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Case Report

Co-Existence of Relapsing Myelitis and Miller Fisher Syndrome: A Case Report

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ABSTRACT

Background: Central and peripheral demyelinating processes were rarely co-existing. Positive anti-GM1 ganglioside antibodies are common in peripheral demyelinating diseases but seldom reported in myelopathy.

Case presentation: In this case, we report a 39-year-old man with a 10-year history of relapsing myelitis and Miller Fisher syndrome. The antibody profiles were tested four times to confirm the disease etiology. Only anti-GM1 IgM antibodies were detected positive, while the antibodies for CNS demyelinating diseases were negative.

Conclusions: We describe a patient with co-existing myelopathy and MFS. The anti-GM1 antibodies should be considered to test in long-term, relapsing, and agnogenic myelopathy.

BACKGROUND

The demyelinating disease could affect the central nervous system (CNS) and peripheral nervous system (PNS), such as myelitis and Miller Fisher syndrome (MFS) [1,2]. In the vast majority of cases, demyelinating diseases are strictly separated, the co-existence of CNS and PNS demyelinating diseases were rare but also exists, such as GBS/ATM overlap syndrome [3,4]. Anti-GM1 ganglioside antibodies are commonly found in peripheral demyelinating diseases but rarely presented in myelopathy [5,6]. We report a case of concomitant MFS and relapsing myelitis. Positive anti-GM1 IgM antibodies were demonstrated in serum, while the antibodies for demyelinating diseases of the CNS were all detected negative in cerebrospinal fluid (CSF).

CASE REPORT

A 39-year-old Chinese man was admitted with progressive bilateral lower extremity numbness in September 2009. He complained about the numbness of his lower limbs for one month and aggravated for ten days. Physical examination revealed decreased acupuncture sensation between the left knee and groin, hypoesthesia below the right groin, and disappeared right proprioception. Bilateral Babinski signs and Chaddock signs were positive. Muscle strength (grade 5/5) and deep tendon reflexes (++) of extremities were normal and symmetrical. No meningeal irritation findings were observed. Visual examination and the rest of the neurological examinations were normal. Laboratory examination including blood biochemistry, urine/feces examination, Vitamin B12, folic acid, rheumatoid factor, antinuclear antibodies, and anti-double-stranded deoxyribonucleic acid antibodies revealed no clinically significant abnormality. Spine magnetic resonance imaging (MRI) revealed multiple abnormal signal lesions in the medulla oblongata and cervicothoracic spinal cord. Spinal cord vascularity showed no abnormity. No significant abnormalities were found on brain MRI. The patient was diagnosed with myelitis and administrated with pulsed intravenous methylprednisolone for 3 days, followed by an oral corticosteroid taper. All the symptoms were completely resolved except hypoesthesia below-left ankle until the discharge.

The same symptoms had not recurred until July 2017. Physical examination revealed normal muscle strength of extremities and deep tendon reflexes and decreased superficial sensibility of the right lower extremity. No pathological reflection was induced. Spine MRI demonstrated abnormal signals in the T8-9 level thoracic cord (Figure 1 A-D). Electro-neurogram of bilateral lower extremities was normal. Electromyography revealed undifferentiated SEPs waveforms of the right lower limb, prolonged latent phase of P40 wave of the left lower limb, prolonged left brainstem conduction

