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LETTER TO THE EDITOR

Bilateral trigeminal root entry zone enhancement in MOG-IgG-associated brainstem encephalitis

Yaoyao Shen[1] · Zhijuan Cheng[2] · Chenguang Zhou[3]

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Dear editor,

Over the past few years, IgG antibodies to myelin oligodendrocyte glycoprotein (MOG-IgG) have attracted more attention in inflammatory demyelinating diseases of the central nervous system (CNS). Recent studies support the viewpoint that MOG-IgG-associated encephalomyelitis (MOG-EM) may be a disease entity in its own right, immunopathogenetically distinct from classic multiple sclerosis (MS) and AQP4-IgG-positive neuromyelitis optica spectrum disorders (NMOSD) [1]. The incidence of brainstem involvement among patients with MOG-EM is estimated to be almost one-third [2]. Up to our knowledge, the pontine trigeminal root entry zone (REZ) abnormality is frequently described in MS but extremely rare in MOG-EM [3]. We herein describe an interesting neuroradiological finding of bilateral trigeminal REZ enhancement in a patient with MOG-IgG-associated brainstem encephalitis.

A previously healthy 51-year-old woman was admitted to local hospital owing to intractable nausea and vomiting (INV) for 1 week. Initially, she was seen by a gastroenterologist and was treated with symptomatically. Tests of blood investigation, chest and abdomen CT, and endoscopy were all negative. Four days later, she complained of right facial numbness and weakness. The patient was subsequently transferred to our center. On admission, neurological examination revealed right-sided peripheral facial paralysis and decreased pain and touch sensation with disappeared corneal reflex, ipsilaterally. Brain and cervical magnetic resonance imaging (MRI) disclosed extensive lesions involving the dorsal medulla oblongata (including area postrema), both middle cerebellar peduncles (MCPs) and aqueduct of midbrain on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images. Bilateral trigeminal REZ enhancement can also be visualized after gadolinium injection (Fig. 1). Visual evoked potentials (VEP) were performed in our patient and did not support a previous evident of subclinical optic nerve involvement. Cerebrospinal fluid (CSF) analysis showed increased cell count (78 cells/mm^3, mononuclear cells dominant) and protein (0.47 g/L) with negative oligoclonal bands (OCBs). Work-up for infectious pathogens (herpesviruses, Mycobacterium tuberculosis, HIV, syphilis, and Lyme disease), autoimmune antibodies (ANA, ENA, ANCA, anti-thyroid, anti-GQ1b, anti-VGKC, anti-NMDAR, anti-LG1, anti-CASPR2, and anti-GABAbR) were all negative. Established cell-based immunoassays revealed that she was positive for anti-MOG antibodies (1:512) and negative for anti-AQP4 in serum. She was administrated with high-dose glucocorticoid (methylprednisolone 1 g/day for 3 days) followed by gradually reduce to oral administration. At 1-month follow-up, MRI showed residual REZ hyperintensity on T2-weight and FLAIR images and the patient was completely recovered except for slightly right facial numbness.

Discussion

Although MOG-IgG-associated optic neuritis (ON) and myelitis has been well documented, less is known about extra-opticospinal manifestations, especially brainstem involvement. It is estimated that the frequency of brainstem involvement among patients with MOG-EM is about 30% and isolated attacks of brainstem encephalitis that occur in the absence of myelitis or optic neuritis account for only 1.8% [2]. In MOG-associated brainstem encephalitis, lesions can locate

✉ Yaoyao Shen
15270881796@163.com

[1] Department of Neurology, The Affiliated Hospital of Jiujiang University, No.57 Xunyang East Rode, Xunyang District, Jiujiang 332000, Jiangxi Province, People's Republic of China

[2] Department of Neurology, The Second Affiliated Hospital of Nanchang University, No.1 Mingde Rode, Donghu District, Nanchang 330006, Jiangxi Province, People's Republic of China

[3] Department of Neurology, The Fifth Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, Henan Province, People's Republic of China

