Clinical characteristics of patients with late-onset NMOSD in a Japanese cohort

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Abstract

Objective

Neuromyelitis optica spectrum disorders (NMOSD), which is characterized by aquaporin-4 (AQP4) autoantibodies, is an autoimmune disorder of the CNS. The objectives of this study were to identify clinical characteristics of late-onset NMOSD (LONMOSD) in a Japanese cohort.

Methods

This study retrospectively included 73 Japanese NMOSD patients, met the international consensus 2015 diagnostic criteria of NMOSD. The patients were divided into two groups: a LONMOSD group (> 50 years of age at onset) included or an early-onset NMOSD (EONMOSD) group (< 50 years of age at onset) included. Moreover, we focused clinical features of three NMOSD patients with onset over 80 years old.

Results

Among total 73 Japanese patients with NMOSD (63 female, 10 male; median age of onset, 44 [IQR 34-54]; seropositivity for AQP4 antibodies, 88%) based on international consensus 2015 diagnostic criteria of NMOSD, a LONMOSD group included 21 patients (29%). The median disease duration was 106 (IQR 48-181) months. All three patients with onset over 80 years old very late-onset NMOSD had the seropositivity of AQP4 antibodies. A LONMOSD group was characterized by higher frequency of male patients (33% vs 5.7%, P = 0.005) and lower frequency of relapses (0.7 vs 3.6 P = 0.0002), compared to an EONMOSD group. Higher frequency of monophasic courses (52% vs 19%), higher frequency of myelitis (43% vs 37%) and higher median EDSS at last follow-up (4.5 vs. 2.3) were present in a LONMOSD group compared to an EONMOSD group. There was a significant negative correlation between age at onset and number of relapses (r = -0.43, P = 0.003). 57 % in a LONMOSD and 22% in an EONMOSD group had complications including opportunistic infection during treatments.

Conclusion

There may be an interaction between NMOSD and age in which less disease activity, but more damage, are present in a late onset.

Our representative publications regarding to NMO and the related disorders

1. Kawachi I, Lassmann H. Neurodegeneration in multiple sclerosis and neuromyelitis optica. ***J Neurol Neurosurg Psychiatry*** 2017; 88: 137-145.
2. Hokari M, Kawachi I, et al.: Clinicopathological Features in Anterior Visual Pathway in Neuromyelitis Optica. ***Ann Neurol*** 2016;79:605-624.
3. Saji E, Kawachi I, et al.: Cognitive impairment and cortical degeneration in neuromyelitis optica. ***Ann Neurol*** 2013; 73: 65-76.
4. Yanagawa K, Kawachi I, et al.: Pathologic and immunologic profiles of a limited form of neuromyelitis optica with myelitis. ***Neurology*** 2009; 73: 1628-37.
5. Yokoseki A, Kawachi I, et al. Relapse of multiple sclerosis in a patient retaining CCR7- expressing T cells in CSF under fingolimod therapy. ***Mult Scler J*** 2013; 19(9):1230-1233.
6. Yokoseki A, Kawachi I, et al. Hypertrophic pachymeningitis: significance of myeloperoxidase anti-neutrophil cytoplasmic antibody. ***Brain*** 2014;137(2):520-536.

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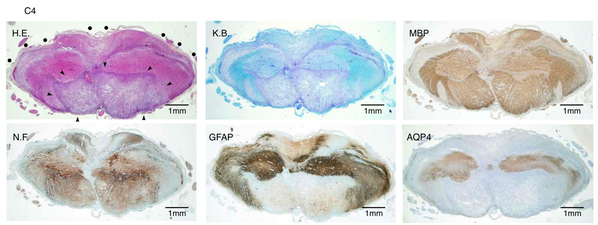
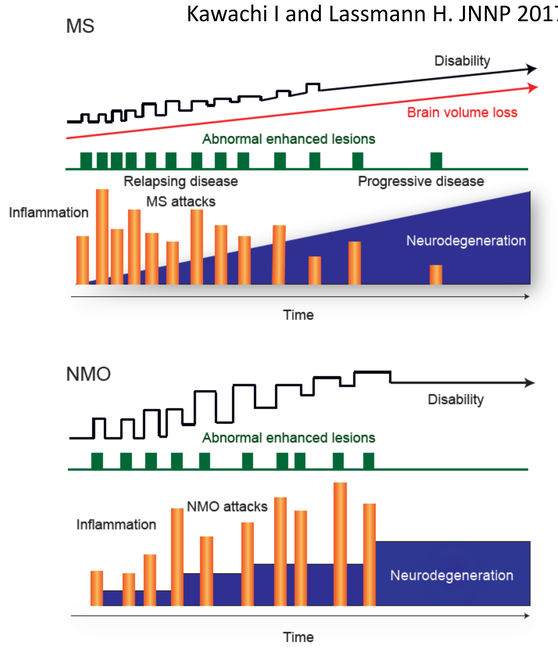
Introduction

