Prognostic Factors for Multiple Sclerosis in Patients with Spinal Isolated Syndromes

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Introduction

•The spinal cord makes up the 15% of the Central Nervous System weight; it has a fundamental role being the main pathway for information connecting the brain and peripheral nervous system and any spinal lesion/damage contributes substantially to a patient's disability;

•At the onset of Multiple Sclerosis (MS) most patients have spinal lesions, which are prognostic for further relapses and cumulative disability;

•Inflammatory conditions with spinal involvement have different clinical course, prognosis, and acute and chronic treatment strategies; an early and accurate diagnosis is important to minimize cumulative disability;

•The aim of the current study was to assess the diagnostic and prognostic factors in patients with a spinal isolated syndromes (SIS);

Methods

•**Cohorts of patients** enrolled into the study:

- Cohort 1: we retrospectively identified patients with a spinal syndromes meeting the following inclusion criteria:
  - A subsequent diagnosis of NMO according to the 2015 NMO diagnostic criteria, serum samples availability from the time of onset and adequate clinical and paraclinical data (18 patients)
  - A subsequent diagnosis of sarcoidosis with a pathological confirmation, serum samples availability from the time of onset and adequate clinical and paraclinical data (11 patients).
  - A subsequent diagnosis of MS according to the 2010 MS diagnostic criteria, serum samples availability from the time of onset and adeguate clinical and paraclinical data (150 patients)
- Cohort 2: we retrospectively identified patients with a spinal isolated syndrome suggestive of MS after a comprehensive work up, with serum samples availability from the time of onset and adequate clinical and paraclinical data (218 patients) .

•**Clinical and paraclinical baseline data:**

- **Clinical**: age, gender, time from onset, symptoms, full vs partial recovery, response to steroids;
- **Brain and spinal MRI**: >3 vs <3 segments, cervical vs dorsal location, meningeal or persistent enhancement, dissemination in space and time critieria for MS;
- **Neurophysiology:** combined somatosensory and motor evoked potential score (4 limbs range 0 – 24);
- **CSF**: cells and proteins count, presence of OCBs;
- **Serum:** AQP4 and neurofilaments status at baseline;

•**Statistical analysis:** standard non/parametric to compare three groups, uni/multivariate Cox for time to event data, NRI and IDI as reclassification indices, and CART learning algorithm for tree development and pruning.

Results

Table 1. Baseline characteristics of the cohorts

Characteristics	NMO (n =18)	Sarcoidosis (n = 11)	MS (n = 150)	p
Clinical variables				
Age at onset, mean years (SD)	46.8 (14.2)	49.7 (16.2)	32.5 (8.5)	< 0.01
Females — %	15 (83.3)	7 (63.6)	98 (65.3)	ns
Time from onset — mean days (SD)	27.3 (14.1)	73.1 (34.2)	51.2 (26.3)	< 0.01
Sensory symptoms — %	5 (27.8)	10 (90.9)	98 (65.3)	< 0.01
Response to steroids — %	10 (55.6)	9 (81.8)	93 (62.0)	ns
Full recovery — %	3 (16.7)	4 (36.4)	84 (56.0)	< 0.01
Serum variables				
AQP4 positive — %	13 (72.2)	0 (0)	0 (0)	< 0.01
Neurofilaments, mean pg/ml (SD)	183.9 (78.2)	16.1 (4.3)	36.2 (19.7)	< 0.01
CSF variables				
Elevated cell count — %	10 (55.6)	9 (81.8)	21 (14.0)	< 0.01
Elevated protein count — %	11 (61.1)	8 (72.7)	16 (10.7)	< 0.01
OCBs — %	4 (22.2)	5 (45.5)	127 (84.7)	< 0.01
Neurophysiological variables				
Sensory-motor EP score, mean (SD)	5.6 (1.2)	2.1 (1.3)	2.1 (1.4)	< 0.01
MRI variables				
> 3 segments — %	15 (83.3)	6 (54.5)	0 (0)	< 0.01
Cervical lesion —- %	7 (38.9)	6 (54.5)	87 (58.0)	ns
Meningeal enhancement — %	0 (0)	6 (54.5)	7 (4.6)	< 0.01
Persistent enhancement — %	3 (16.7)	9 (81.8)	5 (3.3)	< 0.01
DIS criteria fulfilled — %	4 (22.2)	0 (0)	128 (85.3)	< 0.01
DIT criteria fulfilled — %	0 (0)	2 (18.2)	34 (22.7)	ns

