The cerebellar peduncle lesion as an age-independent feature of MOG antibody associated disease

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Abstract

Objective: This study used MRI to compare specific features of myelin oligodendrocyte glycoprotein antibody (MOG-Ab)-associated disease to aquaporin 4 (AQP4)-Ab-associated disease.

Methods: In this cross-sectional study, we used MRIs to compare demyelinating lesion sites in 134 MOG-Ab-positive and 70 AQP4-Ab-positive patients referred to Tohoku University in 2018. The brain was divided into 21 sectors, and an independent neurologist and a neuroradiologist identified the locations of the lesions using MRI.

Results: MOG-Ab-positive patients had a significantly higher ratio of acute disseminated lesions to solitary lesions compared to AQP4-positive patients (108:26 vs 30:40) (P < 0.001). MOG-Ab-positive patients also had significantly higher amounts of subcortical white matter lesions of the temporal lobe (23.1%) and cerebellar peduncle (22.4%) than AQP4-Ab-positive patients (0.0% and 4.3%, respectively). AQP4-Ab-positive patients had more frequent dorsal medulla lesions (30.0 %) compared to MOG-Ab-positive patients (6.0 %) (P < 0.001). By comparing in age group, paediatric MOG-Ab-positive cases had a significantly higher number of temporal lobe lesions compared to adults, but the incidence of cerebellar peduncle lesions was not statistically different.

Conclusions: Lesions in the cerebellar peduncle are a distinctive and age-independent indication of MOG-Ab-associated diseases and could help provide differential diagnosis between these disorders and AQP4-Ab-associated diseases.

Introduction

Brainstem and diencephalic syndrome are key characteristics of neuromyelitis optica (NMOSD).[1)]
However, the specific features of brain MRI in MOGAD are still unknown.
In French group research, pons and thalamus are distinctive features. [2)]
In Chinese group research, subcortical white matter and internal capsule lesions are. [3)]

The aim of this study is to solve the discrepancy by our larger cohort.
And for better understanding the brainstem lesions of MOGAD, superimposed images are needed.

Method

Patients
Patients inclusion flowchart is shown in Figure 1.
Antibody testing
Live CBA using full-length human MOG and M23-AQP4 transfected HEK 293.
Brain MRI analysis
Brain region: divided into 21 parts;
Subcortical white matter (4 lobes), deep white matter (4 lobes),putamen, thalamus, hypothalamus, internal capsule, corpus callosum, midbrain (ventral and dorsal), pons (ventral and dorsal), medulla(ventral and dorsal), cerebellar peduncle and cerebellum.
Statistical analysis
Categorial variables: Pearson's chi-square test or Fisher's exact test.
Quantitative variables: Mann-Whitney *U* test.
P value at brain MRI analysis was multiplied by 21; **Bonferroni's correction**.
P value was set <0.05 statistically significant. (using R)

Results

We finally included **134** MOGAD and **70** NMOSD patients. (Table.1)
MOGAD patients had significantly more **subcortical white matter lesions of the temporal lobe** (23.1%) and **the cerebellar peduncle** (22.4%) than NMOSD patients (0.0% and 4.3%, respectively).
Dorsal medulla lesions were more frequent in the NMOSD patients (30.0%) than in the MOGAD patients (6.0%) (P < 0.001).
In 81 adult patients and 53 paediatric patients diagnosed with MOGAD, we revealed that the subcortical white matter lesions of the temporal lobe were significantly dominant in paediatric patients (P < 0.005). In contrast, there was no significant difference of cerebellar peduncle lesions between the two groups: 23.5% (19/81) of the adult and 20.8% (11/53) of the paediatric patient (P = 0.833).
The superimposed images of brainstem lesions in MOGAD and NMOSD patients showed that the pyramidal and medial medulla lesions were commonly observed in MOGAD, whereas the area postrema lesions were observed in NMOSD (Figure. 2).

