© Aktualn Neurol 2022, 22 (4), p. 185–191
DOI: 10.15557/AN.2022.0023

Katarzyna Zwiernik[1], Magdalena Kwaśniak-Butowska[1,2], Robert Bonek[3], Jarosław Sławek[1,2]

Received: 31.01.2023
Accepted: 14.04.2023
Published: 29.05.2023

Late and very late onset neuromyelitis optica spectrum disorders – a case series

Choroby ze spektrum zapalenia nerwów wzrokowych i rdzenia kręgowego o późnym i bardzo późnym początku – seria przypadków

[1] Department of Neurology and Stroke, St. Adalbert Hospital, Gdańsk, Poland
[2] Division of Neurological and Psychiatric Nursing, Faculty of Health Sciences, Medical University of Gdansk, Gdańsk, Poland
[3] Department of Clinical Neurology and Neuroimmunology, Regional Specialist Hospital, Grudziądz, Poland
Correspondence: Katarzyna Zwiernik, Jana Pawła II 50, 80-462 Gdańsk, Poland, e-mail: katarzyna.zwiernik@op.pl

ORCID iDs
1. Katarzyna Zwiernik https://orcid.org/0000-0002-4159-3717
2. Magdalena Kwaśniak-Butowska https://orcid.org/0000-0002-2322-3376
3. Robert Bonek https://orcid.org/0000-0003-4077-8960
4. Jarosław Sławek https://orcid.org/0000-0001-6816-0877

Abstract

Background and purpose: Neuromyelitis optica spectrum disorders are a group of autoimmune diseases leading to severe visual and motor impairment with a median disease onset at 39 years. **Materials and methods:** We present a case series of four AQP4-Ab positive neuromyelitis optica spectrum disorders patients, with a median age at onset of 67 years (ranging 54–72), in whom neuromyelitis optica spectrum disorder was not suspected at first, given unusual age and age-associated comorbidities. **Results:** Severe spinal cord involvement was the main finding in all patients. Two patients additionally manifested brainstem impairment in the form of area postrema syndrome and double vision. The therapeutic process included intravenous steroid pulses followed by long-term immunosuppression. Two of the patients died within a year of the diagnosis due to respiratory failure (one due to SARS-CoV-2 infection). One patient was started on satralizumab therapy with a significant motor improvement and good tolerance. One patient decided to suspend immunosuppressive treatment due to treatment-related gastrointestinal complaints. **Conclusion:** Based on the presented case series and the literature review, we assume that neuromyelitis optica spectrum disorders diagnosis should be considered regardless of age and comorbidity. New highly effective therapies with monoclonal antibodies are currently available. Early diagnosis and proper treatment may improve the outcome and prevent further visual and motor disability.

Keywords: neuromyelitis optica spectrum disorders (NMOsd), late onset NMOsd, very late onset NMOsd, transverse myelitis, optic neuritis

Streszczenie

Wprowadzenie: Choroby ze spektrum zapalenia nerwów wzrokowych i rdzenia kręgowego (*neuromyelitis optica spectrum disorders*, NMOsd) to grupa rzadkich chorób autoimmunologicznych z kręgu pierwotnych astrocytopatii, które charakteryzują się współwystępowaniem nawracającego zapalenia nerwów wzrokowych oraz zapalenia rdzenia kręgowego. Wiek zachorowania przypada zazwyczaj na trzecią i czwartą dekadę życia, z medianą w 39. roku życia. **Materiał i metoda:** Opis czterech przypadków pacjentów z rozpoznanym późnym początkiem choroby ze spektrum zapalenia nerwów wzrokowych i rdzenia kręgowego, z dodatnim mianem przeciwciał przeciwko akwaporynie 4, z medianą wieku zachorowania w 67. roku życia (54–72 lat). Z uwagi na nietypowy wiek zachorowania oraz współistniejące obciążenia rozpoznanie choroby ze spektrum zapalenia nerwów wzrokowych i rdzenia kręgowego nie było rozważane w pierwszej kolejności. **Wyniki:** Rozległe, poprzeczne zapalenie rdzenia kręgowego było kliniczną manifestacją choroby u wszystkich pacjentów. U dwóch chorych dodatkowo stwierdzono uszkodzenie pnia mózgu w postaci zespołu pola najdalszego oraz podwójnego widzenia. Proces terapeutyczny obejmował podanie dożylnych pulsów sterydowych oraz włączenie leków immunosupresyjnych. Dwóch pacjentów zmarło w ciągu roku od postawienia diagnozy z powodu powikłań infekcyjnych. U jednego pacjenta rozpoczęto terapię satralizumabem, obserwując poprawę sprawności oraz dobrą tolerancję leczenia. Jeden pacjent zdecydował o przerwaniu leczenia immunosupresyjnego z powodu wystąpienia działań niepożądanych. **Wnioski:** Prezentowane przypadki dostarczają dowodów na kliniczną i demograficzną zmienność chorób ze spektrum zapalenia nerwów wzrokowych i rdzenia kręgowego

