Neuromyelitis Optica Spectrum Disorder with Recurrent Intracranial Hemorrhage

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Abstract

The patient was a woman without hypertension who had previously experienced intracranial hemorrhage twice at 48 and 56 years of age. At 59 years of age, she was diagnosed with neuromyelitis optica spectrum disorder (NMOSD) based on the presence of a brain stem lesion and the detection of anti-aquaporin 4 (AQP4) antibodies. After 5 months of continuous treatment with prednisolone (15 mg/day), she presented with optic neuritis and intracranial bleeding. A recurrent attack of NMOSD and intracranial hemorrhage were concurrently diagnosed. We herein report a case of NMOSD with recurrent intracranial hemorrhage, which indicates an association between NMOSD and cerebellar vascular dysfunction.

Key words: neuromyelitis optica spectrum disorder (NMOSD), recurrent intracranial hemorrhage, brain blood barrier (BBB)

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Introduction

Neuromyelitis optica (NMO) is an inflammatory disease that mainly affects the optic nerve and spinal cord. A disease-specific autoantibody, anti-aquaporin 4 (AQP4) antibody, has been found in the sera of patients with NMO (1). Recently, the concept of neuromyelitis optica spectrum disorder (NMOSD) has become more widely accepted than mere optic neuritis or transverse myelitis (2). Sato et al. reported that AQP4 antibody-positive patients with single or recurrent attacks of optic neuritis, myelitis, or brain/brain-stem disease who do not fulfill the current criteria of NMO or NMOSD may not be uncommon and that they should also be included in the NMO spectrum (2). The International Panel for NMO Diagnosis was convened to revise the diagnostic criteria using systematic literature reviews and electronic surveys to facilitate consensus (3). The new nomenclature defines the unifying term “NMOSD”, which is further stratified by serological testing (NMOSD with or without AQP4-IgG) (3). Additionally, some studies on the association between NMO and the brain blood barrier (BBB) have shown that the sera from neuromyelitis optica patients disrupt the BBB (4-6). We herein report a case of NMOSD with recurrent intracranial hemorrhage.

Case Report

The patient was a woman without hypertension who had previously experienced intracranial hemorrhage twice at 48 and 56 years of age (Fig. 1A and B). At that time, cerebral vascular disease including aneurysm and severe arteriosclerosis was not detected by cerebral angiography. She had not been treated with an anticoagulant or antithrombotic agent. At 59 years of age, she presented with muscle atrophy on the right side of her tongue, dysarthria and dysphagia. Sagittal fluid-attenuated inversion recovery (FLAIR) (Fig. 1C), sagittal postgadolinium-enhanced T1 (Fig. 1D) and axial T2-weighted (Fig. 1E) imaging showed areas of hyperintensity in the dorsal medulla along the fourth ventricle. There was no intracranial microbleeding on T2 star-weighted imaging. The patient’s serum was AQP4 antibody-positive. The patient’s serum was negative for blood markers and autoantibodies associated with systemic vasculitis, including antinu...
clear antibody (ANA), SSA, SSB and anti-neutrophil cytoplasmic antibody (ANCA). The prothrombin time (PT), activated partial thromboplastin time (APTT) and D-dimer levels were within the normal limits. Tests for lupus anticoagulant (LAC) and anti-beta-2 glycoprotein 1 antibodies were negative. An examination of the patient’s cerebrospinal fluid did not reveal pleocytosis, an increased total protein concentration, an elevated IgG index, or an increased level of myelin basic protein (MBP). Oligoclonal IgG bands were not detected. The administration of intravenous methylprednisolone (IVMP, 1,000 mg/day) and oral prednisolone (PSL) improved her neurological symptoms, including her tongue at-
Concurrently diagnosed. The current attack of NMOSD and intracranial hemorrhage were the hemispatial neglect. Based on the above findings, a recurrence was evident. Furthermore, the absorption of the hematoma improved her visual acuity and she became able to write letters. Normal limits under treatment of PSL. Treatment with IVMP showed multiple intracranial bleeding in the right frontal lobe and right parietal lobe. Brain CT angiography did not detect cerebral vascular disease including aneurysm or severe arteriosclerosis. Bilateral optic neuritis was diagnosed by an ophthalmologist, and the patient’s visual evoked potentials (VEP) were prolonged in comparison to the previous results. The PT, APTT and D-dimer levels were also within normal limits under treatment of PSL. Treatment with IVMP improved her visual acuity and she became able to write letters. Furthermore, the absorption of the hematoma improved the hemispatial neglect. Based on the above findings, a recurrent attack of NMOSD and intracranial hemorrhage were concurrently diagnosed.