Yanagawa K, et al. Neurology 2009 [4)]



✓ NMOSD is an autoimmune channelopathy/astrocytopathy that targets the water channel aquaporin-4 (AQP4) on astrocytes in the CNS, and AQP4 antibody, which has facilitated the distinction from MS (oligodendrocytopathy).

Kawachi I and Lassmann H. JNNP 2017[1)]



✓ Distinct patterns of disease courses and pathology of neurodegeneration in NMOSD and MS

Methods

✓ Patients were enrolled if they met the 2015 International Panel for NMO Diagnosis criteria for NMOSD5).
✓ Statistical analyses were performed using Mann-Whitney test, Fisher's exact test and Spearman correlation analysis. Relapse-free survival rates were estimated by Kaplan-Meier method. All statistical analyses were considered significant at p values of <0.05.

Results & Discussion

Table 1. Clinical features of patients with LONMOSD and EONMOSD

[a] median (IQR), [b] means ± SD

	Late-onset NMOSD N = 21 (29%)	Early-onset NMOSD N = 52 (71%)	*P*-value
Lesions at onset			
The optic nerves, n (%)	10/21 (48%)	25/52 (48%)	*1.00*
The spinal cord, n (%)	9/21 (43%)	19/52 (37%)	*0.79*
Brainstem, n (%)	1/21 (5%)	4/52 (8%)	*0.65*
The brain parenchyma, n (%)	1/21 (5%)	5/52 (10%)	*0.67*
Multiple region involvement, n (%)	5 /21 (24%)	10/52 (19%)	*0.75*
Clinical courses			
Monophasic courses, n (%)	11/21 (52%)	10/52 (19%)	*0.009*
Disease activities & severity			
Total number of relapses [b]	0.7 ± 0.9	3.6 ± 4.6	*0.0002*
EDSS scores at last follow-up [a]	4.5 (3-6.8)	2.3 (1.1-3.9)	*0.06*

Late onset NMOSD was characterized by

✓ Higher frequency of monophasic courses
✓ Higher median EDSS at last follow up

Figure 1. Age at onset and gender

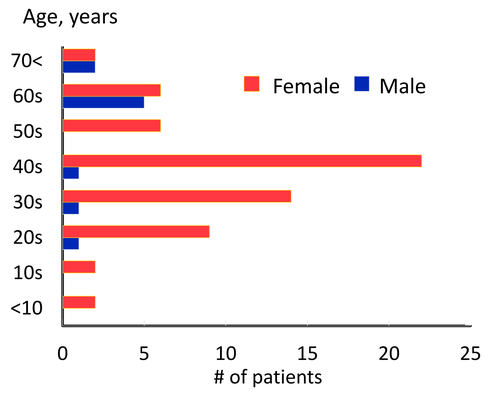
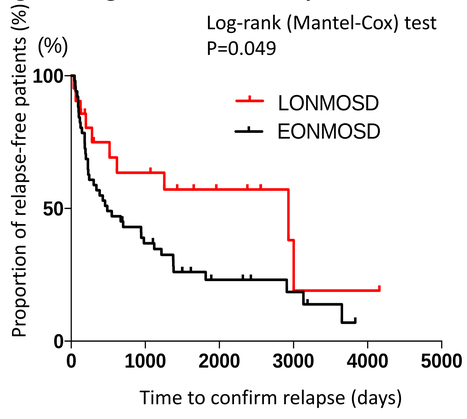


Figure 2. Age at onset and relapses



✓ Autoimmune disorders including NMOSD are characterized by female predominant disorders, and recent reports suggest that mapping the transcriptome and methylome in T lymphocytes and neurons in females could reveal mechanisms underlying gender differences in autoimmunity
✓ Higher frequency of male patients in LONMOSD was present in this study. This was consistent with other autoimmune disorders including RA. Initiation and progression of immune abnormalities in NMOSD might be caused both by sex hormone and age.
✓ There may be an interaction between NMOSD and age in which less disease activity, but more damage, were present in a late onset.
✓ Due to the retrospective design of this study, selection bias may limit the interpretation of our results. Future studies including nation-wide survey of NMOSD are needed.