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UNRECOGNIZED NEUROMYELITIS OPTICA SPECTRUM DISORDER WITH PONTINE AND CORPUS CALLOSUM MICROHEMORRHAGE

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Abstract

Introduction: Neuromyelitis optica spectrum disorder (NMOSD) represents an immune-mediated neuroinflammatory syndrome, classified as separate entity after discovery of aquaporin-4 immunoglobulin G antibodies (AQP4-IgG). The neuroimaging spectrum of NMOSD classically consisted of bilateral optic neuritis and longitudinally extensive transverse myelitis (LETM), recently broadened with lesions in area postrema, diencephalon, brainstem and cerebellum, and extensive cord atrophy.

Case report: Here we present a case of an AntiAQP4-positive 65-year old female patient who initially presented with underappreciated LETM and developed multiple cerebral and cerebellar lytic demyelinating lesions associated with acute long segment optic nerve involvement two years later. Two new imaging findings are described in this case: the involvement of complete cross-sectional area of pons and microhemorrhage in the pons and corpus callosum.

Conclusion: Raising suspicion of NMOSD is of a crucial importance in cases with isolated LETM in order to prevent relapses in Anti-AQP4 positive cases, improve patient outcome and recovery.

Keywords: neuromyelitis optica; magnetic resonance imaging; aquaporin 4; susceptibility-weighted imaging

Apstrakt

Uvod: Neuromijelitis optika spektar (NMOSD) predstavlja imunoposredovan neuroinflamatorni sindrom, koji je klasifikovan kao poseban entitet nakon otkrića akvaporin-4 imunoglobulin G antitela (AQP4-IgG). Spektar nalaza na neuroimindžingu se klasično sastoji od bilateralnog optičkog neuritisa i longitudinalno ekstenzivnog transverznog mijelitisa (LETM), je odskora proširen lezijama u arei postremi,
deiencefalon, moždanog stabla I cerebeluma, te ekstenzivnom atrofijom kičmene moždine.

**Prikaz slučaja:** Prikazujemo slučaj AntiAQP4-pozitivne 65-godišnje ženske osobe sa inicijalnom prezentacijom neuočenog LETM i koja je razvila multiple cerebralne i cerebelarne litičke demijelinacione lezije povezane sa akutnim optičkim neuritisom dugog segmenta dve godine kasnije. Dva nova nalaza na imidžingu su opisana: zahvatanje kompletne transverzalne površine ponsa, te mikrohemoragije u ponsu i korpusu kalozumu.

**Zaključak:** Sumnja na NMOSD je od krucijalnog značaja u slučajevima sa izolovanim LETM da bi se prevenirali relapsi u AntiAQP4-pozitivnim slučajevima, poboljšala prognoza i oporavak.

**Introduction**

Neuromyelitis optica spectrum disorder (NMOSD) represents an immune-mediated neuroinflammatory syndrome that became a separate entity after discovery of aquaporin-4 immunoglobulinG antibodies (AQP4-IgG) (1).

The neuroimaging spectrum of NMOSD, classically consisted of bilateral optic neuritis and longitudinally extensive transverse myelitis (>3 vertebral segments, LETM), has been broadened to include lesions in the area postrema, diencephalon, brainstem and the cerebellum, as well as longitudinally extensive cord atrophy as chronic sequalae (1). Acute LETM spinal cord lesions are, however, the most specific neuroimaging characteristic of NMOSD (2).

Here we present a case of a 65–year old female patient who initially presented with underappreciated LETM, with two new imaging findings described- the involvement of complete cross-sectional area of the pons and hemorrhage in the pons and in the splenium of corpus callosum.
Case report

A 63-year old female presented with lower back pain, spastic paraparesis, gait disorder, and urinary retention. CSF was normal, oligoclonal bands were negative both in CSF and serum. Magnetic resonance imaging (MRI) of the thoracic spine revealed extensive, five segments long inflammatory process of the upper thoracic spinal cord mainly involving the central gray matter, misinterpreted as syringomyelia (Figure 1, A and B).

Six months later, a follow up MRI study revealed disease progression, associated with cord edema and inflammation involving more than 8 segments in the thoracic spinal cord. Imaging of the brain revealed no abnormalities (Figure 1, C and E).

Twenty-seven months later, the patient presented with altered consciousness, dysphagia, anarthria, spastic paraplegia. Brain imaging showed bilateral, almost symmetric abnormalities in the periventricular white matter, corpus callosum, both corticospinal tracts at the level of the posterior limb of capsula interna, mesencephalon, pons, superior and middle cerebellar peduncles and cerebellar white matter adjacent to the fourth ventricle, as well as in the ventral columns of medulla oblongata. Diffusion was restricted at the periphery of the lesions. Susceptibility-weighted imaging (SWI) revealed discrete hemorrhage in the splenium of the corpus callosum and laterally in the pons. Contrast enhancement was vivid and heterogeneous (Figure 2). At this point, long segment left optic nerve atrophy was present, with no contrast enhancement. Five days later, MR spectroscopy was performed in the pontine lesion, showing only elevation of Cho/Cr ratio and a small lactate peak, compatible with anaerobic glycolysis in tumefactive demyelination (Figure 3F). The suspicion of NMOSD was raised and lumbar puncture was repeated - CSF tested positive for AQP4-IgG. Follow up imaging of the thoracic spine showed severe atrophy of the thoracic spinal cord and gliotic lesions surrounding the
dilated central canal as sequelae of LETM (Figure 1, D and F). The patient was initially treated with pulse doses of 1g methylprednisolone for 7 days, which resulted in minimal neurological improvement. Due to unsatisfactory response to treatment, plasma exchange was performed, followed by the introduction of immunosuppressive therapy with prednisone and azathioprine. The outcome was lethal.

