CASE STUDY

CLINICAL CASE OF NEUROMYELITIS OPTICA SPECTRUM DISORDERS IN YOUNG WOMAN TREATED WITH RITUXIMAB

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Iryna M. Poiasnyk, Viktoriia A. Gryb
IVANO-FRANKIVSK NATIONAL MEDICAL UNIVERSITY, IVANO-FRANKIVSK, UKRAINE

ABSTRACT

We report a case of a 28-year-old female who had the clinical manifestation of Neuromyelitis optica spectrum disorders with the area postrema syndrome at 24 years old. The patient presented with decreased vision due to acute optic neuritis, gait impairment, tetraplegia, sensory, and bladder disturbances. Magnetic resonance imaging of the spinal cord showed longitudinal high-intensity signals on a T2-weighted image in cervical and thoracic parts. Her serum and cerebrospinal fluid were positive for the anti-AQP4 antibody. The patient received high-dose methylprednisolone, plasmapheresis, but she remained free from relapses only after prescribing Rituximab.

Prophylactic treatment of Neuromyelitis optica spectrum disorders recurrence must be immediately performed when it is identified because the progression of disability is related to the severity of attacks.

KEY WORDS: Neuromyelitis optica spectrum disorders, aquaporin-4, Rituximab, extensive transverse myelitis, Expanded disability status scale

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INTRODUCTION

Neuromyelitis optica (NMO) is a rare inflammatory disorder of the central nervous system (CNS) that commonly presents with either monophasic or recurrent attacks of optic neuritis (ON) and transverse myelitis (TM) [1, 2].

In 2015, the International Panel for NMO Diagnosis proposed the unifying term of neuromyelitis optica spectrum disorders (NMOSD) for patients presenting selective demyelination of the spinal cord and the optic nerve. Specific criteria were established to facilitate earlier and more accurate diagnoses in water channel aquaporin-4 (AQP4) antibodies seropositive or seronegative patients presenting with ON, TM, or area postrema clinical syndrome (APS) associated with a medullary MRI lesion. The NMOSD term also encompassed the cerebral, and thalamus/hypothalamus (acute diencephalic syndromes, e.g. symptomatic narcolepsy), and brainstem lesions that occur in a minority of patients with otherwise typical NMO. It also included AQP4-IgG-seropositive patients with coexisting autoimmune disorders (e.g., systemic lupus erythematosus or Sjögren syndrome). Finally, NMOSD potentially included patients diagnosed with opticospinal multiple sclerosis (MS), an MS phenotype prominent in Asia and distinguished from Western MS [3].

The median age at presentation is 39 years, but 15–20% of patients may present to pediatricians (under 16 years) or elderly care physicians (greater than 65 years) [4]. Female preponderance is reported in NMOSD patients, in both pediatrics and adults [5]. The disease predilection for females in NMOSD is stronger than in MS, in which gender ratio varies from 1.1:1 to 3.4:1 in Europe and 3.1:1 in United States [6, 7]. A female hormonal basis for this association may be a factor, but requires further study [8].

In most articles on NMOSD, introduction starts with a sentence like 'NMOSD is a severe inflammatory demyelinating disease of the central nervous system.' In fact, NMO (Devic) is classified as a demyelinating disease of the CNS in the International Classification of Diseases (2019 ICD-10-CM Diagnosis Code G36.0) [6]. However, the pathological studies of AQP4-antibody-seropositive NMOSD cases clearly indicate that AQP4-expressing astrocyte is the major target of immune attack and astrocytic destruction is more severe and extensive than demyelination in the disease [9]. These findings strongly confirm that AQP4-antibody-seropositive NMOSD should be classified as an autoimmune astrocytopathic disease rather an inflammatory demyelinating CNS disease. This change of pathological concept of AQP4-antibody-seropositive NMOSD is expected to add a new page in neuropathology and ICD-11 [10].

The AQP4-specific serum autoantibody, NMOIgG, is recognized as a specific biomarker for NMOSD [11]. Although AQP4-Ab is critical in the diagnosis of NMOSD, its involvement in the pathogenesis of the disease remains controversial [12]. Several studies have suggested that AQP4-Ab is generally used as a marker of disease activity in an individual patient [13, 14]. However, many studies have shown that AQP4-Ab is only a diagnostic marker for NMOSD and can only be detected in serum during relapse and remission [15, 16].