oraz występowanie również w podeszłym wieku. Z uwagi na wczesne zajęcie rdzenia kręgowego w omawianej grupie pacjentów i szybszą progresję niepełnosprawności szczególnie ważna jest wczesna diagnoza i wdrożenie skutecznego leczenia.

Słowa kluczowe: choroby ze spektrum zapalenia nerwów wzrokowych i rdzenia kręgowego (NMOsd), NMOsd o późnym początku, zapalenie nerwów wzrokowych, poprzeczne zapalenie rdzenia kręgowego

INTRODUCTION

Neuromyelitis optica spectrum disorders (NMOsd) are a group of rare autoimmunological diseases, characterised by the coexistence of recurrent inflammation of the optic nerves and spinal cord. For many years, it was considered a subtype of multiple sclerosis (MS); however, the discovery of pathogenic antibodies against aquaporin-4 (AQP4) in 2004 allowed to define it as a separate entity. AQP4, the immune target for autoreactive antibodies, is a membrane-forming protein of a water channel with high expression within the central nervous system (CNS) (Gospodarczyk-Szot et al., 2016; Zakrzewska-Pniewska, 2020). High levels of AQP4 occur in the astrocytic processes, which are part of the structures that make up the blood-brain barrier (Jasiak-Zatońska et al., 2022a, 2022b; Waliszewska-Prosół et al., 2021). The autoimmunological process ultimately leads to severe damage to astrocytes and oligodendrocytes. In the CNS, aquaporin-4 is highly expressed in the spinal cord, optic nerves, brain stem, hypothalamus, periventricular regions, subpial regions and area postrema (Jasiak-Zatonska et al., 2016). These structures of the highest AQP4 expression tend to correspond with the localisation of brain lesions.

The presence of AQP4-antibodies is pathognomonic for NMOsd, and these antibodies are found in up to 80% of cases, although their absence does not preclude the diagnosis (Zakrzewska-Pniewska, 2020). In 2015, a meeting of an international group of experts (International Panel for NMO Diagnosis, IPND) formulated the term of "neuromyelitis optica spectrum disorder" (NMOsd), which includes complexes of symptoms related or not related to the presence of AQP4, which do not meet the classic historic criteria of NMO: longitudinally extensive transverse myelitis (LETM), relapsing isolated optic neuritis (RION), bilateral optic neuritis (BON) (Gospodarczyk-Szot et al., 2016). However, the diagnostic work-up in NMOsd patients can be extensive, and careful magnetic resonance imaging (MRI) analysis is often of help. Some cases are extremely atypical, such as tumefactive ones (Juryńczyk et al., 2022; Topkan et al., 2022).

In AQP4 seronegative patients, an antibody against myelin-associated oligodendrocyte glycoprotein (MOG) is most

Study	Number of patients, female/male	Median age at onset [years]	Main clinical manifestations
Collongues et al., 2014	46 41/5	56	LETM 20 (43%) Optic 22 (48%) Both LETM + ON 3 (6%)
Krumbholz et al., 2015	3 2/1	83	LETM 3
Mao et al., 2015	30 26/4	57.5	LETM 15 (50%) Both (LETM + ON) 1 (2%) ON 13 (43%) Mix (e.g. brainstem + LETM) 1 (2%)
Seok et al., 2017	45 40/5	58.1	LETM 29 (64%) ON 10 (22%) Brain 3 (6%) Mixed 3 (6%)
Suchdev et al., 2017	1 1/0	84	LETM 1
Carnero Contentti et al., 2020	16 15/1	60.5	LETM 8 (50%) ON 11 (69%) Brain 1 (7%)
Sepulveda et al., 2019	60 48/12	59	LETM 28 (47%) ON 22 (37%) Both (ON + LETM) 4 (6%) Brainstem 6 (10%)
Fragoso et al., 2019	37 30/7	56	LETM 32 (86%) ON 26 (70%) Brainstem dysfunction 6 (16%)

LETM – longitudinally extensive transverse myelitis; **ON** – optic neuritis.

