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Neuromyelitis optica shorter lesion can cause important pyramidal deficits

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ABSTRACT

Objective: Evaluate the correlation between spinal cord lesion length and pyramidal function system score in a cohort of patients with NMO.
Methodology: Retrospective retrieval of all exams performed in our center from January 2004 to December 2012 for patients with NMO. The exams were evaluated for lesion length, contrast enhancement and T1 hypointensity; these variables were correlated with the functional system score from the EDSS, performed no more than three months from the scan.
Results: 41 patients were included. Although patients with lesion extension ≥2 vertebral segments did not present worse pyramidal scores in a direct comparison, the influence of lesion length was not so strong when patients were separated in 3 groups (≥2, ≥3 or ≥4 vertebral segments) and evaluated with a receiving operating characteristics (ROC) curves. Gadolinium enhancement also contributed to more severe pyramidal system scores, but T1 hypointensity did not.
Conclusion: Although patients with spinal cord lesion extending ≥3 vertebral segments had more pyramidal disability, its difference was not so strong when compared to patients with ≥2 or ≥4 vertebral segments. This suggests that lesion extension might not be the most important factor in favoring a worse prognosis in spinal cord lesions in NMO.

1. Introduction

Neuromyelitis optica (NMO) is an autoimmune disease characterized by recurrent optic neuritis and transverse myelitis [1], but can also present distinct symptoms within a syndromic spectrum, known as NMO spectrum disorders (NMOSD), which include recurrent optic neuritis and recurrent longitudinal myelitis and specific brain and brainstem lesion and syndromes, associated to the anti aquaporin 4 antibody (anti-AQP4-IgG) [2]. The hallmark of the spinal cord lesion in these patients is a longitudinally extensive transverse myelitis (LETM), defined by magnetic resonance imaging (MRI) as a lesion extending for 3 or more vertebral segments [1].

A short transverse myelitis (STM), defined as a MRI spinal cord lesion not extending within and beyond 3 vertebral segments, has recently been shown to be the initial presentation in 14% patients from a large NMO cohort [3]. The incorporation of STM within the NMO-SD might broaden the range of patients who are candidates for AQP4-IgG testing and treatment with early and aggressive immunosuppression, since halting further relapses can prevent neurological disability [4,5].

The goal of this study was to evaluate the influence of spinal cord lesion length on clinical disability, and especially to compare patients with LETM and STM.

2. Methodology

We retrieved all available MRI studies performed at the Department of Radiology, Universidade Federal de São Paulo, from patients followed

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Table 1
Clinical and MRI information relevant for this study.

	Age			Disease duration			Pyramidal functional system*			Longitunal extension**
	All	Patients with lesion ≤ 2***	Patients with lesion ≥ 3***	All	Patients with lesion ≤ 2***	Patients lesion ≥ 3***	All	Patients with lesion ≤ 2***	Patients with lesion ≥ 3***	All
Mean	39.1	35.0	41.2	170.3	115.4	204.3	2.5	1.4	3.1	3.6
Median	37.0	33.0	42.0	54.0	31.5	68.0	3.0	1.0	3.0	3.0
Std. Deviation	10.5	8.6	11.1	364.5	310.9	393.1	1.7	1.8	1.5	3.4
Minimum	24.0	26.0	24.0	0	0	0	0.0	0.0	0.0	0.0
Maximum	61.0	57.0	61.0	1363	1353	1363	5.0	5.0	5.0	14.0

* As per EDSS functional system scores.
** Longitudinal extension: longitudinal extension measured in number of vertebral segments involved in the T2 sagittal plane.
*** 17 subjects had lesion extension ≤2 vertebral segments and 24 had lesion extension ≥3 vertebral segments.

at the Neuroimmunology Clinic at the same institution, from January 2004 to December 2012, diagnosed with NMO according to Wingerchuck 1999 and/or 2006 criteria [1,6]. The exams were performed for diagnostic or regular follow-up, either during an acute attack or remission. In cases with more than one MRI available, the most representative exam was selected.

All patients with available scans from the cervical and thoracic spinal cord were select for this study. Clinical and demographic data were obtained from medical records at the closest time point from the MRI scan (either at acute event or first outpatient clinical evaluation), functional disability was measured with the Expanded Disability Status Scale (EDSS) [7] and NMO-IgG status was obtained by indirect immunofluorescence from a commercial test. We excluded all pediatric cases (<18 years), patients whose MRI studies were inappropriate for analysis, and patients whose clinical information could not be retrieved. Since this is a retrospective clinical analysis, patients had been treated with acute or preventive therapies recommended and available for NMO at the time they were seen, which included, oral or IV pulse steroids, cyclophosphamide, methotrexate, azathioprine and intravenous immunoglobulin [8–10].