However, 10-20% of patients with NMOSD are negative for AQP4-IgG [12]. Recent studies have demonstrated the presence of IgG antibodies to myelin oligodendrocyte gly-

coprotein (MOG-IgG) in a subset of patients with NMOSD as well as in patients with isolated ON or longitudinal extensive transverse myelitis (LETM), syndromes that are often formes frustes of NMOSD [17–19].

A subset of cases with typical NMO is seronegative for AQP4 and MOG antibodies [19]. Some of them may be false-negative based on the currently available assays but it remains unclear whether a third NMO-associated autoantibody is present and this issue is under study [10].

AQP4-IgG–seropositive patients usually have more severe clinical attacks, worse outcome, more relapses (81%–91%), higher female-to-male ratio, and more frequent coexisting autoimmune disorders compared with AQP4-IgG–seronegative patients [20, 21].

CASE REPORT

This young woman first presented in August 2016 at age 24 with an attack of bilateral ON with blurred vision and gait impairment for 1 month. On neurological examination, we found normal mental status and higher functions and no meningismus, but gaze-evoked nystagmus, cerebellar ataxia, hypesthesia of the right arm, deep tendon reflexes were hyperactive, left and the right Babinski sign were positive. A general physical examination was normal. Blood tests as well as liver and kidney function were normal. MRI of the brain (22.08.2016, 1,5 Tl with enhancement) showed focal changes of the right hemisphere of the cerebellum and the white matter of the right frontal lobe, which may correspond to the demyelinating process in the active phase. The diagnosis of MS based on MackDonalds criteria, clinical symptoms, and MRI brain findings was done (expanded disability status scale (EDSS) 2.0). The therapy was started with steroid pulse therapy – intravenous methylprednisolone (IVMP) pulse therapy 1 g for 5 days, with a proton pump inhibitor. The symptoms remitted partially.

In January 2017 and August 2018 the patient presented with a relapse of blurred vision and dizziness, but she independently goes to the Alexander hospital in Kyiv, where she was diagnosed with the vertebral artery syndrome. On the MRI of the brain no apparent change, no optic nerve lesions were detected (16.01.2017, without enhancement, 0,4 Tl). The decompression of the right and left vertebral artery was performed, after which the condition improved by 1.5 years.

In January 2019 she was readmitted to the Ivano-Frankivsk Regional Clinical hospital with complaints of the left hemibody numbness, progressive left-sided weakness accompanied by difficult walking and headache. Examination results were as follows: left-sided spastic hemiparesis with hemyhipestesia, Babinski sign, and MRC grade 3/5 (upper limb) and grade 2.5/5 (lower limb). On the MRI of the brain (23.01.2019, 1,5 Tl without enhancement) were detected lesions of the dorsal part of the medulla oblongata and spinal cord throughout are determined in the form of thickening and increasing the signal on T2-weighted images (T2W), FLAIR, and DWI (Fig.1 (A, B). The patient received high-dose IVMP pulses (1.0 g/day) over 5 days, but the improvement had not become.

The patient on her own applied for rehabilitation to one of the clinics in Kyiv, after which her condition had been improved (according to her words).

11.02.2019 MRI of the cervical and upper thoracic spine (with enhancement, 3,0 Tl) showed signals abnormalities from the medulla oblongata extending to the posterior parts of the spinal cord to 3rd thoracic level – hyperintensity on T2WI and hypointensity on T1-weighted images (T1WI) dimensions 0.6-0.65 cm, length up to 17.2 cm. Postcontrast enhancement was not detected in the lesions.

During all hospitalization, the patient denied the presence of demyelinating disease and considered that she had an ischemic stroke.

Three months later the patient had an episode of TM and was admitted to the hospital with progressive weakness of the legs and inability to walk independently. The pain sensation level was decreased unilateral (right) from the 5th thoracic level. Deep feeling impairment was from the bilateral 7th thoracic level. Lower moderate spastic paraparesis. The right and left Babinski sign was positive. Urinary incontinence. She could not walk on her own, only with bilateral support. An EDSS of 6.5 was noted.