Tab. 1. Summary of publications regarding late onset, very late onset AQP4-Ab(+) NMOsd

DOI: 10.15557/AN.2022.0023

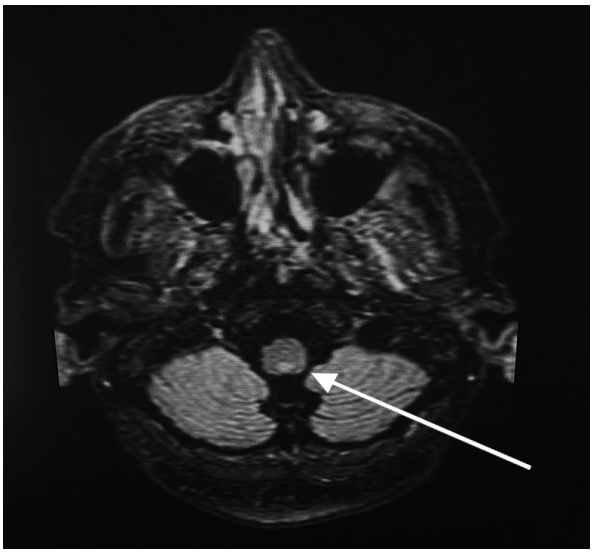

Fig. 1. Case 1. MRI scan showing a T2-hyperintense lesion in the medulla oblongata manifesting as area postrema syndrome

commonly found (Zakrzewska-Pniewska, 2020). MOG-antibody disease (MOGAD) is a demyelinating disease distinct from MS and classic NMO, with the most common clinical presentation of optic neuritis (54–61%), LETM (22%), acute disseminated encephalomyelitis (ADEM) or brainstem/cerebral cortical encephalitis with seizures (Ambrosius et al., 2020). MOG-positive patients tend to be at a lower risk of further relapses than AQP4-positive patients, and the course of the disease is less disabling (Wynford-Thomas et al., 2019). The most common residual features are visual and sphincter disfunction (Juryńczyk et al., 2019).

The typical onset of NMOsd is between third and fourth decade of life, with a median age of 39 years. The disease onset after 50 years of age is relatively rare and usually associated with worse outcomes (Fragoso et al., 2019). In the literature, patients who developed AQP4-Ab(+) NMOsd beyond the age of 50 years were classified as late onset (LO-NMOsd) and beyond the age of 70 years as very late onset (VLO-NMOsd) (Tab. 1). The cut-off point for the "late onset" was based on thresholds associated with other autoimmune disorders, such as myasthenia gravis.

Here, we present four cases of AQP4-Ab positive NMOsd with late and very late disease onset.

CASE 1

A 72-year-old female presented with persistent nausea, vomiting, hiccups and sudden weakness of both lower limbs. Neurological examination revealed psychomotor slowing, recurrent hiccups, horizontal nystagmus to the right, slight paraparesis of the lower limbs.

Her medical history was significant for Hashimoto disease, type 2 diabetes, arterial hypertension and breast cancer 9 years before, successfully treated with surgery and hormonal therapy.

Brain and cervical spine MRI showed paraventricular T2-hyperintense lesions in the left hemisphere, midbrain and medulla oblongata (Fig. 1). All lesions enhanced peripherally post-contrast. MRI of the cervical spine showed an intramedullary lesion from C2 to C3 level. Visual evoked potentials revealed bilateral damage to the visual tract in a form of prolonged P100 potentials. AQP4-Ab was found to be positive.

The patient underwent a 5-day course of intravenous methylprednisolone at a total dose of 5 g. This was followed by long-term oral steroids (prednisone 70 mg/d) and azathioprine (125 mg/d). The patient's condition improved and she was subsequently discharged. A complete resolution of symptoms from area postrema was observed. However, four months after the diagnosis the patient's condition deteriorated rapidly due to the lower respiratory tract infection. She was admitted to the intensive care unit (ICU), where she died after two weeks.

CASE 2

A 71-year-old female was admitted to the hospital due to a sudden onset of double vision with accompanying paresis of the left lower limb.

Previous medical history revealed Addison–Biermer disease, hypothyroidism, obesity, and bilateral hip arthroplasty.

The neurological examination was remarkable for the left abducens paresis and severe proximal paresis of the left lower limb. MRI of brain and lumbar spine detected an area of increased signal in FLAIR and T2 images with linear post-contrast enhancement in the ventral part of the medulla oblongata (Fig. 2). In the lumbosacral part of the spine, an increased signal and post-contrast enhancement was visualized at the level of Th8–L1, the roots of cauda equina and cerebrospinal dura (Fig. 3). CSF analysis revealed white cell count of 54/μL with lymphocyte predominance, mildly elevated protein level (66.5 mg/dL) and no oligoclonal bands. Neuroinfections, including syphilis and neuroborreliosis, were excluded. No atypical cells were found in microscopic examination.