The studies were performed at 1.5T scanners. Most exams were performed at a Siemens Magnetom Sonata 1.5T scanner (Siemens Medical Solutions®, Erlangen, Germany), with the exception of 5 spinal cord studies that were performed at a Philips Gyroscan ACS-NT 1.5T scanner (Philips Medical Systems®, Eindhoven, the Netherlands). Spinal cord MRI protocol was obtained with the following sequences: (1) Turbo spin-echo (TSE) T2-weighted imaging; (2) Short Time Inversion Recovery (STIR); and (3) Spin-echo (SE) T1-weighted imaging pre and post gadolinium injection.

Two experienced neuroradiologists (authors GBS Carvalho and RS Carvalho) reviewed all MRI scans independently and both were blinded to all clinical information except for the diagnosis of NMO; when discordant, final opinion about the findings was reached by consensus. The images were analyzed for the following items: longitudinal extension measured in number of vertebral segments involved in the sagittal plane; the presence or absence of lesion hypointensity on T1-weighted images; and the presence or absence of enhancement lesion on post-gadolinium sequences.

We analyzed the correlation between the MRI characteristics and neurological impairment, focusing on the pyramidal system disability. This functional system was chosen because it is severely affected in patients with NMO and its information can easily be retrieved from clinical charts and has a very low chance of suffering inter-observer variability.

Table 2
MRI characteristics studied in the 41 patients.

	Present (%)	Absence (%)
Lesion extension ≥ 3 vertebral bodies	58.5	41.5
T1 hypointensity	30.0	70.0
Gadolinium enhancement	27.5	72.7

The data was analyzed using Prism 5 (Graphpad Software, Inc.) and the IBM SPSS Statistics, version 21, software. The data were evaluated for normality distribution with the Kolmogorov–Smirnov normality test and the unpaired t test or Mann–Whitney test was used to compare two groups. The Tukey's Hinges test was used to analyze the correlation between MRI characteristics and pyramidal scores and further reassured by checking the area under the curve (AUC) in receiving operating characteristic (ROC) curves. Furthermore, Kendall's tau b test was used to evaluate the correlation between multiple variables.

3. Results

A total of 78 MRI scans from 47 patients were evaluated, 6 patients were excluded (three patients had exams considered inappropriate for analysis and complete clinical data was unavailable for six patients), thus 41 patients were included in the study (Tables 1 and 2); all but one patient had recurrent NMO. 40% of the patients were NMO-IgG positive, 43% negative and 17% were not tested. Reasons for not having been tested for the NMO-IgG were patients lost to follow-up before the exam became available in Brazil (late 2007) or evident NMO clinical confirmation, i.e., index event, typical MRI features [6] and treatment implementation already performed at the time of NMO-IgG availability. Tables 1 and 2 display the clinical and radiological data from these 41 patients. 17 subjects had lesion extension ≤2 vertebral segments (41%) (Fig. 1) and nine patients had their lesion considered shorter than one vertebral segment: one that had the index event during follow-up, thus her spinal cord

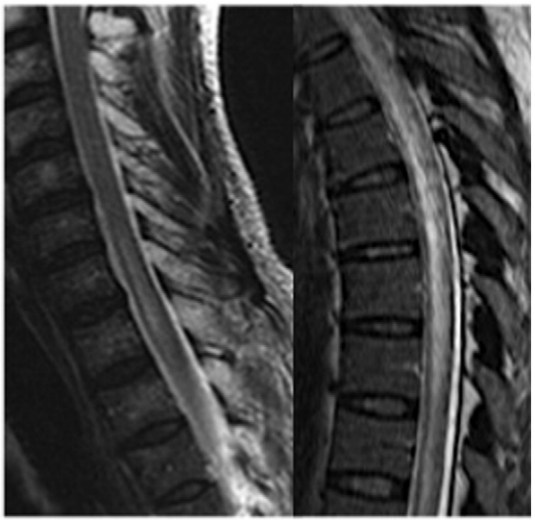

Fig. 1. Magnetic resonance images case examples of short and longitudinally extensive transverse myelitis. T2 magnetic resonance images in the sagittal plane. Left: cervical spinal cord of a patient with short transverse myelitis ≤2 vertebral segments); Right: thoracic spinal cord of a patients with longitudinally extensive transverse myelitis ≥3 vertebral segments).