Extensive spinal leptomeningeal enhancement in neuromyelitis optica spectrum disorders: a case report

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ABSTRACT

Background: Cortical involvement and leptomeningeal enhancement are rare in neuromyelitis optica spectrum disorder (NMOSD). Cerebrospinal fluid (CSF) total protein is usually raised typically ranged between 0.5 and 1.5 g/l.

Case Presentation: A 22-year old lady who was previously well presented with a subacute onset of bilateral lower limb weakness for 1 week, which progressed in an ascending pattern involving the upper limbs. Magnetic resonance imaging spine showed longitudinally extensive transverse myelitis as well as leptomeningeal enhancement of the entire spine. CSF protein was high with 3.33 g/l. Serum Aquaporin-4 IgG was positive. After failed steroid therapy, she responded dramatically with plasma exchange.

Conclusion: The presence of very high CSF protein and the presence of extensive leptomeningeal enhancement should not dissuade clinicians from considering the diagnosis of NMOSD, but merely reflects its severity and may need aggressive immunotherapy such as combination of steroids and plasma exchange.

Keywords: Neuromyelitis optica spectrum disorders, spinal leptomeningeal enhancement, aquaporin-4 IgG, longitudinally extensive transverse myelitis.

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Background

Neuromyelitis optica spectrum disorders (NMOSD) are inflammatory disorders of the central nervous system characterized by episodes of immune-mediated demyelination and axonal damage predominantly affecting optic nerves and spinal cord [1]. Current consensus on diagnosis of NMOSD with Aquaporin-4 (AQP4)-IgG requires present least one of the six core clinical characteristics of NMOSD which include optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy, or acute diencephalic clinical syndrome with NMOSD-typical diencephalic magnetic resonance imaging (MRI) lesions, and symptomatic cerebral syndrome with NMOSD-typical brain lesions [2]. One of the most distinct features in NMOSD is longitudinally extensive transverse myelitis (LETM), which was defined as a lesion that spans over three or more contiguous vertebral segments [3]. Cortical involvement and leptomeningeal enhancement are rare in NMOSD [4]. Cerebrospinal fluid (CSF) total protein is usually raised typically ranged between 0.5 and 1.5 g/l [5]. We present a case of NMOSD, AQP4-IgG positive with LETM with two unusual features which are the extremely high CSF protein and the presence of extensive leptomeningeal enhancement (LME), involving the whole spine.

Case Presentation

A 22-year old lady who was previously well presented with a subacute onset of bilateral lower limb weakness for 1 week which progressed in an ascending pattern involving the upper limbs. There is no bulbar symptoms, diplopia, or blurring of vision. No prior visual loss, hiccups, nausea, or vomiting as well as diencephalic symptoms. She is afebrile otherwise. Upon examination, she was hemodynamically stable and afebrile. Her lower limb power was Medical Research Council (MRC) 0/5 with upper limb power of MRC 4/5. Reflexes were absent and there was a sensory level at T2. Fundoscopy was normal.

Her initial laboratory workout, including full blood count, renal profile, liver function tests, calcium, magnesium, phosphate, thyroid function test, serum complement level for C3 and C4 all were normal. C-reactive protein was not raised, and her Antinuclear antibodies and anti-double stranded DNA (anti-dsDNA) were not detected. Blood cultures were negative. The chest radiograph was normal. CSF analysis showed a very high protein level of 3.33 g/l with normal glucose, and sterile culture. CSF GeneXpert and polymerase chain reaction (PCR) for tuberculosis (TB), and PCR for Herpes Simplex virus were negative. Serum Aquaporin-4 IgG antibody was positive. A few red blood cells were present in CSF, hence unable to proceed with cell counts by our laboratory.

MRI brain showed scattered non-enhanced bilateral frontoparietal T2/fluid-attenuated inversion recovery (FLAIR) hyperintense juxtacortical lesion (Figure 1).