Acute TM was highly suspected. MRI of spinal cord (05.04.19) with intravenous contrast showed on T1WI and T2WI of the cervical part of spinal cord long signal throughout diffusely changed, in the upper without clear contours, occupying 1/3 or 2/3 of the diameter of the cord, in the lower parts (from Th1 to Th12) on the entire diameter. At the level of C1 and C2 there are local extensions of the spinal canal up to 0.2 cm, length 0.9 cm and 0.4 cm, respectively. Conclusion: changes in the spinal cord need to be differentiated between idiopathic TM and demyelinating process (Fig. 2 (A, B).

To investigate the etiology of acute TM, an examination for auto-immune disease and cerebrospinal fluid (CSF) analysis were carried out. The patient had an increased anti-nuclear antibody (ANA) titer of 1:1000 dilution, antibodies to double-stranded DNA, SS-A, SS-B, antiphospholipid antibodies and cardiolipin were undetectable. The results of CSF analysis were unremarkable, with normal protein and glucose, and no pleocytosis (white blood cell count: 3/mm^3). Clinical or laboratory evidence of CSF and serum for syphilis, Lyme disease, HIV, HTLV-1, Mycoplasma, other viral infection (e.g., HSV-1, HSV-2, VZV, EBV, CMV, HHV-6) were negative. The CSF and serum were negative for oligoclonal bands. Because of a high suspicion of NMOSD and for its confirmation, anti-AQP4 antibody was assessed. The serum and CSF sample was positive for anti-AQP4 antibody (titer of 1:320 dilution). Overall, the patient met the definitive diagnostic criteria for NMOSD with the objective evidence of bilateral ON with poor recovery, LETM, and positive anti-AQP4 antibody. She was treated with plasma exchange (PLEX) (3×) followed by high-dose IVMP (1.0 g/day) over 5 days, but her condition had not improved significantly.

In June 2019, the patient had a next episode of TM and was admitted to the hospital with progressive weakness that also

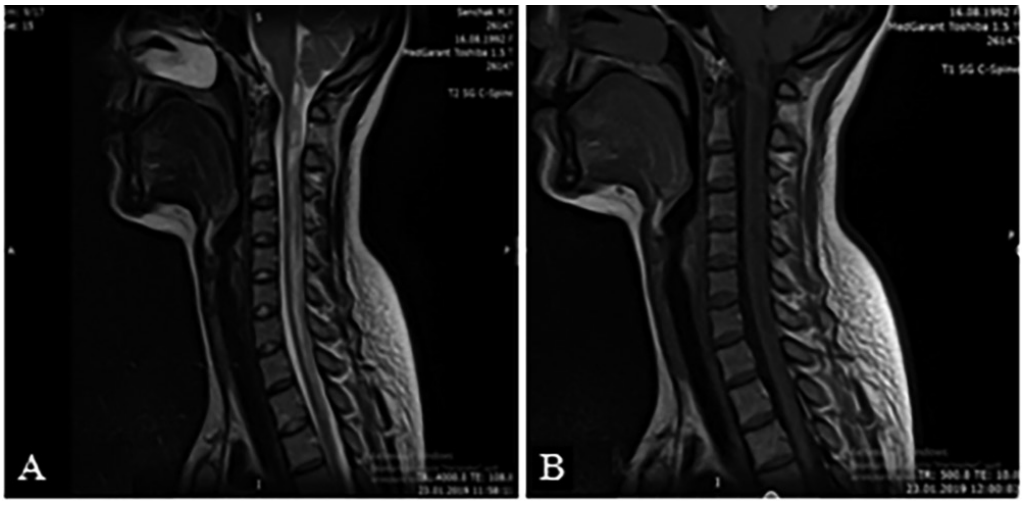

Fig. 1. (A) Sagittal T2-weighted MRI with gadolinium demonstrates an acute lesion associated with APS. (B) Sagittal T1-weighted MRI - LETM extending to Th7 with swelling and contiguous hyperintensity. APS: area postrema syndrome, LETM: longitudinal extensive transverse myelitis.