Figure.1 Flow chart for inclusion of patients with MOG and AQP4-Ab

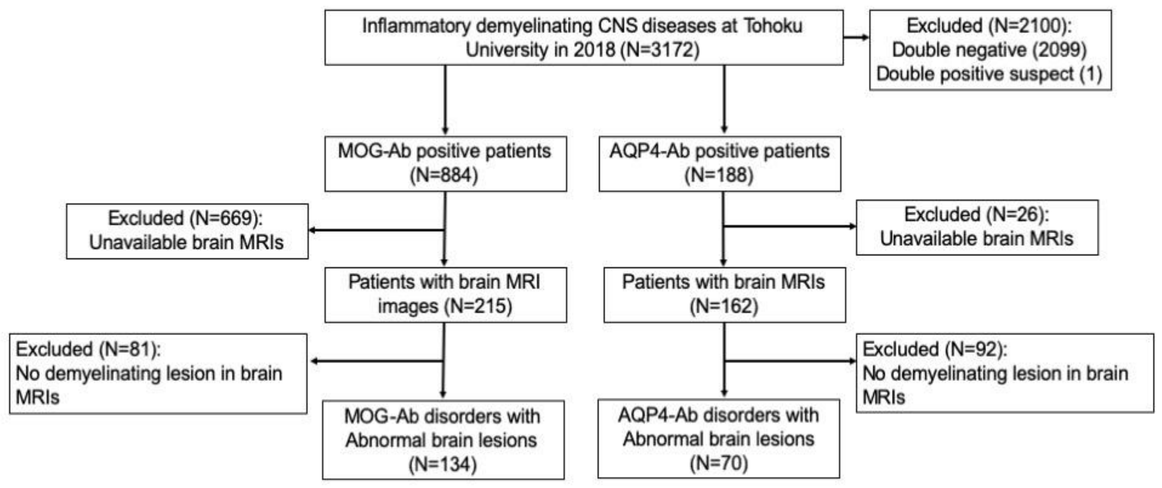
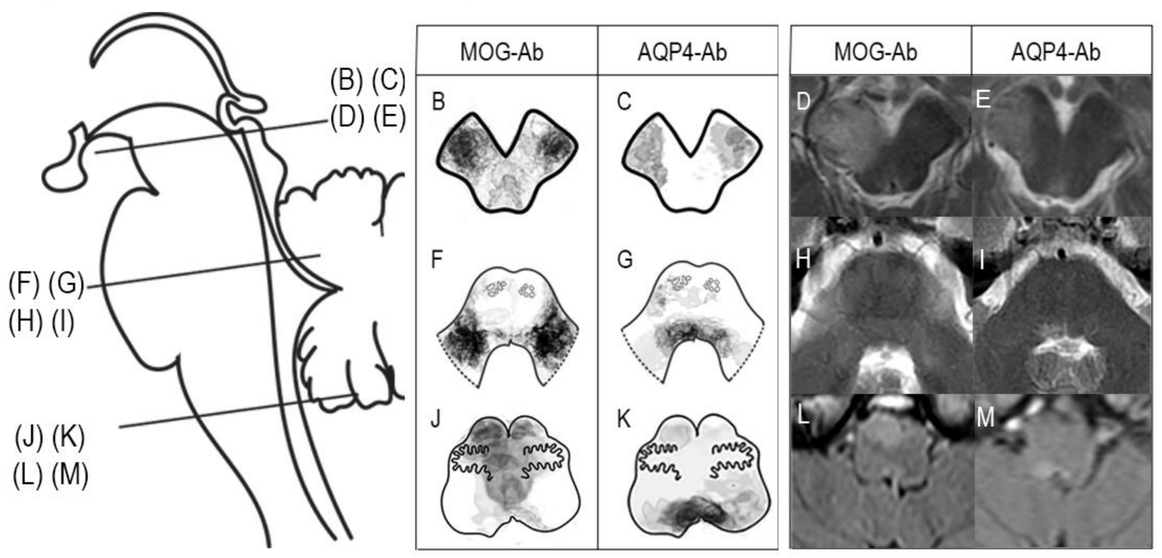