Figure 1. Pruned CART Algorithm for differential diagnosis of SIS

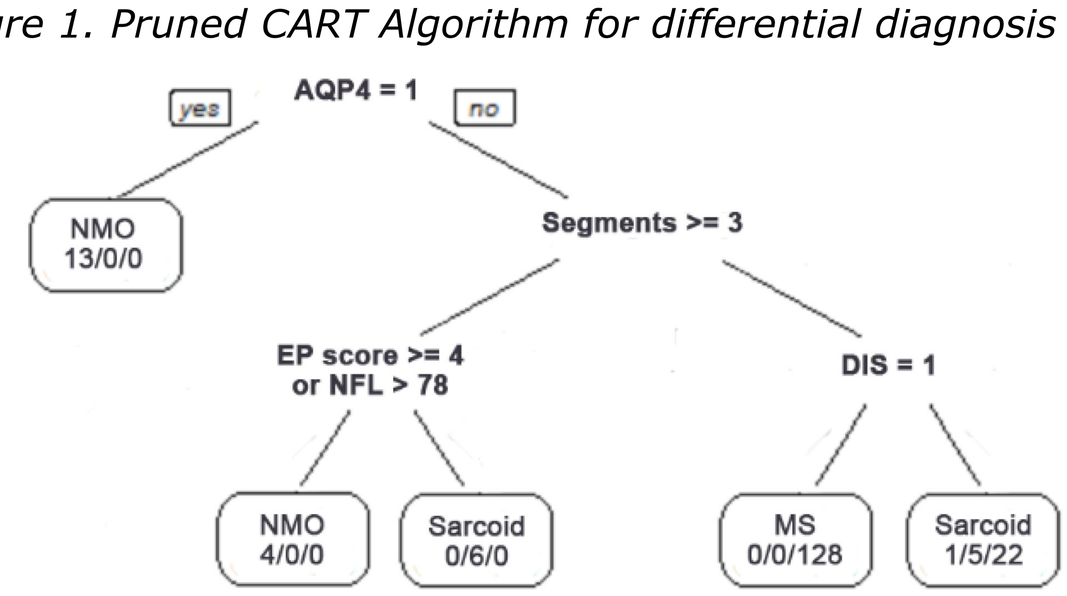
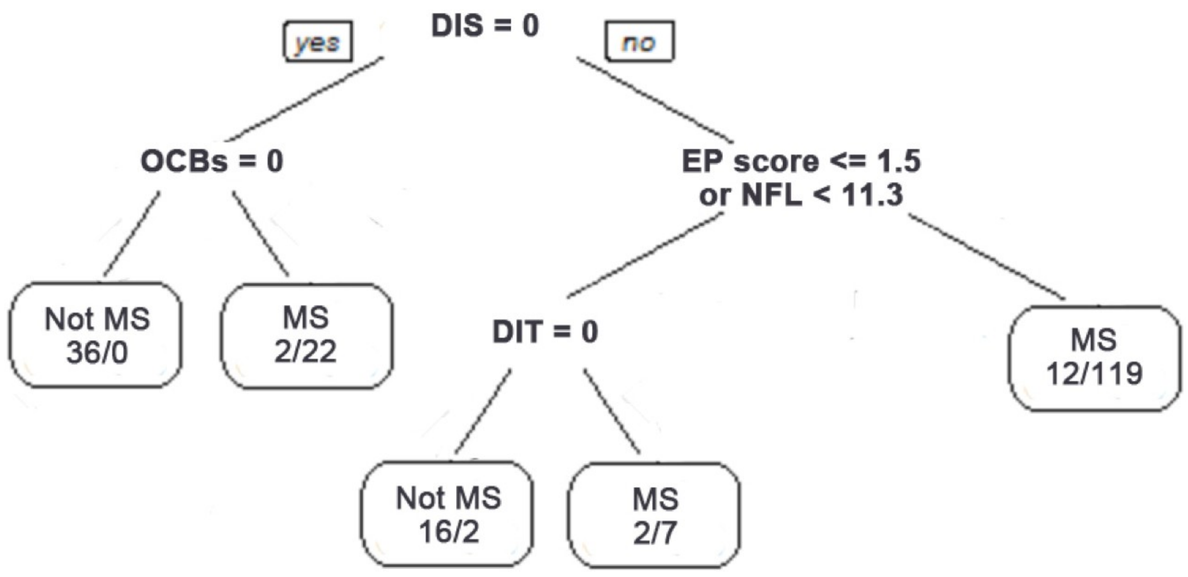


Figure 2. Pruned CART Algorithm for prognostication of MS in SIS



Conclusions

•Positive AQP4 antibodies and extensive longitudinal spinal lesions are the hallmark of NMO disorder, but a high evoked potential score or serum neurofilaments levels and the presence of DIS criteria are important for the differential diagnosis of atypical cases;

•In patients in which different inflammatory disorders have been excluded after a comprehensive work up, the fulfillment of DIS and DIT criteria, the presence of CSF oligoclonal bands, and a high evoked potential score or serum neurofilaments levels are independent prognostic factors for MS;