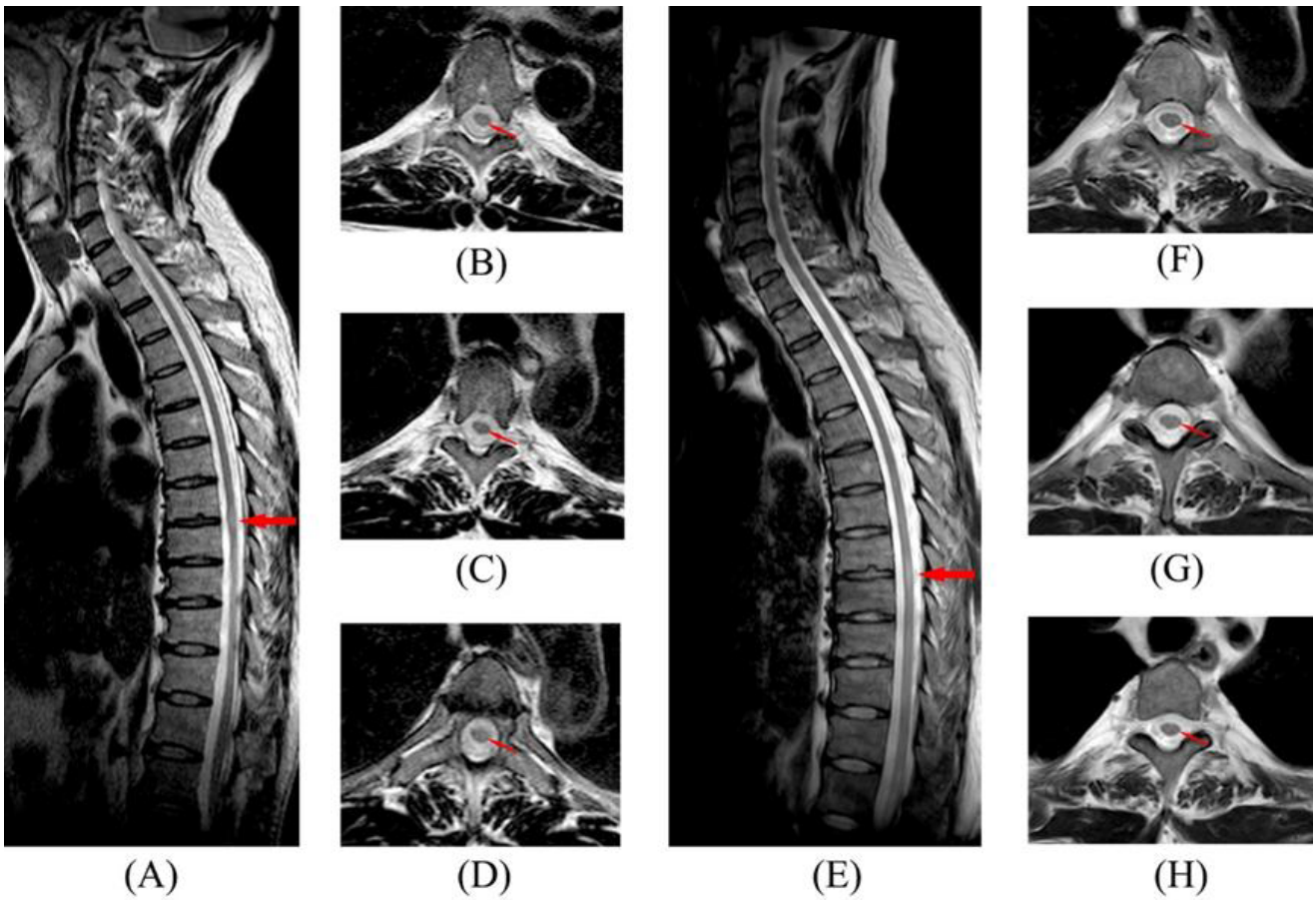

Figure 1: The MRI scanning was performed utilizing 1.5T Siemens MR imaging systems. A-D were finished in July 2017, while the E-H in September 2018. T2WI presented hyperintensities in T8-9 level thoracic cord, accompanied by spinal cord swelling (A) There were patchy area of hyperintensity within the transverse section of spinal cord (B-D). The hyperintensity were remaining detected in T8-9 level thoracic cord, while the spinal cord swelling disappeared (E). Patchy hyperintensity could be detected in the spinal cord (F-H).

times, and bilateral poorly differentiated visual P100 wave with normal latency. Other examinations like blood biochemistry, urine, and tumor marker tests showed no abnormity. Cell counting of cerebrospinal fluid (CSF) revealed no obvious abnormal. CSF albumin (Alb) and immune globulin (Ig) were quantified. The Alb, IgG, IgA, IgM, Alb quotient, and IgG index were in the normal range. There was no oligoclonal banding detected in CSF. Also, the CSF anti-aquaporin-4 (NMO-IgG) antibodies, anti-myelin basic protein (MBP) IgG antibody, and anti-myelin oligodendrocyte glycoprotein (MOG) IgG antibody were synchronously tested, of which results were all negative. The patient was reassessed with multiple sclerosis and receive glucocorticoids and immunosuppressor treatment. The patient was permitted to discharge from the hospital due to the significantly relieving symptoms, and he received azathioprine 100 mg and methylprednisolone 24 mg daily at a subsequent time. The drug dosage was gradually tapered in the outpatient clinic. The patient re-examined the spinal MRI in September 2018. The lesions were remaining detected, while the spinal cord swelling disappeared (Figure 1 E-H).