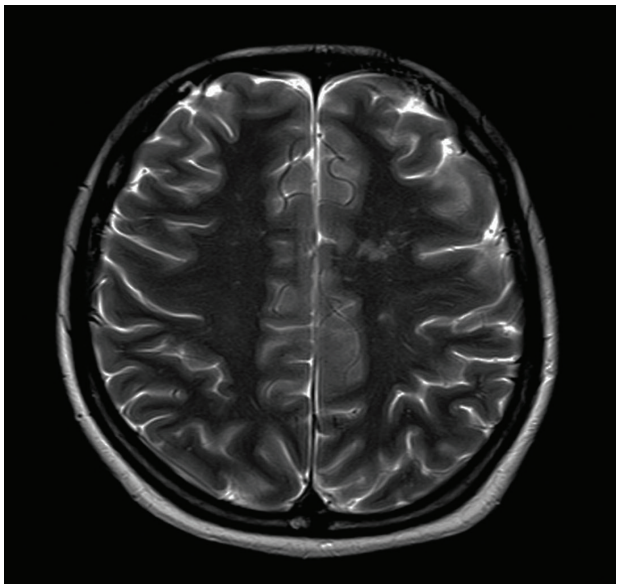

Figure 1. *MRI brain showed scattered non-enhanced bilateral frontoparietal T2/FLAIR hyperintense juxtacortical lesion.*

MRI spine showed LETM as well as smooth leptomeningeal enhancement of entire spine (Figures 2 and 3).

A diagnosis of NMOSD was made. She was treated with methylprednisolone followed by oral prednisolone. However, she showed very minimal improvement in muscle power of the right ankle dorsiflexion and plantar flexion (MRC 2/5) after 2 weeks. She was then undergone five cycles of plasma exchanges via centrifuge method. She showed a significant improvement in muscle power. At the end of the sessions, her strength improved; upper limb MRC 5, lower limb MRC 3 proximally, and MRC 5 distally. The band-like sensation at thoracic region was gone. After undergone in-patient rehabilitation, she was recently discharged with her being able to walk with Zimmer frame.

Discussion

Although there are other differential diagnoses besides NMOSD in patients with LETM [3], NMOSD remains the most common cause of LETM [6]. Other causes of LETM includes systemic autoimmune diseases, such as systemic lupus erythematosus and parainfectious phenomenon, including mycobacterium TB [6,7]. Even though our