Discussion

The diagnosis of NMOSD is based on both clinical and radiologic findings, according to the international consensus diagnostic criteria for NMOSD (1). In this case the patient was a 63-year-old female, and disease followed relapsing course, in concordance with typical NMOSD epidemiologic findings (3). Mortality rates are high in NMOSD, varying from 25-50%, highly associated with neurogenic respiratory failure and extensive brainstem lesions (4).

The initial imaging finding in our patient was an isolated acute LETM, misinterpreted as a syrinx, with no concurrent brain lesions. LETM is typically considered as one of the cardinal clinical findings in NMOSD, in conjunction with optic neuritis (5). At the initial presentation, no signs of optic neuritis were evident, although it developed later during the disease. However, isolated myelitis as the only clinical manifestation has been shown to be more common in male patients (67% vs 28%) (6). Follow-up MRI scans revealed the progression of LETM leading to severe and rapid atrophy of the affected spinal cord. Relapsing course was observed two years later with newly detected lesions in the brain, all classical NMOSD locations (1).

Spinal cord atrophy is considered a chronic manifestation of NMOSD. However, it usually develops over a longer period of time, up to 12 years (5). It is suggested that spinal cord atrophy can potentially help differentiate between Anti-AQP4 and Anti-MOG positive
patients, with anti-AQP4 patients having significantly more severe atrophy, which was true for our patient (5). It must be noted that our patient was under no specific treatment for lesions in the spinal cord due to misinterpretation. Although modern therapy in concordance with the current guidelines was given (high-dosage methylprednisolone therapy for 3-5 days continuously, followed with plasma exchange as a rescue therapy option) (7), the outcome was lethal.

Previously reported brainstem lesions only accounted for focal lesions in the pons (8), while our patient presented with diffuse pontine lesions. This is the finding not so commonly observed in NMOSD patients, given that proposed patterns for brainstem lesions are focal and more dorsally located (9). One previously unreported finding was observed in our patient, a discrete linear hemorrhage in the right aspect of the pons and in the splenium of corpus callosum, visible on SWI. Kamo et al. previously reported a case of major pontine hemorrhage, which was secondary to corticosteroid treatment and hypertension (202/127 mmHg) (10). In our patient, the form of hemorrhage resembled that of microbleeds (Figure 3, D and E) and no elevation of blood pressure was detected. This finding could be associated to the corticosteroid therapy but might also represent the end-stage changes in demyelinating lesions (11).

**Conclusion**

To conclude, raising suspicion of NMOSD is of crucial importance in cases with isolated LETM, especially in cases of Anti-AQP4 seropositivity, even when no lesions in the brain and optic nerves are present, in order to prevent delay in diagnosis and improve patient outcome and recovery.
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Declarations of interest: None.

Abbreviations list:
NMOSD: neuromyelitis optica spectrum disorder
AQP4: aquaporin 4
LETM: longitudinally extensive transverse myelitis
CSF: cerebrospinal fluid
MRI: magnetic resonance imaging
MOG: myelin oligodendrocyte glycoprotein
SWI: susceptibility-weighted imaging

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Figure legends:

Figure 1. An extensive signal abnormality was evident in the upper thoracic spinal cord on T2-weighted (A) and STIR (B) sagittal images, around 5 segments long, with no significant cord swelling. A follow up examination after 6 months showed extension of the lesion in the caudal direction (arrow, C) and bright lesions around the central canal on the axial
image (E). Two years later, an extensive cord atrophy is appreciated on STIR sagittal (D, encircled) and T2-weighted axial (F) images.

**Figure 2.** Extensive signal abnormality reflecting lytic demyelination was observed in periventricular white matter and corpus callosum (A), affecting also both corticospinal tracts symmetrically (B), suggestive for neuromyelitis optica spectrum disorder. Vivid postcontrast enhancement was observed in the initial MR examination in corresponding areas (C, D).

**Figure 3.** A lesion involving a complete cross-sectional area of the pons is evident on FLAIR axial image (A), showing signs of diffusion restriction (B- DWI image, C- ADC map). Discrete signs of hemorrhage are observed in the right lateral aspect of the pons (D) and in the right aspect of the splenium of corpus callosum (E). Long echo time MR spectroscopy is of low quality, showing elevation in Cho/Cr ratio, and a small lactate peak (F), implying the process of increased membrane metabolism and glial proliferation in inflammation.
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