In March 2019, the patient was readmitted with double vision and dizziness. The left eye adduction was limited, and the horizontal nystagmus was elicited when the right eye turned to the right. Tendon reflex of extremities was disappeared. Ataxia was not observed. Examination of the CSF revealed a normal biochemical component with no pleocytosis and normal IgG index. Pathological examination of CSF was sterile and virus-free. Intravenous drip methylprednisolone sodium succinate (500mg daily) was administered following the initial diagnosis of the inflammatory brainstem and peripheral nerve disease. There was no clinical response on the third day of the methylprednisolone treatment, and the patient started to complain about obvious bilateral lower limb weakness. Physical examination reported no added positive pathological signs. Electromyography was carried out and the result indicated H reflex of the bilateral tibial nerve is abnormal (S1 injury was considered). Moreover, the anti-ganglioside antibodies profiles were screened with the patient's serum. The anti-GM1 IgM antibodies were detected positive, while IgG and IgM antibodies to GM2/3/4, GD1a, GD1b, GD2, GD3, GT1a, GT1b, and GQ1b and IgG antibody to GM2 were all negative. Based on these results,

the methylprednisolone treatment was stopped, and the pulse immunoglobulin (IVIG) treatment (400 mg/kg/day, for 5 days) was started was administered. The patient's complaints about double vision and dizziness relieved significantly and the lower extremities strength improved over the following days. At discharge, he had occasional dizziness, the double vision disappeared completely, and the strength of lower limb muscles recovered. The discharge diagnosis was Miller Fisher syndrome. The patient rechecked the antibodies for demyelinating diseases of CNS and the anti-ganglioside antibodies profiles in June 2019. The anti-NMO IgG antibodies, anti-MBP IgG antibody, and anti-MOG IgG antibody remained negative, while there were still only anti-GM1 IgM antibodies positive. Until now, he is still in follow-up treatment and has not developed double vision, dizziness, and lower limb numbness or weakness.

DISCUSSION

Here, we describe a patient with recurrent attacks of myelopathy and later peripheral neuropathy. Antibody testing was repetitiously performed as etiological confirmation. Intriguingly, only anti-GM1 IgM antibodies were detected positive, while the antibodies for demyelinating diseases of the CNS were all negative.

Ganglioside is a sort of acid glycolipid on the mammalian nerve cell membrane. Ganglioside could regulate the function of neurocytes and could also act as the target of autoantibody [7]. Anti-GM1 antibodies are present widely in immune-mediated peripheral demyelinating diseases like Guillain-Barré syndrome (GBS) and Miller Fisher syndrome [8]. MFS, which is featured as ophthalmoplegia, ataxia, and areflexia, is a variant of GBS. Anti-GM1 antibodies are rarely reported with MFS but were useful in establishing a diagnosis [9]. Nevertheless, the identity of the antigens to which anti-GM1 antibodies bind in myeloid tissue is poorly understood. In vitro experiments, Corbo et al. [10] confirmed that the binding of human anti-GM1 antibodies to GM1 in spinal cord gray matter, white matter, and myelin may be the molecular basis of the bio-effect of anti-GM1 antibodies partly. As for clinical cases, there were few reports of anti-GM1 antibodies-induced myelopathy (spinal demyelinating diseases or myelitis), which more tend to observe in child patients, particularly following an intestinal bacterial infection. After the infection, an immune response is processed, which stimulates producing of serum anti-GM1 antibodies, resulting in neuroimmune injury. For example, Zhiling Wang and colleagues reported two cases of myelitis in children with a positive anti-GM1 antibody. They also summarized the reports of acute myelitis with positive anti-GM1 antibodies in the literature [6].

In this case, a patient with a 10-year history of relapsing myelitis and MFS were analysed, with no infection before symptoms. Antibody testing had been performed repeatedly (twice for demyelinating diseases of CNS and twice for PNS) to confirm the etiology of the disease. According to monism, the anti-GM1 antibody probably led to relapsing myelitis and MFS. The interplay between the demyelinating disease of CNS and PNS presumably due to the shared common immune-pathogenic features, for example, activation of the nonspecific inflammatory cascade, which is responsible for demyelination, axonal loss, and disease progression [11]. Despite that peripheral and central myelin have different protein compositions, they seem to share some common protein antigens [12,13]. That may explain some co-occurring cases of myelopathy and peripheral demyelinating diseases, although rarely reported [14].

CONCLUSION

To the best of our knowledge, this is the first report describing positive anti-GM1 antibodies co-exist myelopathy and MFS. Our findings might be suggestive of a linkage between the two diseases [14]. The anti-GM1 antibodies should be added to test when comes to long-term, relapsing, and agnogenic myelopathy.

The limitation of this report is that it doesn't rule out coincidences. So further studies ought to reveal the molecular pathogenesis of anti-GM1 antibodies-induced myelopathy, based on which novel diagnostic and therapeutic strategy could be established.

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CONFLICT OF INTEREST

The authors declare no competing interests.

AVAILABILITY OF DATA AND MATERIALS

Data sharing does not apply to this article as no datasets were generated or analysed during the current study.

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