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Case report

Long spinal cord lesions in a patient with pathologically proven multiple sclerosis

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ABSTRACT

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system. We report the case of a 50-year-old man who presented with progressive gait ataxia. Brain magnetic resonance imaging (MRI) on fluid-attenuated inversion recovery revealed a hyperintense lesion in the right temporal white matter. The spinal cord showed a long hyperintense lesion between the vertebral levels C6 and L1 on T2-weighted MRI. Biopsied tissues from the brain lesion demonstrated features of inflammatory demyelination with preservation of astrocytes, consistent with typical MS. This is the first reported case of pathologically proven MS with longitudinally extensive spinal cord lesions.

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1. Introduction

Multiple sclerosis (MS) is a disease characterized by inflammatory demyelination in the central nervous system (CNS). Patients with MS have multiple lesions throughout the CNS tissues. Neuromyelitis optica spectrum disorder (NMOSD) shares many points of similarity to MS, such as a relapse-remitting clinical course and CNS lesions. However, NMOSD is pathologically characterized by astrocytopathy with the presence of an anti-aquaporin 4 (AQP4) antibody in serum [1]. In the previous clinical diagnostic criteria for NMOSD, the presence of anti-AQP4 antibody, longitudinally extensive spinal cord lesions (LESCL) on spinal cord magnetic resonance imaging (MRI), and optic neuritis were essential features to consider in the diagnosis of NMOSD [2]. Differentiation of MS from NMOSD is sometimes difficult because some patients with NMOSD were found to show negative results for AQP4 antibody in serum [3], and some MS patients were reported to show LESCL [4,5]. Although LESCL in patients with MS was recognized to be conglomerations of short spinal cord lesions [5], the pathological back-

grounds of MS patients with LESCL have been unclear in terms of differentiation from MS to NMOSD. Here, we describe the first reported case of pathologically proven MS with LESCL on MRI.

2. Case presentation

A 50-year-old Japanese man who had a 4-month history of progressive ataxia was admitted to our hospital. Neurological examination revealed acoustic hyperesthesia, truncal ataxia, and myoclonic jerky involuntary movement in bilateral upper extremities. Serum anti-AQP4 antibody was not elevated. Mild pleocytosis (27 cells/ μ L; reference, <3 cells/ μ L), elevated protein levels (57 mg/dL; reference, <40 mg/dL), and oligoclonal bands were found in the cerebrospinal fluid (CSF). T2-weighted spinal cord MRI revealed a long hyperintense lesion with gadolinium enhancement between the vertebral levels of C6 and L1 (Fig. 1A–B). Brain MRI on fluid-attenuated inversion recovery revealed a hyperintense lesion in the right temporal white matter with gadolinium enhancement (Fig. 1C). Considering that malignant disorders could not be excluded, a brain biopsy of a specimen from the right temporal white matter lesion was performed.

Histological findings showed features of inflammatory demyelination, including infiltration of macrophages and lymphocytes, damage of myelin, and preservation of neurofilaments, astrocyte, and AQP4 (Fig. 2A–E). Most of the perivascular lymphocytes were CD20-positive B cells. However, most of the lymphocytes infiltrating the brain parenchyma were CD4- or CD8-positive T cells (Fig. 2F–H). We made a diagnosis of MS based on the clinical and

Abbreviations: MS, multiple sclerosis; MRI, magnetic resonance imaging; CNS, central nervous system; NMOSD, neuromyelitis optica spectrum disorder; AQP4, anti-aquaporin 4; LESCL, longitudinally extensive spinal cord lesions; CSF, cerebrospinal fluid.