Visual evoked potentials showed bilateral, axonal-demyelinating damage to the visual tract. Serum AQP4-Ab tested positive.

The patient received five pulses of intravenous methylprednisolone 1 g/d, followed by oral prednisolone (90 mg/d), with clinical improvement. She was discharged and subsequently received satralizumab treatment, while the dose of oral steroid therapy was reduced. A further significant neurological improvement was observed, and the therapy was well-tolerated.

CASE 3

A 63-year-old woman was admitted to the neurological ward due to a sudden left lower limb weakness with

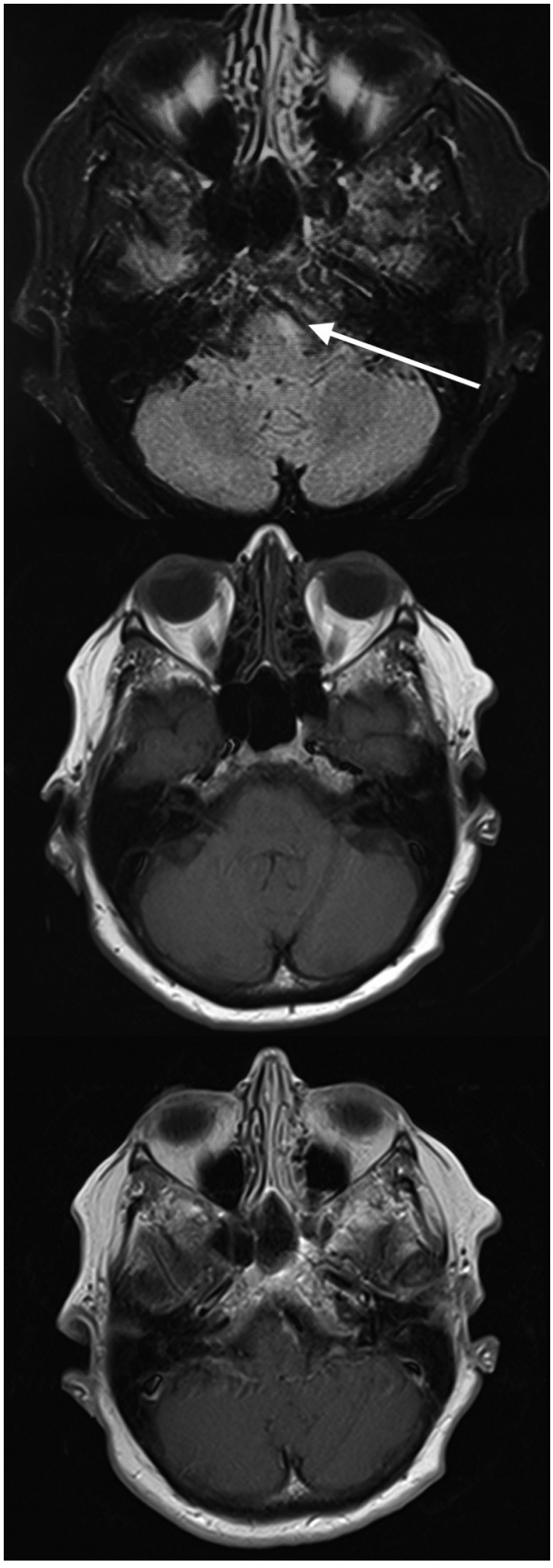

Fig. 2. Case 2. MRI scan showing FLAIR and T1 images before and after contrast, with linear enhancement after contrast in the ventral left part of the medulla oblongata