Table.1 The patient characteristics of MOGAD and NMOSD

Clinical and MRI features				
		MOG (134)	AQP4 (70)	P value
Age at MRI, years, median (IQR)		23 (9, 42)	47 (33, 63)	<0.001*
Children, n (%)		53 (39.6)	4 (5.7)	<0.001*
Female, n (%)		72 (53.7)	61 (87.1)	<0.005*
EDSS in acute phase, median (IQR)		2.5 (1.0, 5.0)	5.0 (2.0, 6.0)	<0.005*
Brain MRI obtained at onset: at relapse		103:31	49:21	0.369
Case with Gd-enhanced vs non-enhanced		55:56	22:13	0.238
Case with disseminated vs solitary lesions		108:26	30:40	<0.001*
Lesion distribution on brain MRI				
Cortex/subcortical white matter, n (%)	Whole brain	87 (64.9)	32 (45.7)	NA
	Frontal	82 (61.2)	31 (44.3)	0.649
	Temporal	31 (23.1)	0 (0.0)	<0.001*
	Parietal	51 (38.1)	12 (17.1)	0.076
	Occipital	10 (7.5)	1 (1.4)	>0.999
Deep white matter, n (%)	Whole brain	67 (50.0)	38 (54.3)	NA
	Frontal	54 (40.3)	36 (51.4)	>0.999
	Temporal	40 (29.9)	12 (17.1)	>0.999
	Parietal	34 (25.4)	22 (31.4)	>0.999
	Occipital	9 (6.7)	1 (1.4)	>0.999
Corpus callosum, n (%)		19 (14.2)	16 (22.9)	>0.999
Putamen, n (%)		10 (7.5)	1 (1.4)	>0.999
Thalamus, n (%)		15 (11.2)	9 (12.9)	>0.999
Hypothalamus, n (%)		5 (3.7)	4 (5.7)	>0.999
Internal capsule, n (%)		27 (20.1)	14 (20.0)	>0.999
Midbrain, n (%)	Whole	33 (24.6)	8 (11.4)	NA
	Ventral	28 (20.9)	8 (11.4)	>0.999
	Dorsal	14 (10.4)	3 (4.3)	>0.999
Pons, n (%)	Whole	30 (22.4)	10 (14.3)	NA
	Ventral	20 (14.9)	3 (4.3)	>0.999
	Dorsal	20 (14.9)	9 (12.9)	>0.999
Medulla oblongata, n (%)	Whole	21 (15.7)	24 (34.3)	NA
	Ventral	19 (14.2)	6 (8.6)	>0.999
	Dorsal	8 (6.0)	21 (30.0)	<0.001*
Cerebellar peduncle, n (%)		30 (22.4)	3 (4.3)	<0.05*
Cerebellum, n (%)		17 (12.7)	1 (1.4)	0.315

Figure.2 The superimposed images of brainstem lesions of MOGAD and NMOSD

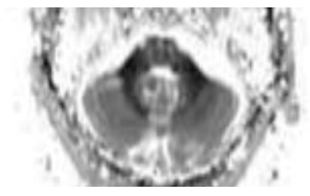


Discussions

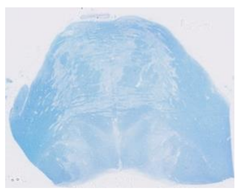
- Why is subcortical whiter matter frequently involved in MOGAD patients than in NMOSD patients?
  Most of the patients of MOGAD had multiple lesions (Table 1)
  ADEM, Cortical encephalitis 4) more common in MOGAD than NMOSD.

- Why is cerebellar peduncle frequently involved in MOGAD patients than in NMOSD patients?
  Cerebellar peduncle is the highest expression area of myelin [4)5)]
  MOG expressed the most outer layer of myelin
  →cerebellar peduncle are more likely to be involved in MOGAD

Myelin mapping



Klüver-Barrera（KB）staining



Conclusions

the existence of lesions in the subcortical white matter of the temporal lobe and cerebellar peduncle distinguished MOGAD from NMOSD, especially the cerebellar peduncle was a common feature regardless of age in MOGAD.

1) Wingerchuk DM, Neurology 2015.
2) Cobo-Calvo A. Neurology 2018
3) Chen C. J Neurol Sci 2019.
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5) Ashikaga R. AJNR Am J Neuroradiol 1999