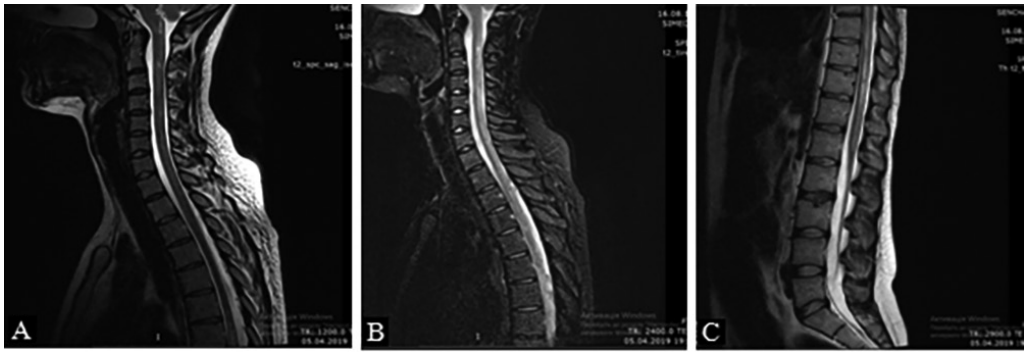

Fig. 2. (A) Sagittal spinal T2-weighted MRI on the level C1 show leptomeningeal gadolinium enhancement. (B, C) Sagittal spinal contrast-enhanced T2-weighted MRI in patient with acute LETM show patchy areas of enhancement extending longitudinally from medulla.

involved the arms, almost complete visual loss in her right eye, urinary incontinence The patient weakness graded 5 in lower limbs and about 3/4 in the upper limbs. Sensory testing demonstrated loss of sensation to all modalities below the 5 th thoracic level. At last follow-up, severe spastic paralysis of the lower limbs and moderate of the upper limbs. Her EDSS score was 9.0. This episode was considered as a new relapse, and she underwent another course of PLEX (4×) but there was no improvement again. The patient was offered treatment with rituximab (RTX). She received four doses of intravenous administration RTX 500 mg (initially 375 mg/m^2 body surface) administered every week over a period of 4 weeks. Over the next 6 months, the patient remained free from relapses .

RTX is considered the sole treatment modality for future relapses, as a result in December 2019 she was hospitalized for receiving another dose of RTX – 1,000 mg with an interval of 2 weeks. Treatment by RTX was followed by incomplete remission of the symptoms. Consequently, her B-cell counts are monitored periodically to allow the timing of further dosing to be planned.

In the dynamics of July 2019, the patient increased strength in the upper extremities – right and left upper limbs proximal muscle strength 3,5, distal muscle strength 3,5, left lower limb muscle strength 2,5, right lower limb proximal muscle strength 2,5, distal muscle strength 2. The superficial sensitivity on the left side and deep sensitivity on both sides partially restored, she could sit down on her own, feels urge to urinate, can bend the legs at the knees but she almost completely lost sight in her right eye. Follow-up MRI (18.06.20) with intravenous contrast revealed residual signal changes, but no new lesions (Fig. 3). At the latest clinical follow-up, the patient had remained relapse free for 12 months after initiation of RTX (EDSS 8.0).

In addition to the caudal medulla oblongata that is affected in the context of LETM originating from the cervical spine, NMOSD can also primarily affect the brainstem. The classical localization is the area postrema (due to the strong expression of aquaporin-4) [22]. There are clinical manifestation of APS results in intractable nausea, vomiting and/or hiccoughs secondary to inflammation in the emetic reflex center located in the rhomboid fossa of the 4th ventricle [23]. Patients may initially present with suspected gastroenteritis or a cyclical vomiting syndrome. APS is the initial presenting feature of NMOSD in approximately 12% of cases [24]. The first symptom of the disease in our patient can be considered retrospectively incomprehensible and unsubstantiated diagnostic vomiting, which occurred in 2015 and met the criteria APS.

ON is one of the most frequent manifestations of NMOSD and is therefore also listed as a "core criterion" in the new diagnostic criteria. The clinical signs and symptoms of NMOSD are similar to those of MS but the NMOSD-ON has certain characteristic features. The presence of bilateral manifestation is highly suspicious, but unilateral inflammation occurs in about 80% of the cases of initial manifestation [25]. Clinically, NMOSD-ON impresses with a high degree of loss of visual acuity to blindness and very limited