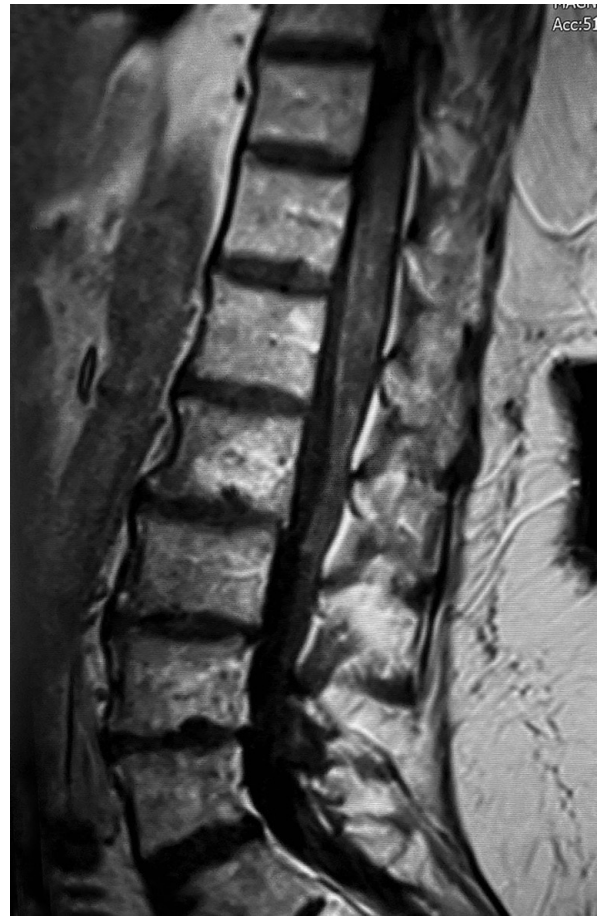

Fig. 3. Case 2. Sagittal T1-weighted image shows a longitudinally extensive lesion extending from Th8–L1 with contrast enhancement

a decreased sensation below the Th4 dermatome on the left and L4 on the right. Her MRI revealed extensive inflammatory changes from C2 to Th6 level (Fig. 4), and small non-specific lesions in the white matter of both hemispheres of the brain (Fig. 5). The examination of the cerebrospinal fluid revealed white cell count of 286/μL with lymphocyte predominance, protein level of 88.5 mg/dL. The infectious aetiology was also excluded. Visual evoked potentials (VEP) examination revealed bilateral, axonal-demyelinating dysfunction of the visual tract with left-sided predominance. Serum test for AQP-4-Ab was positive.

She was treated with intravenous methylprednisolone 1 g daily over 5 days with oral tapering over two weeks. She was maintained on mycophenolate mofetil (MMF) (2 × 1,000 mg) combined with oral methylprednisolone 16 mg/d. Improvement in muscle strength was observed. Nine months after the diagnosis was made the patient was infected with SARS-CoV-2. Her condition deteriorated rapidly during the infection. She was admitted to ICU, intubated and vasopressor support was used. She died three weeks following the admission.

DOI: 10.15557/AN.2022.0023

Age/Sex	Clinical characteristics	MRI lesions localisation	VEP	Treatment
72/Female	LETM: paraparesis Brainstem: area postrema syndrome	Periventricular medulla oblongata Spinal cord (C2–C3)	Bilateral demyelinating damage of visual pathways (P100 123.3 ms L, P100 129.8 ms R)	Methylprednisolone i.v. 1 g daily over 5 days Prednisolone 70 mg p.o. Azathioprine 120 mg p.o.
71/Female	Brainstem: double vision LETM: left lower limb paresis	Medulla oblongata Spinal cord (Th8–L1)	Bilateral demyelinating-axonal damage of visual pathways (P100 220 ms R, P100 219.3 ms L)	Methylprednisolone i.v. 1 g daily over 5 days Prednisolone 90 mg p.o. Satralizumab 120 mg s.c./month
63/Female	LETM: left lower limb paresis, decreased sensation	Spinal cord (C2–Th6) Non-specific bilateral supratentorial T2-hyperintense lesions	Bilateral demyelinating-axonal damage to visual pathways (P100 126 ms L, P100 128.5 ms R)	Methylprednisolone i.v. 1 g daily over 5 days Mycophenolate mofetil 2 × 1,000 mg p.o. Methylprednisolone 16 mg p.o.
52/Female	LETM: left lower limb paresis	Spinal cord Th1–Th5	Bilateral demyelinating-axonal damage to visual pathways (P100 118.5 ms L, P100 142.8 ms R)	Methylprednisolone i.v. 1 g daily over 5 days Prednisolone 90 mg Methylprednisolone 16 mg p.o./ Mycophenolate mofetil 2 × 1,000 mg
LETM – longitudinally extensive transverse myelitis; **ON** – optic neuritis; **VEP** – visual evoked potentials.				

Tab. 2. Clinical and MRI characteristic summary of the reported patients

CASE 4

A 54-year-old previously healthy woman developed sudden paresis of the left lower limb with a positive Babinski sign and numbness below the Th5 dermatome on the right. MRI scan of the cervical and thoracic spine demonstrated a thickening of the spinal cord at the Th1–Th5 level and an intramedullary lesion with increased signal in the T2 and TIRM sequences, occupying the two-thirds of the spinal cord area cross-section, with a clear peripheral enhancement following contrast administration. The lumbar puncture revealed lymphocytic pleocytosis (30/μL) and a slightly increased protein level (64.1 mg/dL). AQP4-Abs were confirmed in serum. Visual evoked potentials revealed bilateral damage to visual tracts. The patient underwent a course of intravenous methylprednisolone therapy (1 g/d over 5 days) and was maintained on oral prednisolone, with the initial dose of 60 mg/day. After 10 days of treatment a follow-up thoracic spine MRI showed partial regression of the lesions, which corresponded with clinical improvement. The patient was started on MMF 1,000 mg twice a day. A year and a half following the diagnosis no relapses were observed. Due to the gastrointestinal complaints related to MMF treatment, the patient decided to suspend treatment.