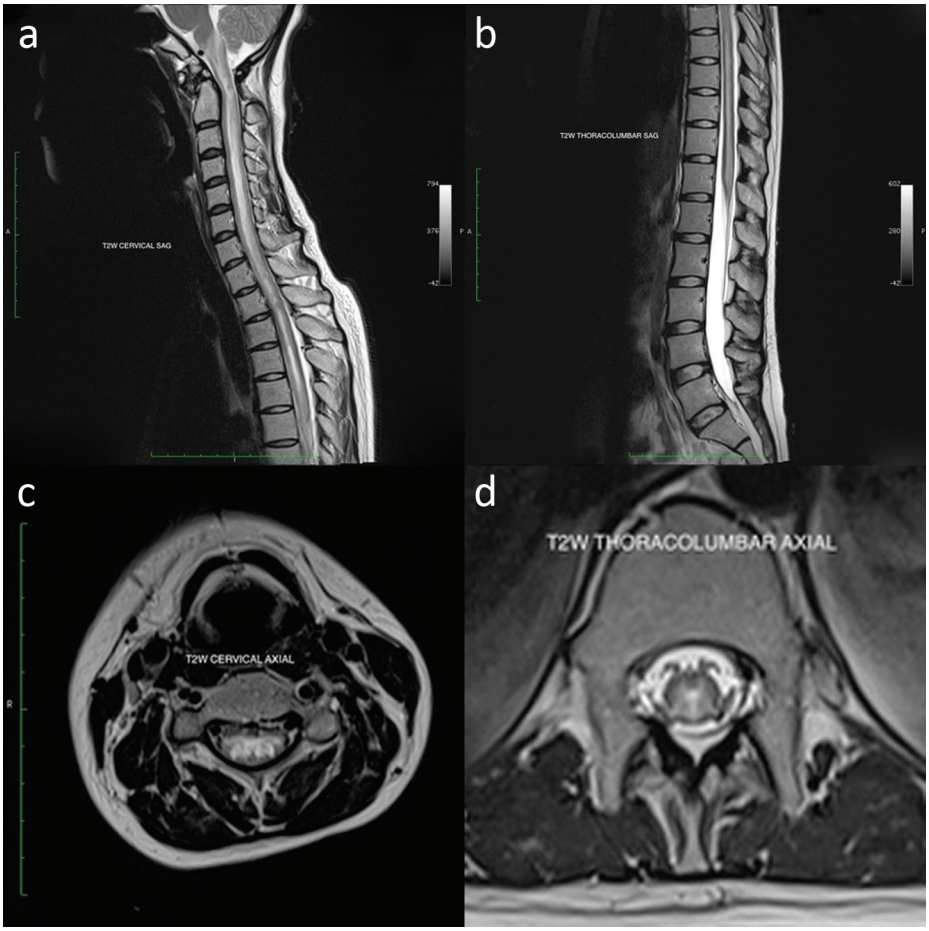

Figure 2. *(a and b) MRI whole spine shows longitudinally extensive intramedullary T2 hyperintensity (entire spinal cord with extension into the brain stem). (c) MRI T2-weighted image of the cervical spine at the axial view, showing hyperintensities signal within the grey matter (bright spotty lesions, BSL). (d) Similar findings at the thoracolumbar axial view.*