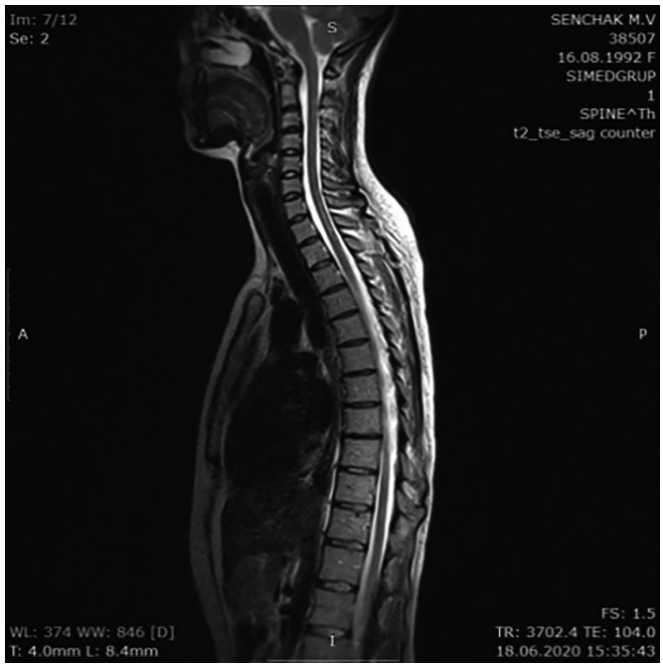

Fig. 3. Sagittal spinal contrast-enhanced T2-weighted MRI at the level C6-Th11 in the central parts of the spinal cord, an elongated form with relatively clear contours, 26.5 cm long and up to 0.26 cm wide, is visualized without pattern of enhancement.

recovery. Radiologically, it is often associated with long-term affection of the corresponding optic nerve, extending into the optic chiasm [26]. In our patient, the disease manifested itself from the usual manifestations of MS, and has typical symptoms – impaired vision, gait impairment until 2018. In 2019, vision began to deteriorate – and there was a decrease, and then a complete loss of vision in the right eye. At the same time, the patient had left-sided moderate spastic hemiparesis, although MRI of the brain and spinal cord already had lesions of the cervical and thoracic spinal cord, namely unilateral lesions and the absence of pelvic disorders were regarded as MS. Most notably, a gradually progressive course of neurologic worsening over months to years is very uncommon (1%–2%) in NMOSD [3]. This feature of the disease was present in our patient.

The symptoms that made our patient's diagnosis of MS incorrect was the progression to spastic moderate-severe lower paraparesis and upper mild paraparesis, the detection of transverse myelitis on MRI extending over more than 3 segments, and the finding of lesions in the brainstem. (Fig. 1, 2 (A, B). An additional criterion was the absence of oligoclonal bands in the CSF and serum, which denied this diagnosis. The gradual deterioration occurred over 4 years with the increase of new symptoms, which can be considered relapsing NMOSD.

LETM is the most specific presentation of NMOSD and is uncommon in MS. LETM typically consists of inflammation affecting the central gray matter, extending over three or more contiguous vertebral bodies [27]. The central gray matter along the central canal of the spinal cord is the preferred area of involvement, as it corresponds to the most prominent expression of the AQP4 antigen [28]. At MRI, these lesions are located centrally or both centrally and peripherally on axial images and involve more than 50% of the cord area, representing transversely extensive lesions. Cervical, thoracic, or cervicothoracic spinal segments are usually compromised [29]. When the cervical spine is involved, extension into the brainstem, typically to the area postrema, is commonly observed [28]. Two of the most typical MRI features that assist NMOSD diagnosis are bright spotty lesions on T2WI and corresponding dark lesions on T1WI. These imaging features have been described as relatively specific for distinguishing NMOSD from other entities, including MS. Bright spotty lesions are defined as spotty lesions with strong hyperintensity on axial T2WI, typically with higher signal intensity than that of the surrounding CSF without flow void effects [30]. Spinal cord atrophy and a distinctive pattern of lesions that tend to fragment into shorter segments along the spinal cord can be observed during remission or after administration of high-dose steroids [28].

Although less common, leptomeningeal and nodular enhancement has also been observed in NMOSD [29, 31]. Such changes were found on the T2WI of our patient (Fig.2 A, B). Blood–brain barrier microvasculature consists of two capillary cell components (pericytes and endothelia), which are typically surrounded by astrocytic end-feet processes [32]. The dominant water channel protein, AQP4, is confined to the astrocytes end-feet processes. Antibody to AQP4 binds to surface of microvessels, pia, and Virchow–Robin sheaths and damages the astrocytes. Thus, leptomeningeal enhancement may be thick or linear and is probably a result of functional impairment of AQP4 water channels in the pial and subpial surfaces [33, 34].