DISCUSSION

The onset of NMOsd after the fifth decade of life is relatively rarely described. Here, we report four cases of late onset NMOsd patients hospitalised in our department, emphasising the demographic and clinical variability of this entity. For the summary of clinical and MRI data, see Tab. 2. In the diagnostic process of the above cases, when taking into account the age and medical history, cerebrovascular

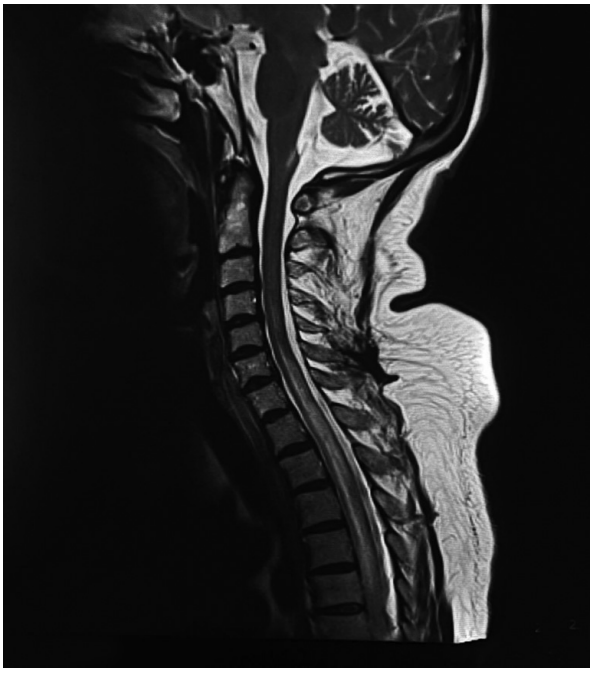

Fig. 4. Case 3. T2-weighted image of a C2–Th6 lesion

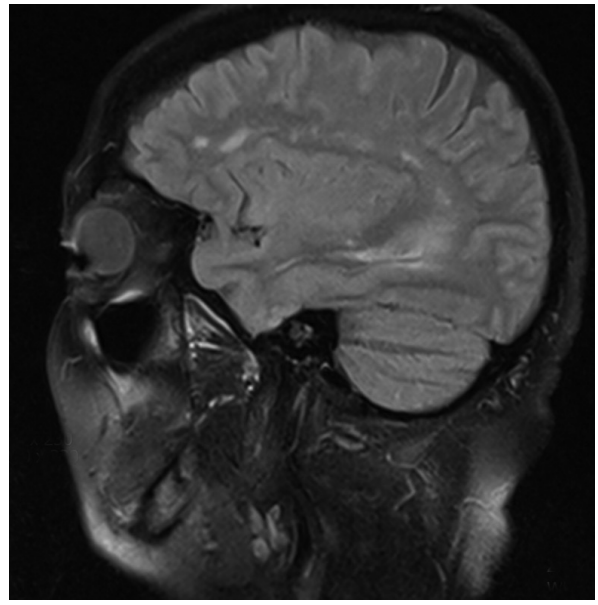

Fig. 5. Case 3. T2-weighted images of non-specific, white matter lesions that do not fulfil neuroimaging criteria for MS diagnosis

 DOI: 10.15557/AN.2022.0023

incidents were considered as the most likely aetiology of sudden paresis. It should be noted that in this age group the first clinical symptoms of NMOsd are rather related to the spinal cord lesions, unlike in the younger population, in whom visual impairment is a more frequent initial symptom (Pandit et al., 2015). Apart from cerebrovascular incidents, infectious causes, diabetic neuropathy, paraneoplastic syndromes and orthopaedic pathology were also considered. Due to the comorbidities in LO- and VLO-NMOsd patients, the condition can easily be misdiagnosed, resulting in a delay of the proper treatment. Older age at onset correlates with severe clinical course of NMOsd and leads to early motor disability. Besides the age at onset, Sepulveda et al. (2019) found a worse recovery from the first attack as an independent predictor of disability in LO-NMOSD. Impaired recovery mechanisms, less immune tolerance and worse anti-inflammatory response aggravate clinical outcomes. The aforementioned study also found that AQP4-seronegative LO-NMOSD patients had worse outcomes than AQP4-seropositive ones.

