CASE REPORT

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Unrecognized neuromyelitis optica spectrum disorder with pontine and *corpus callosum* microhemorrhage

Neprepoznati poremećaj spektra optičkog neuromijelitisa sa mikrokrvarenjem u ponsu i *corpus*-u *callosum*-u

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Abstract

Introduction. Neuromyelitis optica spectrum disorder (NMOSD) represents an immune-mediated neuroinflammatory syndrome, classified as a separate entity after the discovery of aquaporin-4 immunoglobulin G (anti-AQP4-IgG). The magnetic resonance neuroimaging spectrum of NMOSD classically consists 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.** The case presents an anti-AQP4 autoantibody-positive 65-year-old female patient who initially presented with underestimated 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 were described in this case: the involvement of a complete cross-sectional area of pons and microhemorrhage in the pons and *corpus callosum*. **Conclusion.** Raising suspicion of NMOSD is of crucial importance in cases with isolated LETM in order to prevent relapses in anti-AQP4-IgG positive cases and improve patient outcomes and recovery.

Key words:
anti-aquaporin 4 autoantibody; magnetic resonance imaging; neuroinflammatory diseases; neuromyelitis optica; treatment outcome.

Apstrakt

Uvod. Neuromijelitis optika – spektar poremećaja (NMOSP) predstavlja neuroinflamatorni sindrom, posredovan imunskim mehanizmima, klasifikovan kao poseban entitet nakon otkrića akvaporin-4 imunoglobulina klase G (anti-AQP4-IgG). Spektar nalaza NMOSP na snimcima magnetne resonance klasično uključuje bilateralni optički neuritis i longitudinalno ekstenzivni transverzalni mijelitis (LETM), a odskora je proširen lezijama u *area postrema,* dijencefalonu, moždanom stablu i cerebelumu, i ekstenzivnom atrofijom kičmene moždine. **Prikaz bolesnika.** Prikazana je bolesnica sa prisutnim anti-AQP4 autoantitelima, starosti 65 godina, sa inicijalnom, potcenjenom, prezentacijom LETM koja je razvila multiple cerebralne i cerebelarne litičke demijelinizacione lezije povezane sa akutnim neuritisom dugog segmenta optičkog nerva dve godine kasnije. Dva nova nalaza na snimcima opisana su kao zahvatanje kompletne transverzalne površine ponsa i mikrokrvarenja u ponsu i *corpus*-u *callosum*-u. **Zaključak.** Sumnja na NMOSP je od velikog značaja kod bolesnika sa izolovanim LETM da bi se sprečili relapsi u anti-AQP4-IgG pozitivnim slučajevima i poboljšala prognoza i oporavak.

Ključne reči:
anti-akvaporin 4 autoantitela; magnetna rezonanca, snimanje; bolesti, neuroinflamatorne; neuromijelitis optika; lečenje, ishod.

Introduction

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

The neuroimaging spectrum of NMOSD, classically consisting of bilateral optic neuritis and longitudinally extensive

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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 sequelae [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 a complete cross-sectional area of the pons and hemorrhage in the pons and the splenium of the *corpus callosum*.

Case report

A 65-year-old female presented with lower back pain, spastic paraparesis, gait disorder, and urinary retention. Cerebrospinal fluid (CSF) was normal, and oligoclonal bands were negative both in CSF and serum. Magnetic resonance imaging (MRI) of the thoracic spine revealed an extensive, five segments long inflammatory process of the upper thoracic spinal cord mainly involving the central gray matter, misinterpreted as syringomyelia (Figures 1A and 1B).

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 (Figures 1C and 1E).

Twenty-seven months later, the patient presented with altered consciousness, dysphagia, anarthria, and 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* (Figures 2A and 2B), mesencephalon, pons, superior and middle cerebellar peduncles and cerebellar white matter adjacent to the fourth ventricle, as well as in the ventral columns of the 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 (Figures 2C and 2D). At this point, a long segment of left optic nerve atrophy was pre-

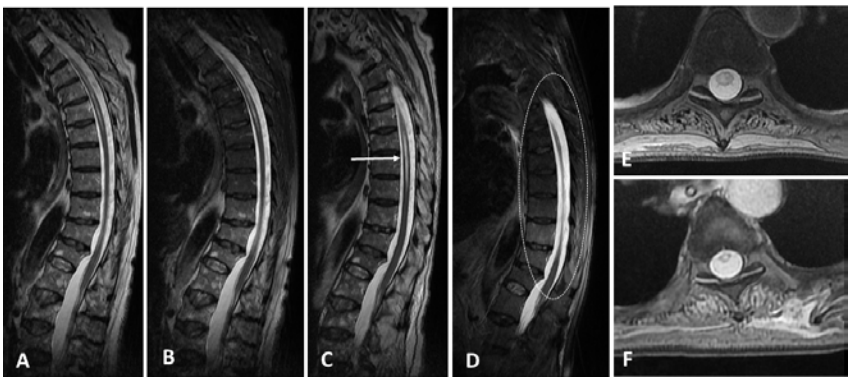

Fig. 1 – An extensive signal abnormality was evident in the upper thoracic spinal cord on the following: (A) T2-weighted and (B) STIR sagittal images, around 5 segments long, with significant cord swelling. A follow-up examination after 6 months (C) showed an extension of the lesion in the caudal direction (arrow) and (E) bright lesions around the central canal on the axial image. Two years later (D) extensive cord atrophy is registered on STIR sagittal (encircled) and (F) T2-weighted axial images. STIR – short tau inversion recovery.