The criterion of temporal dissemination in time the diagnosis of NMOSD does not exist because of the existence of monophasic disease courses. This appears to be meaningful in the face of an accumulation of severe disabilities during disease exacerbation and the associated necessity to start a disease-modifying therapy quickly [35].

Current treatment of NMOSD is classified as follows: to hasten recovery from acute exacerbation; to prevent relapse in the long-term; and to minimize chronic sequelae. Acute treatment of an NMOSD attack consists of high dose steroids (HDS), typically 1 gram of IVMP daily for 5 days; oral prednisolone 1 mg/kg is then continued for weeks, followed by a gradual taper over the months. Earlier treatment is ideal and with severe neurological deficits, if improvement is not seen within days of HDS, PLEX (5 cycles) should be commenced. Escalation therapy has been shown to increase response/remission rates and should be offered in appropriate cases [36].

Patients who are AQP4-IgG-seropositive should be assumed to be at risk for relapse indefinitely and preventive treatment should be considered, even in the setting of a prolonged clinical remission [3].

Currently RTX seems to be the most effective treatment in NMOSD, although some studies describe a rebound in disease activity shortly after RTX induction [37]. RTX has accept-

able tolerance, reduces the relapse frequency, and improves disability in most patients with NMOSD [39]. In patients with myelitis, RTX is recommended from an earlier stage as a myelitis often leads to severe residual deficits [39]. As an alternative to a fixed dosing regimen every 6 months, monitoring of CD19+/CD20+ B-lymphocytes and administration of RTX in the case of reconstitution of these cells are possible. Another option is the administration of RTX depending on monitoring of CD27+ memory B-cells, which might in some cases allow to lower the cumulative RTX dose [40].

The use of HDS in combination with cycles of PLEX is recommended for the management of acute attacks of NMOSD. Our patient continued to experience relapses while receiving the other proposed therapies for NMOSD, but she became stable on RTX.

Over the last year and a half, the management of the NMOSD has undergone a sea change with the approval of three new therapies – eculizumab (Soliris), inebilizumab (Uplizna), and satralizumab (Enspryng). On June 27, 2019, the U.S. Food and Drug Administration (FDA) approved Soliris (eculizumab) injection for intravenous use for the treatment of NMOSD in adult patients who are anti-aquaporin-4 (AQP4) antibody-positive [41]. On June 11, 2020, FDA approved Uplizna (inebilizumab-cdon) injection for intravenous use for the treatment of NMOSD in adult patients with a particular antibody (patients who are AQP4 antibody-positive) [42]. On August 15, 2020, FDA has approved Enspryng (satralizumab-mwge) as the first and only subcutaneous treatment for adults living with AQP4 antibody-positive NMOSD [43].

CONCLUSIONS

Clinical judgment remains necessary because no characteristic is pathognomonic. All patients with acute TM associated with a LETM lesion on spinal cord MRI, regardless of brain MRI abnormalities, in cases of "idiopathic" acute TM is that lack other features of MS, and even if the cord lesion is less than the three vertebral segments required to meet LETM criteria routine diagnostic testing for AQP4-IgG must be done. AQP4-IgG should be considered in cases of severe ON with poor visual recovery, bilateral simultaneous acute optic neuritis, or detection of a long segment of the optic nerve or chiasmatic signal abnormality on T2- or T1-gadolinium orbital MRI sequences. Testing is also reasonable in patients with intractable nausea, vomiting or hiccups in whom a gastrointestinal cause is not detected, or in whom a dorsal medullary (area postrema) MRI lesion is found.