Furthermore, chronic corticosteroids can exacerbate comorbidities, such as diabetes, osteoporosis or hypertension, which are frequently observed in elderly patients (Ambrosius et al., 2020). The increased mortality in LO-NMOsd patients is often secondary to infections resulting from immunosuppression. Collongues et al. (2014) reported that in a group of 108 LO-NMOsd patients that was followed for 4.5 years, 14 patients died during follow-up due to severe opportunistic infections or respiratory failure. The study indicated that older age at onset and higher annualised relapse rate (ARR) were independent factors of mortality.

NMOsd should be considered regardless of patient's age (Krumbholz et al., 2015). Routine therapeutic management includes relapse treatment and remission maintenance (Selmaj and Selmaj, 2019). Traditionally, intravenous steroid pulses and plasma exchange followed by immunosuppressive drugs are recommended. Until now, oral steroids and azathioprine (AZA) have been considered as the first-line relapse prevention treatment, but their use is limited by side effects (Selmaj and Selmaj, 2019; Waliszewska-Prosół et al., 2021). Also, since AZA itself requires up to 6 months to achieve its immunosuppressive effect, oral steroids are needed as co-therapy (Selmaj and Selmaj, 2019; Waliszewska-Prosół et al., 2021). A more effective but also not licensed option was intravenous rituximab, which is a monoclonal antibody leading to the selective depletion of the CD20-positive B lymphocyte subpopulation (Selmaj and Selmaj, 2019; Zhang et al., 2017). Mycophenolate mofetil, cyclophosphamide and mitoxantrone have also been used as long-term treatment options (Selmaj and Selmaj, 2019).

In the recent years, a significant progress has been made in NMOsd treatment.

Better recognition of the immune mechanism of the disease allowed for the introduction of more targeted therapies. The year 2019 turned out to be a breakthrough year for NMOsd, when the first promising reports on the new therapies were released. These included: eculizumab (antibody against C5 complement), satralizumab (antibody against IL-6 receptor) and inebilizumab (antibody against the CD19 receptor on the B-cell lineage). The high effectiveness in relapse prevention and a good safety profile of these three drugs have been proven in AQP4-Ab seropositive patients (Bennett et al., 2019; Cree et al., 2019; Pittock et al., 2019; Velasco et al., 2021). The development of new therapies with high efficacy and tolerability is a milestone for NMOsd patients.

In relation to LO, VLO-NMOsd patients, the availability of targeted therapies may increase the safety of treatment, as this group is particularly susceptible to serious infectious complications of immunosuppressive therapy. Moreover, it should be kept in mind that frequent comorbidities and impaired restorative processes lead to a worse response to the immunological treatment in the elderly NMOsd patients (Sepulveda et al., 2019).

CONCLUSION

The presented cases of LO-NMO patients provide evidence for the clinical and demographic variability of this disease, which should increase diagnostic vigilance and consideration of NMO irrespective of age under appropriate clinical conditions. Due to the relatively rare occurrence, LO-NMO and VLO-NMO symptoms could have been easily attributed to more frequent diseases in this age group and lead to its misdiagnosis. Due to the recent progress in NMO treatment, early diagnosis is particularly important, as the sooner the appropriate treatment is introduced, the better outcome might be observed.

Conflict of interest

The authors have no conflict of interest to declare.

References

Ambrosius W, Michalak S, Kozubski W et al.: Myelin oligodendrocyte glycoprotein antibody-associated disease: current insights into the disease pathophysiology, diagnosis and management. Int J Mol Sci 2020; 22: 100.

Bennett JL, Greenberg B, Traboulsee A et al.: Efficacy of satralizumab as monotherapy in pre-specified subgroups of SAkuraStar, a double-blind placebo-controlled phase 3 clinical study in patients with neuromyelitis optica spectrum disorder (NMOSD). J Neurol Sci 2019; 405 (Suppl): 172.

Carnero Contentti E, Daccach Marques V, Soto de Castillo I et al.: Clinical features and prognosis of late-onset neuromyelitis optica spectrum disorders in a Latin American cohort. J Neurol 2020; 267: 1260–1268.

Collongues N, Marignier R, Jacob A et al.: Characterization of neuromyelitis optica and neuromyelitis optica spectrum disorder patients with a late onset. Mult Scler 2014; 20: 1086–1094.

Cree BAC, Bennett JL, Kim HJ et al.; N-MOmentum study investigators: Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-MOmentum): a double-blind, randomised placebo-controlled phase 2/3 trial. Lancet 2019; 394: 1352–1363.