Discussion

The present case shows a possible association between NMOSD and intracranial bleeding. Recently, the concept of NMOSD has become wider than mere optic neuritis and transverse myelitis (2). The International Panel for NMO Diagnosis was convened to revise the diagnostic criteria using systematic literature reviews and electronic surveys to facilitate a consensus (3). The new nomenclature defines the unifying term, “NMOSD”, which is further stratified by serological testing (NMOSD with or without AQP4-IgG) (3). Thus, this case could be diagnosed as NMOSD. Clinically, enhanced lesions on brain MRI have occasionally been found in cases of NMO (7). Besides, we previously reported a case in which NMOSD accompanied subarachnoid hemorrhage (8). The patient in that case, a 48-year-old man, also had a brainstem lesion that was diagnosed as NMOSD. Furthermore, the onset of intracranial hemorrhage in that case occurred immediately after the NMOSD attack, the same as in this case. It is difficult to prove an association between NMOSD and intracranial hemorrhage. However, in the present case, the patient presented no risk factors for intracranial hemorrhage. Venous thrombosis in the intracranial region was not detected on CT or T2-star images and no coagulation disorders were detected.

Some studies on the association between NMO and the BBB have shown that the sera from NMO patients disrupts the BBB (4, 5). Vincent et al. reported that NMO-IgG by itself could account for the BBB dysfunction observed in NMO (6). Furthermore, Shimizu et al. suggested that antibodies to brain microvascular endothelial cells disrupt the BBB through the upregulation of vascular endothelial growth factor (VEGF) in NMO patients (4). NMOSD patients may include patients with brain microvascular dysfunction. Thus, the possibility that the disruption of the BBB through NMO is associated with intracranial hemorrhage cannot be ruled out.

Cerebral amyloid angiopathy (CAA) and CAA-related inflammation are the important differential diagnoses (9). Our patient did not show any microbleeding on T2-star MR images that were obtained before bleeding (Fig. 2A) in comparison to T2-star images that were obtained after bleeding (Fig. 2B). Moftakhar et al. reported that the expression of AQP4 was enhanced in cases of CAA in comparison to age- and sex-matched controls (10). Although we cannot deny the possibility of some form of angiopathy, we could not find any cases in which NMOSD was accompanied by CAA.

Acute hemorrhagic leukoencephalitis (AHL) and acute necrotizing hemorrhagic leukoencephalitis (ANHLE) of Weston Hurst are variants of an acute, rapidly progressive, and frequently fulminant inflammatory hemorrhagic demyelination of the central nervous system white matter (11).
AHL is considered to be one of the hyperacute variants of acute disseminated encephalomyelitis (ADEM) (11). Although recurrent forms of ADEM have occasionally been reported, ADEM usually has a monophasic course. Robinson et al. reported a case of AHL that presented widespread astrocytic injury, similar to NMO (12). Further studies should be conducted to investigate the association between AQP4 antibodies and AHL.

Blood components (e.g. thrombin, hemoglobin, iron) and the inflammatory response to those components play a large role in intracranial bleeding-induced BBB dysfunction (13). We herein reported a case of NMOSD with recurrent intracranial hemorrhage. In the future, we should pay attention to whether intracranial hemorrhage is associated with NMO or whether it occurs incidentally.

The authors state that they have no Conflict of Interest (COI).

References

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