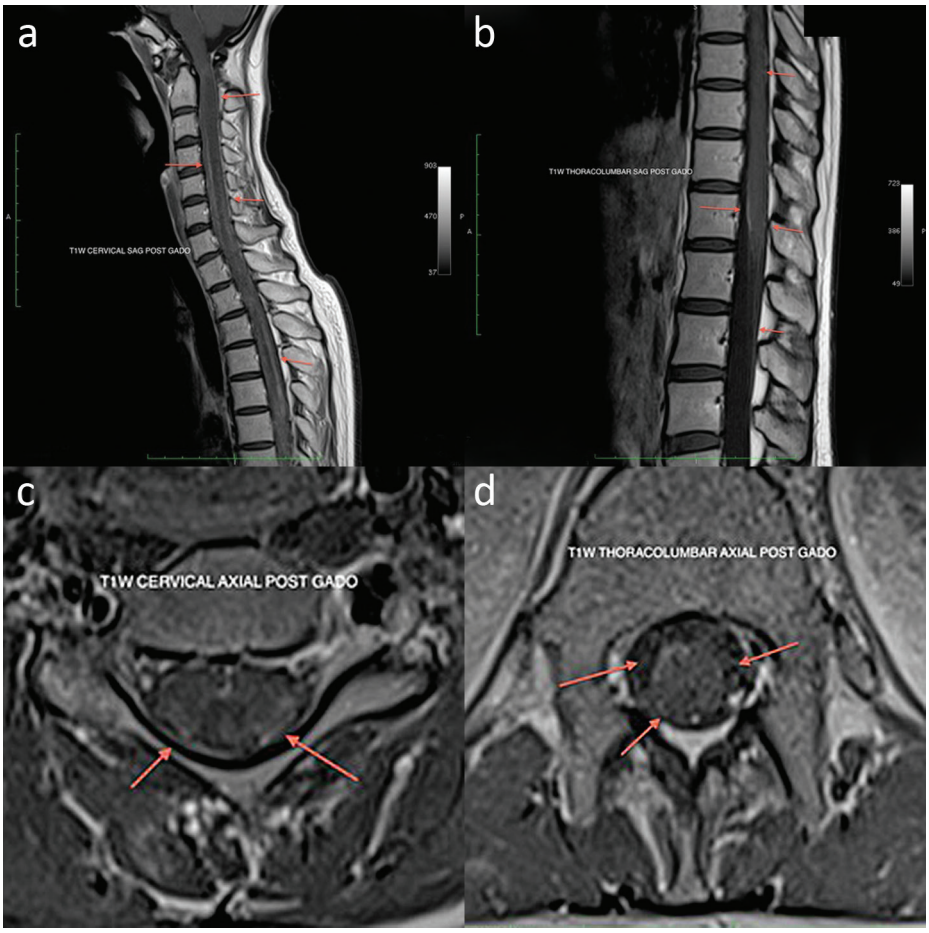

Figure 3. *(a and b) MRI whole spine shows longitudinally extensive intramedullary T1 (post gadolinium) hypo-intensity (entire spinal cord with extension into the brain stem) with smooth leptomeningeal enhancement (red arrows). (c) MRI T1-weighted post-gadolinium image of the cervical spine at the axial view, showing leptomeningeal enhancement (red arrows) and intraparenchymal lesion. (d) Similar findings at the thoracolumbar axial view.*

patient has the evidence of LETM, the diagnosis became in doubt with the presence of extensive leptomeningeal enhancement involving the whole spine. Typical causes of spinal leptomeningeal enhancement include malignancy either primary or secondary metastases, neurosarcoidosis and infection such as TB [8–11].

Although not common, LME has been described with the exact frequency yet to be known. Chen et al [12] described six patients with LME around the brainstem. A retrospective case series of 11 AQP4-IgG-positive NMOSD patients with LME by Asgari et al [13], described its involved 5–17 vertebral segments length. Our patient had LME of the entire spine, with also the presence of bright spotty lesions (BSLs) in the cervical axial images which are clues to the diagnosis. Gadolinium enhancement in NMOSD occurred as a result of disruption of the blood-brain barrier attribute to the ventricular margin containing ependymal cells and astrocytes abundant in AQP4 [13]. Similarly, intense immunoreactivity in the astrocytic end feet, which abut the leptomeninges contributes to LME [14].

Elevated CSF protein is not uncommon in NMOSD, especially during the severe myelitis attack. This is the result of the disruption of the blood CSF barrier which opens the sanctuary areas to the extrathecally-produced aquaporin-4 antibodies. CSF total protein is usually raised typically ranged between 0.5 and 1.5 g/l [5].

Traditionally, the acute treatment for NMOSD is high-dose corticosteroids, usually intravenous methylprednisolone 1 g/day for 3 to 5 days, followed by a slowly tapering course of oral steroids. If initial treatment fails, plasma exchange is the next option [1]. Our patient responded poorly to steroid but dramatically improves with plasma exchange. The extremely high CSF protein and extensive LME may reflect the severity of inflammation and thus failed steroid therapy.

Conclusion

The presence of very high CSF protein and the presence of extensive smooth LME, although unusual but a possible presentation and should not dissuade clinicians from considering the diagnosis of NMOSD. These changes merely reflect the severity and more extensive inflammation. These features may prompt the clinician to initiate an aggressive immunotherapy upfront such as a combination of steroids and plasma exchange. Our patient responded dramatically to plasma exchange and steroids.

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List of Abbreviations
AQP4-IgG	Aquaporin-4 IgG
CSF	Cerebrospinal fluid
FLAIR	Fluid-attenuated inversion recovery
LETM	longitudinally extensive transverse myelitis
LME	leptomeningeal enhancement
MRC	Medical Research Council
MRI	Magnetic resonance imaging
NMOSD	Neuromyelitis Optica Spectrum Disorders

Consent for publication
Written informed consent for the paper to be published (including images, case history and data) was obtained from the patient for publication of this paper.

Ethical approval
Ethical approval is not required at our institute to publish an anonymous case report.

