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Case Report

Very Late-Onset Neuromyelitis Optica Spectrum Disorder Associated with Latent Syphilis: A Case and Literature Review

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SUMMARY

Neuromyelitis optica spectrum disorder (NMOSD) in elderly patients is an uncommon but severely disabling disease. Rapid diagnosis and treatment are warranted. However, due to the different comorbidities present in the elderly, it is likely to result in misdiagnosis or delayed diagnosis. Herein, we report a case of very-late-onset NMOSD with latent syphilis misdiagnosed as lumbosacral spondylolisthesis in an 80-year-old woman. Our case highlights that timely treatment of co-existing latent syphilis and aquaporin-4 antibody(AQP4-Ab)-positive NMOSD results in an excellent prognosis. NMOSD should be considered in the differential diagnosis of elderly patients with transverse myelitis. In addition, comprehensive investigation and treatment of diseases co-existing with NMOSD are essential.

1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory demyelinating disease of the central nervous system.[1] Several cases of NMOSD co-existing with or preceding autoimmune diseases, infections, and cancers have been reported.[2] Usually, NMOSD develops in the patients aged 30–40 years and rarely occurs in elderly patients.[3] The NMOSD in the elderly warrants attention because it seems to be a distinct disease entity compared to the early-onset NMOSD.[4] Moreover, it is difficult to make an exact diagnosis in the elderly due to the presence of many comorbid conditions. The systemic infection may trigger or exacerbate the development of NMOSD in elderly patients.[5] The progression is rapid and the morbidity and mortality rates are high, leading to the requirement of immediate treatment.

Herein, we report a case of parainfectious very late-onset (VLO)-NMOSD associated with latent syphilis in an 80-year-old woman who was hospitalized in the orthopedics ward because of lumbosacral spondylolisthesis.

2. Case report

An 80-year-old woman was admitted to the orthopedics ward due to the complaint of back pain and radiating paresthesia in the right lower limb. She had been diagnosed with spinal stenosis a week before. However, she complained of stabbing chest pain and nausea from the day of hospitalization, and began vomiting continuously. There were no abnormal findings on the intestinal endoscopy and abdominal pelvic CT. After a week, urinary retention and difficulty in defecation developed.

The patient had no medical history except hyperlipidemia and flu-like symptoms that developed a month before. Neurologic examination revealed paraparesis of motor grade 2/2, impaired sensation, and paresthesia below T4. The Babinski sign on the right was positive. The patient experienced painful muscle spasms in both hands. The Expanded Disability Status Scale (EDSS) score was 8.5. Spinal cord magnetic resonance imaging (MRI) on the T2-weighted imaging (T2WI) demonstrated longitudinally extensive hyper-intensity lesions at C2–C6 extending to the cervicomedullary junction and at T2–T4 and T10–T11 (Figure 1). The lesions showed multifocal central gadolinium enhancement at the C2–L1 level (Figures 1 and 2). Brain MRI revealed no lesions, suggesting demyelinating disease except of the area postrema. Cerebrospinal fluid (CSF) analysis revealed mild protein elevation (60.52 mg/dL) with pleocytosis (7 cells/μL) and normal glucose levels (59 mg/dL). The oligoclonal bands were negative and the immunoglobulin G (IgG) index was elevated to 3.28. Serological tests showed high venereal disease research laboratory (VDRL) titer (≥ 1:32) and high *Treponema pallidum* latex agglutination-*Treponema pallidum* hemagglutination (TPLA-TPHA) levels (29 T.U.; 1 T.U. equals 2 mIU according to WHO reference material).

The patient was transferred to the neurology ward and was treated with ceftriaxone IV (2 mg) for 2 weeks. Simultaneously, she received a high-dose intravenous steroid (methylprednisolone, 1 g/day) for 5 days, followed by oral prednisolone daily. Subsequently, the CSF VDRL and the fluorescent treponemal antibody absorption test (FTA-ABS) were negative. Serological tests to exclude autoimmune and infectious diseases were negative. The serum AQP4-Ab test result on the 10th day of treatment was positive (1:10, intensity 3+, cell-based direct immunofluorescence). Thus, the patient was diagnosed with parainfectious NMOSD associated with latent syphilis.

