Neuromyelitis Optica Spectrum Disorders

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KEYWORDS

• Neuromyelitis optica spectrum disorders • Anti-aquaporin-4 antibody
• Anti-myelin oligodendrocyte glycoprotein antibody • MR imaging • Optical coherence tomography

KEY POINTS

- Neuromyelitis optica spectrum disorders (NMOSD) is now divided into anti-aquaporin-4-antibody (anti-AQP4-Ab)-seropositive NMOSD and -seronegative NMOSD (or unknown serostatus).
- In anti-AQP4-Ab-seropositive NMOSD, optic neuritis (ON) is often severe and may involve the optic chiasm, and acute myelitis is longitudinally extensive (>3 vertebral segments) and preferentially involves the central gray matter. Area postrema lesions associated with intractable hiccup, nausea, and vomiting, and other brain syndromes may develop in some patients.
- A fraction of anti-AQP4-Ab-seronegative patients with NMOSD are positive for anti-myelin oligodendrocyte glycoprotein-antibody (anti-MOG-Ab), and anti-MOG-Ab-seropositive NMOSD has some unique features as compared with anti-AQP4-Ab-seropositive NMOSD (fewer relapses and better prognosis, simultaneous bilateral ON, lumbosacral myelitis). Double-seronegative NMOSD might include heterogeneous groups of diseases.
- Optical coherence tomography shows relatively milder neuronal damage in anti-MOG-Ab-seropositive ON than in anti-AQP4-Ab-seropositive ON.
- MR imaging and OCT are powerful tools to diagnose and evaluate both types of autoantibody-associated NMOSD.

INTRODUCTION

Neuromyelitis optica (NMO) is clinically characterized by severe optic neuritis (ON) and transverse myelitis. NMO spectrum disorder (NMOSD) is a newly emerging disease spectrum with or without anti-aquaporin-4-autoantibody (anti-AQP4-Ab) and includes typical NMO. Until recently, ON (often severe and simultaneous bilateral) and acute transverse myelitis (mostly longitudinally extensive, >3 vertebral segments) have been the cardinal clinical symptoms of NMO and were absolutely needed for the diagnosis. Then the term NMOSD was introduced for anti-AQP4-Ab-seropositive cases with

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typical NMO, ON (recurrent or simultaneous bilateral), longitudinally extensive transverse myelitis (LETM), or ON/LETM with systemic autoimmune diseases or brain lesions typical of NMO (hypothalamic, corpus callosal, periventricular, or brainstem). However, it has been recognized that cerebral and brainstem lesions occasionally develop as the onset events in some anti-AQP4-Ab-seropositive patients. Based on those observations, NMOSD has recently been redefined, and certain types of brain syndromes were also included as core clinical characteristics of NMOSD in the 2015 international consensus diagnostic criteria.[1] The MR imaging findings in AQP4-Ab-seropositive NMOSD are usually distinct from those in typical multiple sclerosis (MS). Differential diagnosis between NMOSD and MS are critically important because such disease-modifying drugs for MS as interferon-β, natalizumab, and fingolimod may aggravate anti-AQP4-Ab-seropositive NMOSD.

Another serum autoantibody called anti-myelin oligodendrocyte glycoprotein-antibody (anti-MOG-Ab) has been detected in a fraction of patients with NMOSD without anti-AQP4-Ab. Patients with anti-AQP4-Ab and those with anti-MOG-Ab seem to have distinct pathophysiologies, although there are some overlaps of their clinical manifestations. Massive astrocytic destruction associated with autoimmunity to AQP4 is a dominant pathology in patients with anti-AQP4-Ab,[2] whereas anti-MOG-Ab-associated NMOSD seems to be an inflammatory demyelinating disease,[3] and immunosuppression is needed in the relapsing form of both antibody-associated NMOSD. Distributions and other features of the MR imaging lesions in cases with anti-AQP4-Ab and anti-MOG-Ab are distinguishable to some extent.

This article presents the clinical manifestations, MR imaging findings, and optical coherence tomography (OCT) findings in the patients with anti-AQP4-Ab-seropositive NMOSD and those with anti-MOG-Ab-seropositive NMOSD. All MR imaging shown here is derived from our own database of NMOSD at Tohoku University Hospital, a center of NMOSD research in Japan. Patients with NMOSD without those two autoantibodies certainly exist, but such a disease entity is heterogeneous and is not mentioned here.

ANTI-AQUAPORIN-4-AUTOANTIBODY-SEROPOSITIVE NEUROMYELITIS OPTICA SPECTRUM DISORDER

More than half of the patients with anti-AQP4-Ab develop typical NMO (ON and LETM), but some of the patients develop LETM or ON alone for unknown reasons. In addition to these conventional central nervous system (CNS) lesions, brainstem lesions including area postrema syndrome and certain types of cerebral lesions have also been recognized as the CNS lesions unique to NMOSD. Patients with anti-AQP4-Ab show high rates of relapses if untreated, and thus soon after the patients develop those CNS lesions and are found to be anti-AQP4-Ab-seropositive, immunosuppressive therapy to prevent relapse should be considered.

MR Imaging Findings

Optic neuritis

Distribution ON lesions in anti-AQP4-Ab-seropositive NMOSD are often longer than half of the optic nerve length and the optic chiasmal involvement is not uncommon. The distribution of T2-ON lesions in the subsegments of optic nerves on orbital MR imaging from 26 ON eyes in 23 patients with anti-AQP4-Ab NMOSD seen at Tohoku University Hospital is shown in **Table 1**. The numbers of affected subsegments in each patient were 2.8 ± 1.5, and thus the sum of the percentages in **Table 1** exceeds 100%. The incidence of ON was the highest in the intraorbital portion, and the chiasmal lesions were seen in about one out of four lesions.

Characteristics in the acute phase Affected optic nerves in the acute phase of ON in patients with anti-AQP4-Ab show on orbital MR imaging long lesions (≥2 subsegments in **Table 1**) and swelling and contrast enhancement.[4] To detect ON, short tau inversion recovery (STIR) and fat-suppressed gadolinium-enhanced T1-weighted image are useful (**Fig. 1**). Axial fast spin echo T2-weighted imaging could also be used in depicting ON lesions with adequate sensitivity.[5]

Characteristics in the chronic phase Affected optic nerves in the chronic phase of ON in patients with anti-AQP4-Ab often show long-segmental atrophy with high signal on T2-weighted images, fluid attenuated inversion recovery, and STIR (**Fig. 2**).

Table 1
Lesion distribution of anti-AQP4-Ab-seropositive optic neuritis in the subsegments of optic nerves

Subsegment	Midorbit	Retro-orbit	Canalicular	Intracranial	Chiasmal	Optic Tract
Incidence (percentage)	17/26 (65.0)	18/26 (69.0)	14/26 (53.8)	13/26 (50.0)	7/26 (26.9)	3/26 (11.5)