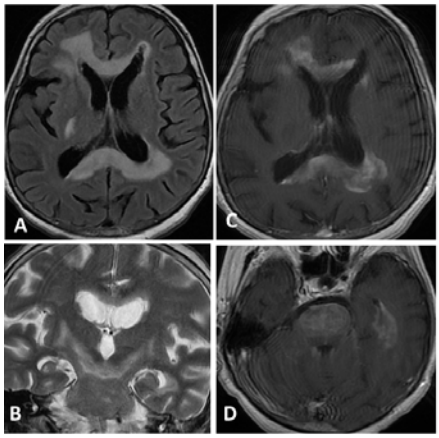

Fig. 2 – Extensive signal abnormality reflecting lytic demyelination was observed in the following: (A) periventricular white matter and *corpus callosum*; (B) affecting also both corticospinal tracts symmetrically suggestive of neuromyelitis optica spectrum disorder; (C, D) Vivid postcontrast enhancement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

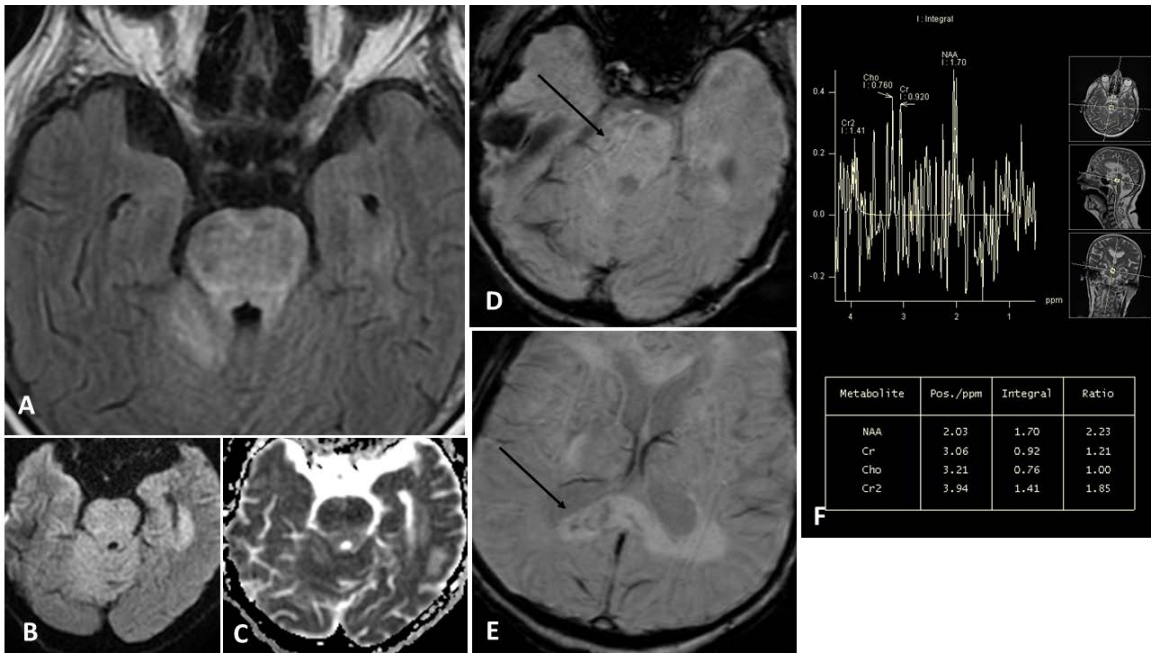

Fig. 3 – A lesion involving a complete cross-sectional area of the pons is evident on FLAIR axial image (A); showing signs of diffusion restriction − DWI image (B); (C) ADC map. Discrete signs of hemorrhage are observed in the right lateral aspect of the pons (D) and the right aspect of the splenium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

sent, with no contrast enhancement. Five days later, MR spectroscopy was performed in the pontine lesion (Figures 3A-3E), showing only an elevation of the 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 (Figures 1D and 1F). The patient was initially treated with pulse doses of 1 g methylprednisolone for 7 days, which resulted in minimal neurological improvement. Due to an 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 65-year-old female, and the disease followed a relapsing course in concordance with typical NMOSD epidemiologic findings [3]. Mortality rates are high in NMOSD, varying from 25–50%, and 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 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 is 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. A 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 by 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 the splenium of the *corpus callosum*, visible on SWI. Kamo et al. [10] previously reported a case of major pontine hemorrhage, which was secondary to corticosteroid treatment and hypertension (202/127 mmHg). In our patient, the form of hemorrhage resembled that of microbleeds (Figures 3D and 3E), and no elevation of blood pressure was detected. This finding could be associated with corticosteroid therapy but might also represent the end-stage changes in demyelinating lesions [11].

Conclusion

Raising suspicion of NMOSD is essential 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.

Conflict of interest

The authors declare no conflict of interest.

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