The patient's neurological symptoms gradually improved. Muscle strength also improved to grade 4, and sitting balance recovered. Follow-up spinal MRI a month after the beginning of treatment

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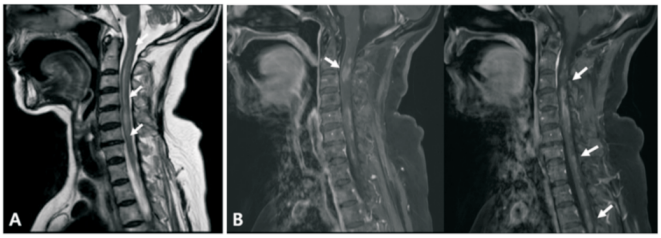

Figure 1. Cervical spine magnetic resonance imaging. (A) Sagittal T2-weighted image showing hyper-intense lesions at C2–C6 level extending longitudinally to the cervicomedullary junction (arrow). (B) Sagittal T1-weighted gadolinium-enhanced images showing a patchy enhancement (arrow) and longitudinally extensive enhancement through the entire spinal cord.

showed remarkable regression of longitudinally extensive transverse myelitis (LETM), except at the C5 level (Figure 3). After the 70th day of admission, the patient could almost stand independently and her EDSS score improved to 5.5. She had no relapse for 12 months with mycophenolate mofetil treatment (1 g/day) and was followed-up with VDRL titer for syphilis treatment.

3. Discussion

In the multicenter studies, NMOSD has been classified based on the age of onset as early-onset NMOSD (EO-NMOSD: < 50 years), late-onset NMOSD (LO-NMOSD: 50–69 or 74 years), and VLO-NMOSD (≥ 70 or 75 years).[6,7] Distinct hallmarks at disease onset have been consistently reported across all studies. Patients with LO-NMOSD and VLO-NMOSD frequently manifested with transverse myelitis (TM) at disease onset, while optic neuritis (ON) was more prevalent in patients with EO-NMOSD. Furthermore, prior reports demonstrated that the length of the spinal cord lesion from cervical to thoracic level was significantly longer in patients with VLO-NMOSD than others.[8,9] In contrast, abnormal findings in brain MRI were less frequently detected in patients with LO-NMOSD and VLO-NMOSD. These discrepancies across age groups may be explained by anatomical susceptibility to inflammation based on the age at onset.[7,10] Patients with LO-NMOSD and VLO-NMOSD tended to display more severe EDSS scores within a short duration after onset. These severe clinical courses in the elderly onset group may be related to the characteristics of the initial presentation, such as LETM invading the long spinal cord. In addition, the elderly onset group may have a higher possibility of underlying co-morbidities.[10]

In our patient, typical features of NMOSD in elderly patients were observed. The EDSS score deteriorated rapidly to 8.5 in a few days and the spinal MRI findings revealed a very long extended myelitis from cervical to lumbar level. Initially, the patient was misdiagnosed with severe lumbosacral spondylolisthesis with multiple nerve root compressions. Moreover, a positive blood test result for syphilis interfered with the correct diagnosis of NMOSD. However, as the CSF tests for VDRL and FTA-ABS were ultimately negative, the patient was diagnosed with chronic, untreated latent syphilis requiring treatment and parainfectious NMOSD associated with latent syphilis. Although the exact mechanism is still unknown, we think that certain pathogens of latent syphilis could have potentially triggered and exacerbated the autoimmune cascade leading to NMOSD in her central nervous system.[5,11] Fortunately, the patient was able to regain walking ability with clear improvements following antibiotic treatment for syphilis and simultaneous high-dose steroid therapy. There was no evidence of relapse or recurrence during follow-up period at the out-patient clinic.

Most cases of VLO-NMOSD in patients aged over 75 years reported over the past decade, extracted from a PubMed search, are

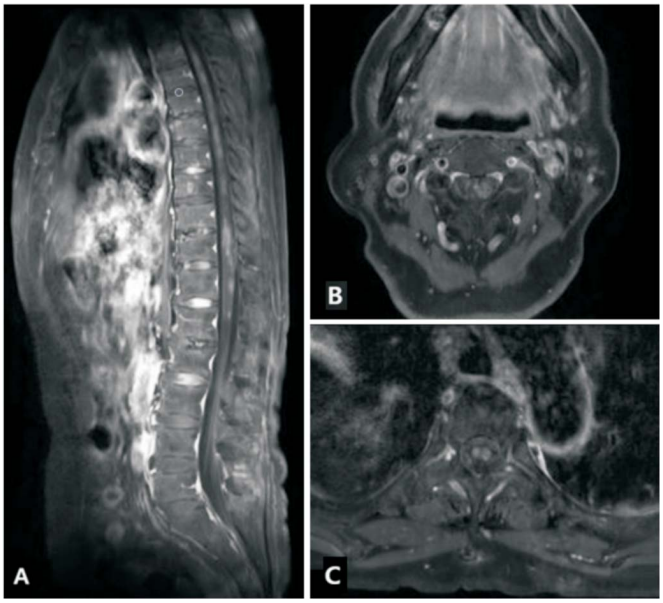

Figure 2. Whole spine magnetic resonance imaging and T1-weighted gadolinium-enhanced images. (A) The sagittal view shows longitudinal high-signal intensity along the spinal cord throughout the thoracic spinal cord. Axial views of (B) cervical cord and (C) thoracic cord show hyper-signal lesions predominant at the center of the cord with peripheral enhancement.