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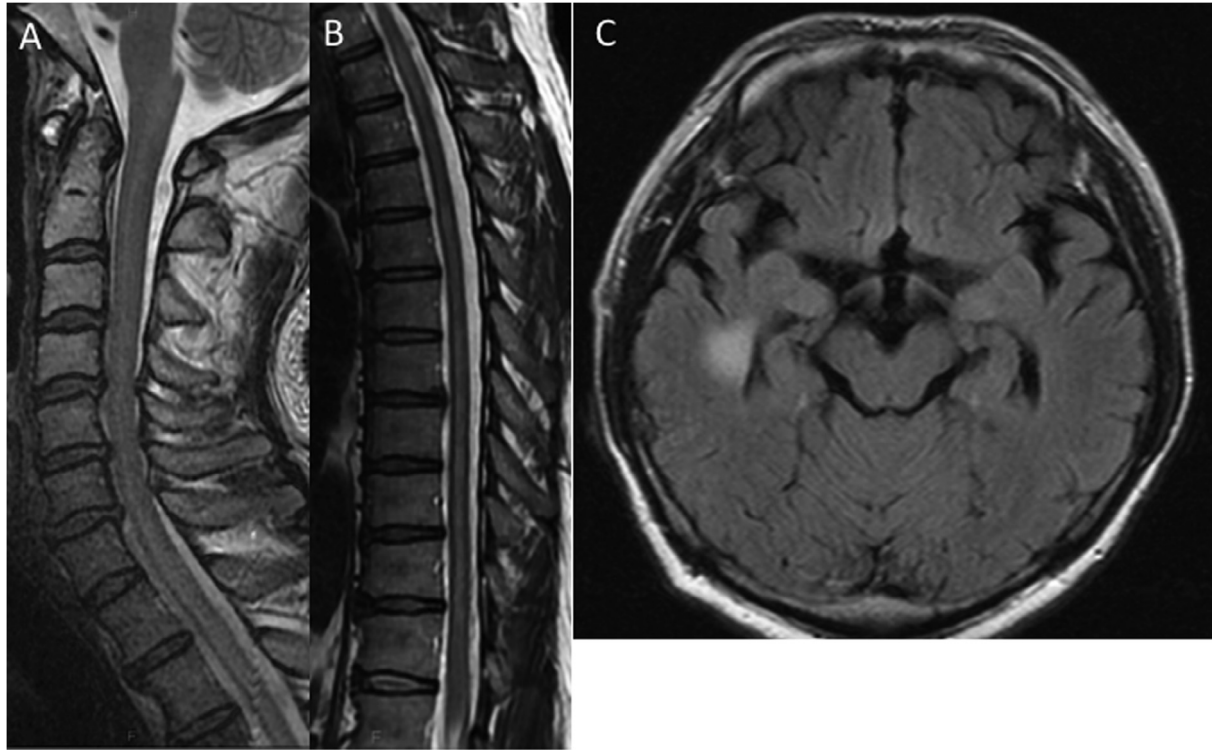


Fig. 1. Findings from magnetic resonance images (A–C). T2-weighted magnetic resonance images showing a long hyperintense lesion between the vertebral levels C6 and L1 (A, B). A fluid-attenuated inversion recovery image showing hyperintense lesion in the right temporal white matter (C).