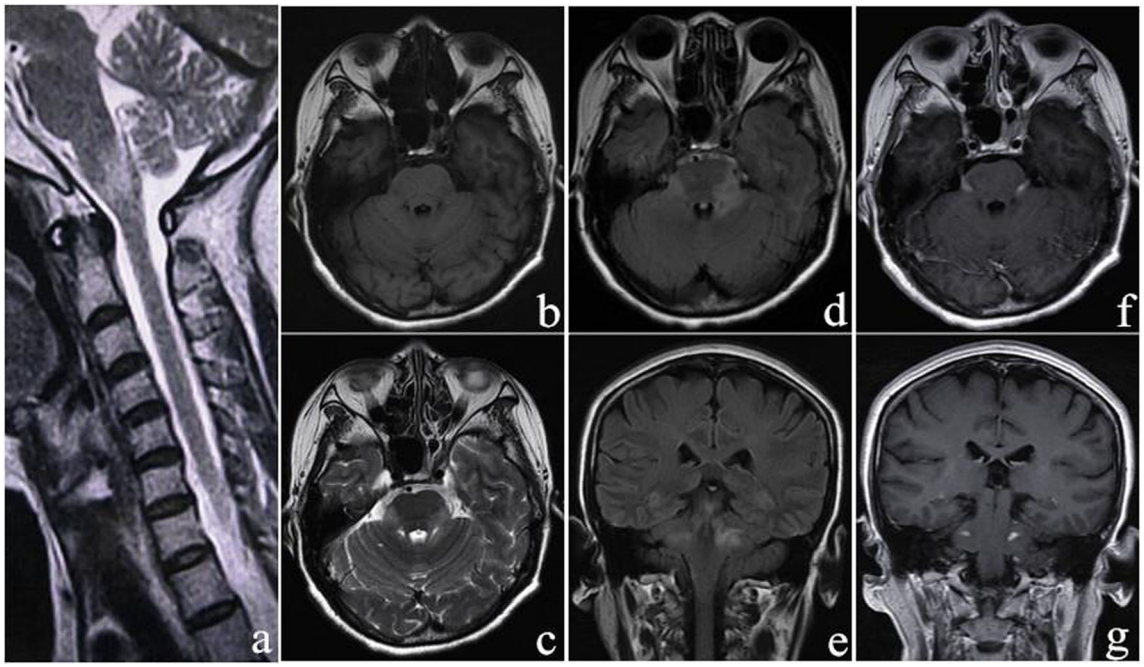

Fig. 1 Sagittal T2-weighted image of the spinal cord demonstrated hyperintensity in the dorsal medulla oblongata (area postrema) (**a**). Brain MRI showed abnormal signal intensities in bilateral middle cerebellar peduncles (MCPs) with T1-weighted hypointensity and T2-weighted hyperintensity (**b**, **c**). FLAIR images showed hyperintensity involving MCPs and aqueduct of midbrain (**d**, **e**). Bilateral trigeminal root entry zone (REZ) enhancement can also be visualized on gadolinium-enhanced T1-weighted images (**f**, **g**)

in different area of the brainstem and the pons is the commonest (84.6%). Other lesions are more commonly located in the medulla oblongata (57.1%), cerebellar peduncles (35.7%), and mesencephalon (14.3%) [2]. Accordingly, clinical manifestations of brainstem involvement are diverse due to lesions distribution. INV is caused by lesions in the dorsal medulla oblongata (area postrema), which has high value for the diagnosis of AQP4-IgG-positive NMOSD. Other symptoms include cranial nerve palsy, central hypoventilation, balance difficulties, and ataxia.

Here, we present a case of brainstem encephalitis with diffused lesion including the dorsal medulla oblongata, both MCPs, and aqueduct of midbrain, characterized by enhancing RZE, positive antibodies against MOG and steroid-responsiveness. A diagnosis of MOG-EM can be established according to the international recommendations proposed by Jarius et al. in 2018 [4]. There are distinct differences between patients with MOG antibodies and those with AQP4 antibodies. Compared with patients with AQP4 antibodies, patients with MOG antibodies are more frequently male (female:male ratio of 0.6:1.0) and more often have bilateral simultaneous ON. In addition, there is a difference in the spatial distribution of spinal cord lesions on MRI between the two groups. The patients with AQP4 antibodies frequently had cervical lesions, including some extending to the medullary region, whereas patients with MOG antibodies more frequently had long lesions extending to the lumbar spinal cord. Furthermore, patients with MOG antibodies usually demonstrated better functional recovery after a single attack [5].

In previous MRI studies, trigeminal REZ abnormality has been reported in MS and NMO, particularly in those with symptoms and signs related to the trigeminal nerve. Sugiyama et al. performed a study of 128 consecutive MS patients and 46 NMO patients. Trigeminal REZ abnormality was present in 11 (8.6%) of MS patients and two (4.3%) of NMO patients [3]. However, our case is the first to emphasize that symmetrical trigeminal REZ enhancement can also been seen in MOG-EM. As MOG is expressed in both the central and peripheral nervous systems, the trigeminal REZ may be a target of anti-MOG antibodies.

In conclusion, this case study suggests that MOG-EM should be taken into consideration when MR findings of brainstem encephalitis, especially in trigeminal REZ affecting. Further investigation of larger numbers of MOG-IgG-positive patients using advanced MRI techniques is needed.

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