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References
1. Bruscolini A, Sacchetti M, La Cava M, Gharbiya M, Ralli M, Lambiase A, et al. Diagnosis and management of neuromyelitis optica spectrum disorders-an update. Autoimmun Rev. 2018;17(3):195–200. https://doi.org/10.1016/j.autrev.2018.01.001
2. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015;85(2):177–89. https://doi.org/10.1212/WNL.0000000000001729
3. Kim HJ, Paul F, Lana-Peixoto MA, Tenembaum S, Asgari N, Palace J, et al. MRI characteristics of neuromyelitis optica spectrum disorder: an international update. Neurology. 2015;84(11):1165–73. https://doi.org/10.1212/WNL.0000000000001367
4. Kim W, Kim SH, Huh SY, Kim HJ. Brain abnormalities in neuromyelitis optica spectrum disorder. Mult Scler Int. 2012;2012. https://doi.org/10.1155/2012/735486
5. Jarius S, Paul F, Franciotta D, Ruprecht K, Ringelstein M, Bergamaschi R, et al. Cerebrospinal fluid findings in aquaporin-4 antibody positive neuromyelitis optica: results from 211 lumbar punctures. J Neurol Sci. 2011;306(1–2):82–90. https://doi.org/10.1016/j.jns.2011.03.038
6. Eckstein C, Syc S, Saidha S. Differential diagnosis of longitudinally extensive transverse myelitis in adults. Eur Neurol J. 2011;3(1):27. https://doi.org/10.1136/bcr.10.2010.3444
7. Kitley JL, Leite MI, George JS, Palace JA. The differential diagnosis of longitudinally extensive transverse myelitis. Mult Scler J. 2012;18(3):271–85. https://doi.org/10.1177/1352458511406165
8. Georgy BA, Snow RD, Hesselink JR. MR imaging of spinal nerve roots: techniques, enhancement patterns, and imaging findings. AJR Am J Roentgenol. 1996;166(1):173–9. https://doi.org/10.2214/ajr.166.1.8571871
9. Garg RK, Malhotra HS, Gupta R. Spinal cord involvement in tuberculous meningitis. Spinal Cord. 2015;53(9):649. https://doi.org/10.1038/sc.2015.58
10. Nayar G, Ejikeme T, Chongsathidkiet P, Elsamadicy AA, Blackwell KL, Clarke JM, et al. Leptomeningeal disease: current diagnostic and therapeutic strategies. Oncotarget. 2017;8(42):73312. https://doi.org/10.18632/oncotarget.20272
11. Smith JK, Matheus MG, Castillo M. Imaging manifestations of neurosarcoidosis. Am J Roentgenol. 2004;182(2):289–95. https://doi.org/10.2214/ajr.182.2.1820289
12. Chen M, Zhang B, Gao C, Zheng Y, Xie L, Gao Q, 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(1–2):62–7. https://doi.org/10.1016/j.jneuroim.2014.02.006
13. Asgari N, Flanagan EP, Fujihara K, Kim HJ, Skejoe HP, Wuerfel J, et al. Disruption of the leptomeningeal blood barrier in neuromyelitis optica spectrum disorder. Neurol Neuroimmunol Neuroinflamm. 2017;4(4):e343. https://doi.org/10.1212/NXI.0000000000000343
14. Pittock SJ, Weinshenker BG, Lucchinetti CF, Wingerchuk DM, Corboy JR, Lennon VA. Neuromyelitis optica brain lesions localized at sites of high aquaporin 4 expression. Arch Neurol. 2006;63(7):964–8. https://doi.org/10.1001/archneur.63.7.964

Summary of the case
1	**Patient (gender, age)**	Female, 22
2	**Final diagnosis**	Neuromyelitis Optica Spectrum Disorders
3	**Symptoms**	Subacute onset of bilateral lower limb weakness for 1 week which progressed in an ascending pattern involving the upper limbs.
4	**Medications**	Methylprednisolone and prednisolone
5	**Clinical procedure**	Steroids followed by 5 cycles of exchange transfusion
6	**Specialty**	Neurology