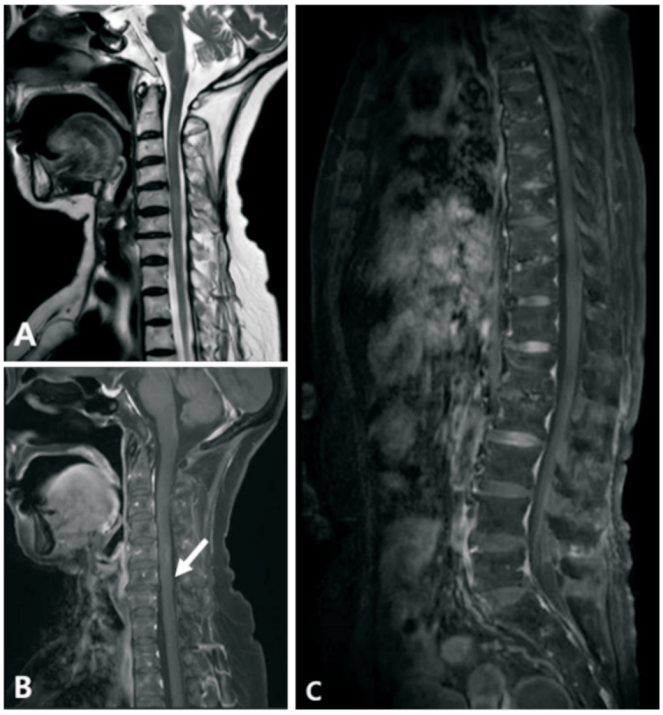

Figure 3. Follow-up spine magnetic resonance imaging after 1 month. (A) Sagittal T2-weighted image shows that cervical cord lesions extending to cervicomedullary junction nearly disappeared. Sagittal T1-weighted gadolinium-enhanced image (B) shows that only dimly enhanced C5 lesions remained (arrow). (C) The previous extensive longitudinally enhanced lesions almost disappeared.

summarized in Table 1.[8,9,12–15] Many elderly patients had frequent relapses, continued to present disabilities, while only about half were able to recover to a walkable status, confirming the poor prognosis of NMOSD in the elderly. In particular, for some patients, death occurred if a rapid diagnosis was not done or NMOSD recurred.[9,12] In a report by Krumbolz et al., the first attack in the second patient was misdiagnosed as compressive myelopathy, and the patient reco-

Table 1
The literature review of reported cases of very-late-onset NMOSD with present case.

Author	Age/ gender	Coexisting disease	Clinical features at onset	Treatment	Prognosis
Fujiwara et al.[8]	82/F	-	T1-T2, T7-T9	IVmPD, PE	Cane walk
	80/M	-	T9-12	PE, OralPD	Bed ridden
Krumbholz et al.[9]	79/M	=	C1-4, T3-4 (1st attack)	IVG	Assisted walk
			ON, Brainstem(medulla)-C5 (2nd attack)	IVG	Wheelchair bound
			ON, Brainstem-entire myelon (3rd attack)	PE	3rd recur/expire
	88/F	Compression myelopathy	T6-9 (1st attack)	No treatment	Spontaneous partial recovery
		TIA Hx.	T10-12 (2nd attack)	IVmPD, PE, Azathioprine(*SE*)	2nd recur/expire # (*PCP/IB*)
	83/F	=	C4, T6-9	Antibiotics treatment	Cane walk
				IVmPD, Azathioprine(*SE*)	(*CMV Pn., hepatopathy*)
				Mycophenolate mofetil	
Otani et al.[12]	79/F	Anti-SS-A/-B Ab: high	Bilateral WMLs	IVmPD, PE	Assisted walk
		Sjogren's sydrome			No relapse
	84/M	-	Lt.WMLs (1st attack)	No treatment	Spontaneous recovery
			LETM (2nd attack)	IVmPD	Expire
Li et al.[13]	81/M	-	C3-7	IVmPD, IVIG	Improve of weakness
				Mycophenolated(*SE*)	Expire # (*pulmonary infection*)
Machado et al.[14]	77/F	VZV infection	C2-T12 (1st attack)	Acyclovir IV, steroid	Wheelchair bound
		Autoimmune thyroiditis Hx	Brain lesions (cbll. & MCP) (2nd attack)	OralPD, Azathioprine	Indwelling urinary cathether
Takewaki et al.[15]	85/F	Stomach cancer	Rt.ON, C3-T4	IVmPD, PE	Partial recovery
Present case	80/F	Latent syphilis	Brainstem lesion (area postrema)	IVmPD, Ceftriaxone IV	Walkable
		LS spondylolisthesis	C2-6, T2-4, T10-L1	Mycophenolated mofetil	