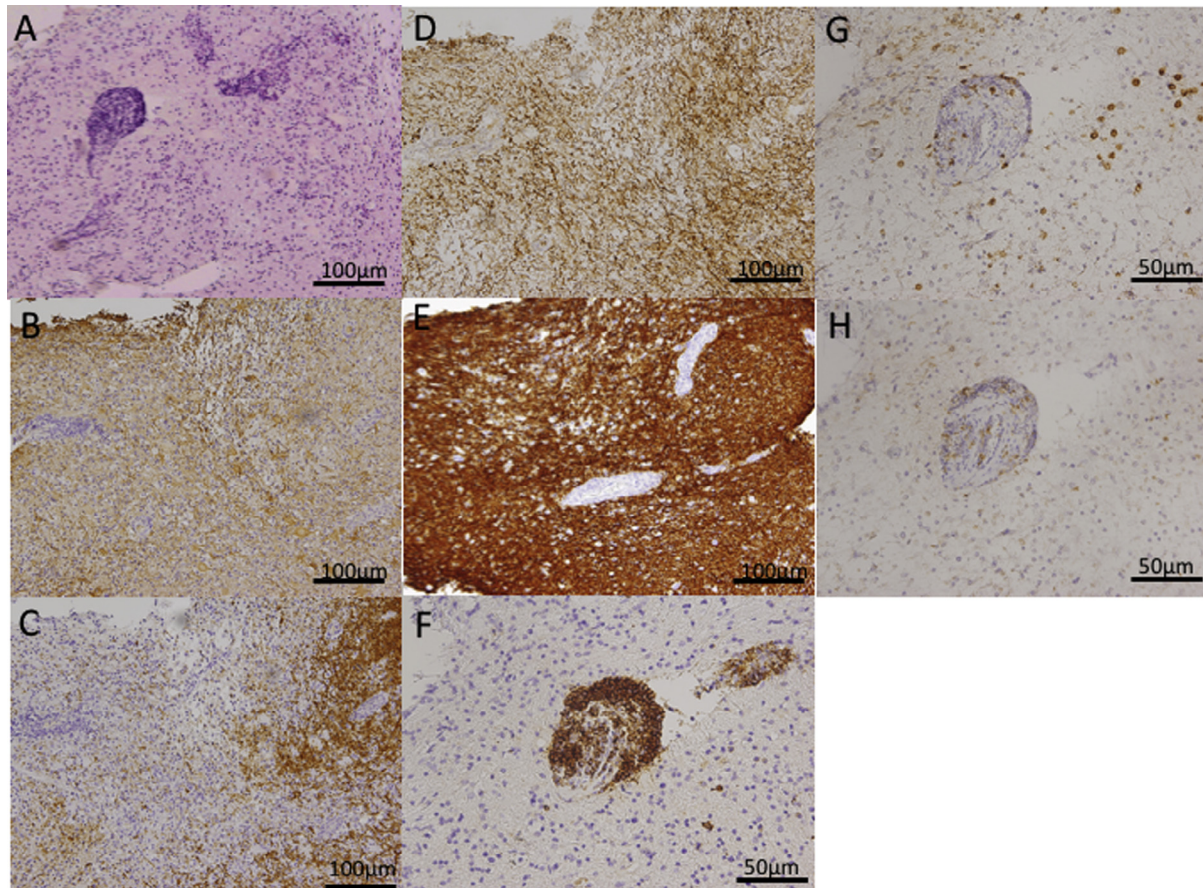


Fig. 2. A biopsy tissue from the left temporal lobe showing infiltration of macrophages and lymphocytes in parenchyma and perivascular on hematoxylin and eosin (A). Reactive astrocyte is obvious (B). Myelin sheath loss with well preserved axons and AQP4 (C, D, E). Prominent B-cell accumulation in the perivascular space (F). Some CD8-positive T cells (G) and sparse CD4-positive T cells (H) in the brain parenchyma. Immunostaining using antibodies against glial fibrillary acidic protein (GFAP) (B), the myelin basic protein (MBP) (C), phosphorylated neurofilament (SMI-31) (D), aquaporin 4 (AQP4) (E), CD20 (F), CD8 (G), and CD4 (H).

pathological features. After treatment with corticosteroid, his clinical manifestations and the neuroradiological findings improved gradually. The brain MRI performed 1 year after treatment initiation revealed a new small demyelinating lesion in the left basal ganglia.

3. Discussion

In this case report, we described a Japanese patient with pathologically proven MS who showed LESCL on MRI. Pathological data from the cerebral white matter revealed inflammatory demyelination with preservation of astrocytes, which led to a diagnosis of MS.

Although some reports described that MS patients showed LESCL [4,5], the diagnoses of these cases were made based on clinical data only. It is obvious that clinical differentiation between MS and NMOSD could be difficult owing to some similarities in clinical and radiological features. Spinal cord lesions of NMOSD typically involve the central gray matter accompanied by frequent cord swelling [6]. By contrast, MS cord lesions usually occupy the peripheral white matter, with an occasional swollen cord. Furthermore, spinal MS lesions could be asymptomatic [7]. In this case, LESCL demonstrated no obvious cord swelling. The clinical symptom was relatively milder than that for the length of the spinal cord lesions, suggesting that the demyelination could be the prime pathology in the spinal cord.

Pathological examination is crucial to exclude the possibility of NMOSD in patients with MS showing LESCL; however, histological investigation is always difficult to perform. In MS lesions, perivascular inflammatory cuffs consisted predominantly of T cells, and B cells were generically sparse and less numerous than T cells in perivascular inflammation. The perivascular aggregation of CD20-positive B cells was the characteristic neuropathological finding of this case. In an experimental rodent model of experimental autoimmune encephalomyelitis, activation of B cells resulted in

the development of encephalitis and myelitis with long cord lesions [8]. The B-cell activity described in our patient might have an important role in the formation of LESCL. Further comprehensive studies are essential to clarify the association between MS, LESCL formation, and the profiles of the inflammatory cells in demyelinated tissues.

In conclusion, we describe for the first time a case of a patient with pathologically proven MS and LESCL. B-cell activation could be related to the development of LESCL in patients with MS.

Conflict of interest/Disclosures

The Authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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