REFERENCES

1. Wingerchuk D.M., Lennon V.A., Lucchinetti C.F. et al. The spectrum of neuromyelitis optica. Lancet Neurol. 2007; 6:805–815.
2. Wingerchuk D.M., Hogancamp W.F., O'Brien P.C., Weinshenker B.G. The clinical course of neuromyelitis optica (Devic's syndrome). Neurology. 1999; 53:1107–1114.
3. Wingerchuk D.M., Banwell B., Bennett J.L., et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015;85:177.
4. Quek A.M.L., Mckeon A., Lennon V.A. et al. Effects of age and sex on aquaporin-4 autoimmunity. Arch. Neurol. 2012; 69:1039–1043.
5. Derle E., Güneş H.N., Konuşkan B., Tuncer-Kurne A. Neuromyelitis optica in children: A review of the literature. Turk J Pediatr. 2014;56:573.
6. Boström I., Stawiarz L., Landtblom A.M. Sex ratio of multiple sclerosis in the national swedish MS register (SMSreg). Mult Scler. 2013;19:46-52.
7. Dilokthornsakul P., Valuck R.J., Nair K.V. et al. Multiple sclerosis prevalence in the united states commercially insured population. Neurology. 2016;86:1014-1021.
8. Bove R., Elsone L., Alvarez E. et al. Female hormonal exposures and neuromyelitis optica symptom onset in a multicentre study . Neurol Neuroimmunol Neuroinflamm. 2017; 4: e339.
9. Fujihara K., Misu T., Nakashima I. et al. Neuromyelitis optica should be classified as an astrocytopathic disease rather than a demyelinating disease. Clin Exp Neuroimmunol. 2012; 3:58–73.
10. Fujihara K. Neuromyelitis optica spectrum disorders: still evolving and broadening. Demyelinating diseases. 2019; 32(3): 385-394.
11. Estrada K., Whelan C.W., Zhao F. et al. A whole-genome sequence study identifies genetic risk factors for neuromyelitis optica. Nat Commun. 2018; 9(1):1929.
12. Jarius S., Franciotta D., Paul F. et al. Testing for antibodies to human aquaporin-4 by ELISA: Sensitivity, specificity, and direct comparison with immunohistochemistry. J Neurol Sci. 2012;320:32–37.
13. Yang Y., Wang C.J., Wang B.J. et al. Comparison of efficacy and tolerability of azathioprine, mycophenolate mofetil, and lower dosages of rituximab among patients with neuromyelitis optica spectrum disorder. J Neurol Sci. 2018;385:192.
14. Nakajima H., Motomura M., Tanaka K. et al. Antibodies to myelin oligodendrocyte glycoprotein in idiopathic optic neuritis. BMJ Open. 2015;5:e007766.
15. Waters P., Woodhall M., O'Connor K.C. et al. MOG cell-based assay detects non-MS patients with inflammatory neurologic disease. Neurol Neuroimmunol Neuroinflamm. 2015;2:e89.
16. Evangelopoulos M.E., Andreadou E., Koutsis G. et al. Treatment of neuromyelitis optica and neuromyelitis optica spectrum disorders with rituximab using a maintenance treatment regimen and close CD 19 B cell monitoring. A six-year follow-up. J Neurol Sci. 2017; 372:92–96.
17. Mader S., Gredler V., Schanda K. et al. Complement activating antibodies to myelin oligodendrocyte glycoprotein in neuromyelitis optica and related disorders. J Neuroinflammation. 2011;8:184.
18. Kitley J., Waters P., Woodhall M. et al. Neuromyelitis optica spectrum disorders with aquaporin-4 and myelin-oligodendrocyte glycoprotein antibodies: a comparative study. JAMA Neurol. 2014;71:276.
19. Sato D.K., Callegaro D., Lana-Peixoto M.A. et al. Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders. Neurology. 2014;82:474–481.
20. Jarius S., Ruprecht K., Wildemann B. et al. Contrasting disease patterns in seropositive and seronegative neuromyelitis optica: a multicentre study of 175 patients. J Neuroinflammation. 2012;9:14.
21. Pandit L, Asgari N., Apiwattanakul M. et al. Demographic and clinical features of neuromyelitis optica: a review. Mult Scler. 2015;21(7):845–853.
22. Popescu B.F., Lennon V.A., Parisi J.E. et al. Neuromyelitis optica unique area postrema lesions: Nausea, vomiting, and pathogenic implications. Neurology. 2011; 76: 1229–1237.
23. Duvernoy H.M., Risold P.Y. The circumventricular organs: An atlas of comparative anatomy and vascularization. Brain Research Reviews. 2007; 56: 119 – 147.