BOOP, Bronchiolitis Oblisterans Organizing Pneumonia; Ca, cancer; Cbll, cerebellum; CMV, cytomegalovirus; F, female; Hx, history; IB, intestinal bleeding; IVG, intravenous glucocorticoids; LS, lumbosacral; Lt, left; M, male; MCP, middle cerebellar peduncles; mPD, methylPD; PCP, pancytopenia; PD, prednisolone; Pn, pneumonia; Rt, right; SE, side effect; Sx, symptom; VZV, varicella zoster virus; WML, white matter lesion; YL, years later.
Expire due to side effect of immunosuppressant, - no commented, = not detected.

vered spontaneously without treatment, but NMOSD recurred and the patient died.[9] The second patient reported by Otani et al. also died due to a similar recurrence.[12] Furthermore, besides NMOSD itself, co-existing diseases are also crucial for deciding treatment in elderly patients with NMOSD. Moreover, elderly patients may not only be resistant to drugs but the drug response may also be poor. The patients reported side effects of immunosuppressive treatment, who finally died due to pancytopenia and intestinal bleeding.[9,12] Physicians should consider that treatment in elderly patients leads to many complications such as bleeding, infections, and even death.

In conclusion, there are numerous pitfalls and complications in correct diagnosis and treatment of elderly patients with NMOSD. Therefore, early comprehensive differential diagnoses for co-existing diseases are necessary. Moreover, proper individualized treatment of diseases co-existing with NMOSD is the most essential factor to achieve a better prognosis for these elderly patients.

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Conflict of interest

The authors declare that they have no competing interests.

References

1. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology.* 2015;85(2):177–189.
2. Chen HQ, Zhang Y, Wang SB, et al. Concurrent aquaporin-4-positive NMOSD and neurosyphilis: A case report. *Mult Scler Relat Disord.* 2019; 34:137–140.
3. Pandit L, Asgari N, Apiwattanakul M, et al. Demographic and clinical features of neuromyelitis optica: A review. *Mult Scler.* 2015;21(7):845–853.
4. Oliveira R, Oliveira S. Letter to the Editor - Late-onset neuromyelitis optica associated with cryptogenic organizing pneumonia. *Mult Scler Relat Disord.* 2019;36:101398.
5. Zhong X, Zhou Y, Lu T, et al. Infections in neuromyelitis optica spectrum disorder. *J Clin Neurosci.* 2018;47:14–19.
6. 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.
7. Nakahara K, Nakane S, Ando Y. Aging, immunosenescense, and very late-onset neuromyelitis optica spectrum disorders. 2020. doi: 10.21203/rs.3.rs-21569/v1.
8. Fujiwara S, Manabe Y, Morihara R, et al. Two cases of very-late-onset neuromyelitis optica spectrum disorder (NMOSD) in patients over the age of 80. *Case Rep Neurol.* 2020;12(1):13–17.
9. 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(5):1379–1384.
10. 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(13):1748–1756.
11. Sellner J, Hemmer B, Mühlau M. The clinical spectrum and immunobiology of parainfectious neuromyelitis optica (Devic) syndromes. *J Autoimmun*. 2010;34(4):371–379.
12. Otani T, Irioka T, Takahashi YK, et al. Two cases of late-onset neuromyelitis optica spectrum disorder initially presenting with isolated cerebral white matter lesions. *eNeurologicalSci.* 2018;13:35–37.
13. Li L, Fang GL, Zheng Y, et al. Late-onset neuromyelitis optica spectrum disorder mimicking stroke in an elderly Chinese man: Case report. *J Spinal Cord Med.* 2020:1–3.
14. Machado C, Amorim J, Rocha J, et al. Neuromyelitis optica spectrum disorder and varicella-zoster infection. *J Neurol Sci.* 2015;358(1–2):520–521.
15. Takewaki D, Kasai T, Itoh K, et al. Case of neuromyelitis optica with recurrent stomach carcinoma. *Clin Exp Neuroimmunol.* 2017;8(4):327–330.