Fragoso YD, Ruocco HH, Dias RM et al.: Late onset of neuromyelitis optica spectrum disorders. Neurol Ther 2019; 8: 477–482.
Gospodarczyk-Szot K, Nojszewska M, Podlecka-Piętowska A et al.: Zapalenie nerwów wzrokowych i rdzenia Devica (NMO) oraz choroby ze spektrum NMO. Pol Przegl Neurol 2016; 12: 196–205.
Jasiak-Zatonska M, Kalinowska-Lyszczarz A, Michalak S et al.: The immunology of neuromyelitis optica – current knowledge, clinical implications, controversies and future perspectives. Int J Mol Sci 2016; 17: 273.
Jasiak-Zatońska M, Michalak S, Osztynowicz K et al.: Relationship between blood-brain permeability and antibodies against aquaporins in neuromyelitis optica spectrum disorders and multiple sclerosis patients. Neurol Neurochir Pol 2022a; 56: 308–317.
Jasiak-Zatońska M, Pietrzak A, Wyciszkiewicz A et al.: Different blood-brain-barrier disruption profiles in multiple sclerosis, neuromyelitis optica spectrum disorders, and neuropsychiatric systemic lupus erythematosus. Neurol Neurochir Pol 2022b; 56: 246–255.
Juryńczyk M, Jacob A, Fujihara K et al.: Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease: practical considerations. Pract Neurol 2019; 19: 187–195.
Juryńczyk M, Jakuszyk P, Kurkowska-Jastrzębska I et al.: Increasing role of imaging in differentiating MS from non-MS and defining indeterminate borderline cases. Neurol Neurochir Pol 2022; 56: 210–219.
Krumbholz M, Hofstadt-van Oy U, Angstwurm K et al.: Very late-onset neuromyelitis optica spectrum disorder beyond the age of 75. J Neurol 2015; 262: 1379–1384.
Mao Z, Yin J, Zhong X et al.: Late-onset neuromyelitis optica spectrum disorder in AQP4-seropositive patients in a Chinese population. BMC Neurol 2015; 15: 160.
Pandit L, Asgari N, Apiwattanakul M et al.; GJCF International Clinical Consortium & Biorepository for Neuromyelitis Optica: Demographic and clinical features of neuromyelitis optica: a review. Mult Scler 2015; 21: 845–853.
Pittock SJ, Berthele A, Fujihara K et al.: Eculizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder. N Engl J Med 2019; 381: 614–625.
Selmaj K, Selmaj I: Novel emerging treatments for NMOSD. Neurol Neurochir Pol 2019; 53: 317–326.
Seok JM, Cho HJ, Ahn SW et al.: Clinical characteristics of late-onset neuromyelitis optica spectrum disorder: a multicenter retrospective study in Korea. Mult Scler 2017; 23: 1748–1756.
Sepulveda M, Delgado-García G, Blanco Y et al.: Late-onset neuromyelitis optica spectrum disorder: the importance of autoantibody serostatus. Neurol Neuroimmunol Neuroinflamm 2019; 6: e607.
Suchdev K, Razmjou S, Venkatachalam P et al.: Late onset neuromyelitis optica mimicking an acute stroke in an elderly patient. J Neuroimmunol 2017; 309: 1–3.
Topkan TA, Sokmen O, Kocer B et al.: Tumefactive demyelinating lesion in patient with neuromyelitis optica spectrum disorder. Neurol Neurochir Pol 2022; 56: 285–287.
Velasco M, Zarco LA, Agudelo-Arrieta M et al.: Effectiveness of treatments in Neuromyelitis optica to modify the course of disease in adult patients. Systematic review of literature. Mult Scler Relat Disord 2021; 50: 102869.
Waliszewska-Prosół M, Chojdak-Łukasiewicz J, Budrewicz S et al.: Neuromyelitis optica spectrum disorder treatment – current and future prospects. Int J Mol Sci 2021; 22: 2801.
Wynford-Thomas R, Jacob A, Tomassini V: Neurological update: MOG antibody disease. J Neurol 2019; 266: 1280–1286.
Zakrzewska-Pniewska B: Kompendium chorób ze spektrum zapalenia nerwów wzrokowych i rdzenia (NMOSD). Via Medica, Gdańsk 2020.
Zhang M, Zhang C, Bai P et al.: Effectiveness of low dose of rituximab compared with azathioprine in Chinese patients with neuromyelitis optica: an over 2-year follow-up study. Acta Neurol Belg 2017; 117: 695–702.