab treatment was planned for the patient who was evaluated as the coexistence of SLE, neuromyelitis optica, and miyasthenia gravis (MG). On follow-up with Rituximab prophylaxis in the third year the patient is clinically and radiologically stable.

The procedures used in this study adhere to the tenets of the Declaration of Helsinki. All participants gave their written informed consent to participate in this study.

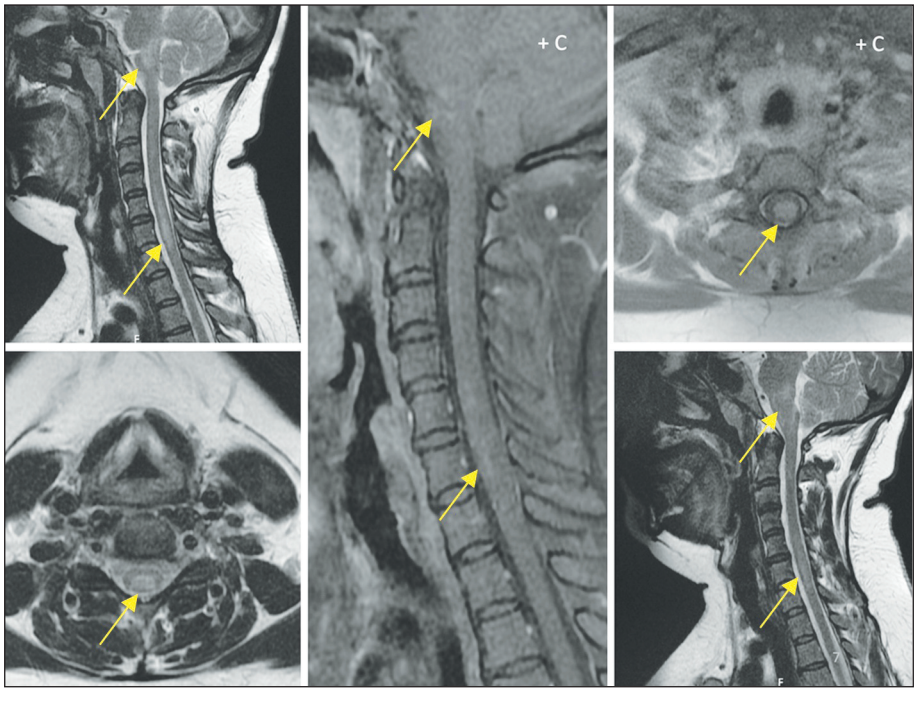

FIGURE 2: In the cervical spinal MRI sagittal and axial sequences showed lesions (yellow arrows) extending from C3 to C7 vertebra level which was hyperintense on T2W images and minimally enhanced on postcontrast images. The presence of parenchymal enhancements in the anterior part of the medulla and superiorly at the pontomedullary junction level in the brainstem in the post-contrast images were noted.
MRI: Magnetic resonance imaging.

DISCUSSION

In this report, a female patient with a history of Hashimoto's thyroiditis, whose neurological findings were found to be compatible with NMOSD and MG, and who was also diagnosed with SLE during the differential diagnosis is presented. Literature about this form of polyautoimmunity is limited to case reports.[3] Recently, this extraordinary form of polyautoimmunity has received attention from neurologists and rheumatologists. The frequency of autoimmune diseases in patients with NMOSD is estimated to be 27.3%.[4] Autoimmune thyroid diseases are the most reported non-neurological organ-specific disease accompanying autoimmune neurological diseases.[5] Sjogren's syndrome and SLE are the most frequently reported comorbid systemic autoimmune diseases and MG is the most reported neurological disease accompanying NMOSD.[5-7]

The pathological mechanism of the SLE and MG association is not clearly known. SLE may develop after thymectomy in MG patients, but there was no thymectomy history in our case since there was no thymoma. The relationship between these diseases seems to be complex.[8] In the literature, we found only two case reports reporting the coexistence of three diseases NMOSD, MG, and SLE.[9,10] In one of them, unlike our case, the anti-musk antibody was positive.[9] The importance of the case we present herein is that NMOSD, SLE, MG, and Hashimoto's thyroiditis diseases were coexisting all together. Therefore, it can be considered as Type 3 multiple autoimmune syndrome (MAS). MAS is defined by the coexistence of 3 autoimmune diseases in the same patient and this rare syndrome has 3 types according to the prevalence of their associations with one another. Type 3 MAS includes autoimmune thyroid disease, myasthenia gravis and/or thymoma, Sjögren's syndrome, pernicious anemia, idiopathic thrombopenic purpura, Addison's disease, Type 1 diabetes mellitus, vitiligo, autoimmune hemolytic anemia, SLE, and dermatitis herpetiformis.[2,4]

In NMOSD, first-line therapy consists of intravenous, high-dose corticosteroids and plasmapheresis/intravenous Ig.[1] Data is lacking on which is optimum in patients with MAS, so the choice is largely dictated by personal preference and experience. Early and effective treatment is important for the prognosis.[2] To avoid delay we preferred to use high-dose pulse steroid therapy in combination with plasmapheresis in the acute period. As the neurological findings of the patient were severe, we preferred Rituximab for prophylaxis in follow-up because of the need for an aggresive treatment approach in MAS.

In conclusion, patients diagnosed with NMOSD may have more than one immune-mediated disorder at the same time. Therefore, in the diagnosis and treatment processes of patients with NMOSD, it should be kept in mind that in addition to systemic autoimmune diseases, another neurological autoimmune disease such as MG may also be present. Aggressive treatment plan and management are important in the prognosis of these cases, which require a multidisciplinary approach.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Vildan Tunçbilek Akın, Aysun Ünal, Bengü Altunan;* ***Design:*** *Vildan Tunçbilek Akın, Aysun Ünal, Bengü Altunan;* ***Control/Supervision:*** *Vildan Tunçbilek Akın, Aysun Ünal, Bengü Altunan;* ***Data Collection and/or Processing:*** *Vildan Tunçbilek Akın, Aysun Ünal;* ***Analysis and/or Interpretation:*** *Aysun Ünal, Rıdvan Mercan;* ***Literature Review:*** *Vildan Tunçbilek Akın, Aysun Ünal, Bengü Altunan;* ***Writing the Article:*** *Vildan Tunçbilek Akın, Aysun Ünal, Bengü Altunan;* ***Critical Review:*** *Bengü Altunan, Aysun Ünal;* ***References and Fundings:*** *Aysun Ünal, Rıdvan Mercan;* ***Materials:*** *Vildan Tunçbilek Akın, Aysun Ünal, Bengü Altunan.*

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