24. Pittock S.J., Lucchinetti C.F. Neuromyelitis optica and the evolving spectrum of autoimmune aquaporin-4 channelopathies: a decade later. Annals of the New York Academy of Sciences. 2016; 1366: 20–39.
25. Piccolo L., Woodhall M., Tackley G. et al. Isolated new onset 'atypical' optic neuritis in the NMO clinic: serum antibodies, prognoses and diagnoses at follow-up. J Neurol. 2016; 263: 370–379.
26. Kim H.J., Paul F., Lana-Peixoto M.A. et al. MRI characteristics of neuromyelitis optica spectrum disorder: An international update. Neurology 2015; 84: 1165–1173.
27. Elsone L, Townsend T., Mutch K. et al. Neuropathic pruritus (itch) in neuromyelitis optica . Mult Scler J. 2012; 19: 475 – 479.
28. Kim H.J., Paul F., Lana-Peixoto M.A. et al. MRI characteristics of neuromyelitis optica spectrum disorder: an international update. Neurology. 2015;84(11):1165–1173.
29. Dumrikarnlert C., Siritho S., Chulapimphan P. et al. The characteristics of spinal imaging in different types of demyelinating diseases. J Neurol Sci. 2017;372:138–143.
30. Yonezu T., Ito S., Mori M. et al. "Bright spotty lesions" on spinal magnetic resonance imaging differentiate neuromyelitis optica from multiple sclerosis. Mult Scler. 2014;20(3):331–337.
31. Kim W., Park M.S., Lee S.H. et al. Characteristic brain magnetic resonance imaging abnormalities in central nervous system aquaporin-4 autoimmunity. Mult Scler. 2010;16(10):1229–1236.
32. Daneman R., Prat A. The Blood–Brain Barrier. Cold Spring Harb Perspect Biol. 2015; 7(1): a020412.
33. Long Y., Chen M., Zhang B. et al. Brain gadolinium enhancement along the ventricular and leptomeningeal regions in patients with aquaporin-4 antibodies in cerebral spinal fluid. J Neuroimmunol. 2014; 269:62–67.
34. Pekcevik Y., Orman G., Lee I.H. et al. What do we know about brain contrast enhancement patterns in neuromyelitis optica? Clin Imaging. 2016;40(3):573–580.
35. Pfeuffer S. et al. NMO Spectrum Disorders. Neurology International Open. 2017; 1: E36–E47.
36. Kleiter I., Gahlen A., Borisow N. et al. Neuromyelitis optica: Evaluation of 871 attacks and 1,153 treatment courses. Ann Neurol. 2016;79:206–216.
37. Perumal J.S., Kister I., Howard J., Herbert J. Disease exacerbation after rituximab induction in neuromyelitis optica. Neurol Neuroimmunol Neuroinflamm. 2015; 2:e61.
38. Fulin G., Bingyan C., Cheng G. et al. Effectiveness of rituximab in neuromyelitis optica: a meta-analysis. BMC Neurology. 2019;19(36):1-7.
39. Ramanathan S., Mohammad S., Tantsis E. et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. J Neurol Neurosurg Psychiatry. 2018;89:127.
40. Cohen M., Romero G., Bas J. et al. Monitoring CD27+ memory B-cells in neuromyelitis optica spectrum disorders patients treated with rituximab: results from a bicentric study. J Neurol Sci. 2017; 373:335–338.
41. Alexion receives FDA approval of Soliris® (eculizumab) for the treatment of adults with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive. News release. Alexion Pharmaceuticals. 2019. https://news.alexion.com/press-release/product-news/alexion-receives-fda-approval-soliris-eculizumab-treatment-adults-neuromy . [date access 20.12.2019]
42. FDA Approves New Therapy for Rare Disease Affecting Optic Nerve, Spinal Cord. News release. FDA. 2020. https://www.fda.gov/news-events/press-announcements/fda-approves-new-therapy-rare-disease-affecting-optic-nerve-spinal-cord [date access 20.03.2020]
43. FDA approves Genentech's Enspryng for neuromyelitis optica spectrum disorder. News release. Genentech. 2020. https://www.businesswire.com/news/home/20200814005501/en/ADDING-MULTIMEDIA%C2%A0FDA-Approves-Genentech%E2%80%99s-Enspryng-Neuromyelitis-Optica. [date access 20.03.2020]

ORCID and contributionship:
Poiasnyk Iryna: 0000-0002-6965-8631 [A, B, D- F]
Gryb Viktoriia: 0000-0001-6111-7921 [E, F]

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CORRESPONDING AUTHOR
Iryna M. Poiasnyk
Ivano-Frankivsk National Medical University
2 Galitska st., 76000 Ivano-Frankivsk, Ukraine
tel: +380973837008
e-mail: sof.3425@gmail.com

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