Evaluation of Prognostic Factors in Pediatric Transverse Myelitis: A Multicenter Cohort Study

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Introduction:

Acute transverse myelitis (ATM) is a rare disease with clinical findings related to immune-induced inflammation of the spinal cord. It may be idiopathic or a component of another disease (1). It may cause severe disability, limiting daily living skills, in children.

Objectives:

In this multicenter study, it was aimed to determine the demographic and clinical findings and prognostic factors of ATM patients in the pediatric age group.

Materials and methods:

Data from 193 individuals (99 boys, 94 girls) with their first episode of ATM who presented between 2010-2021 were collected from 27 centers. Data from the entire cohort, and etiologic subgroups with Rankin scores (RS) at last follow-up ≥ 3 (HRS) and < 3 (LRS), were statistically compared in terms of clinical and immunologic parameters, and treatment modalities (plasmapheresis, IVMP, and IVIG).

Diagnostic criteria for transverse myelitis (in line with the recommendations of the 'Transverse Myelitis Consortium Working Group') (2) were determined as follows: 1- Presence of clinical findings associated with spinal cord pathology: - Sensory, motor or autonomic dysfunction - Bilateral findings, although not symmetrical, - Having a sensory deficit that shows a level 2- Findings indicating inflammation: - CSF pleocytosis or increased IgG index or contrast enhancement on spinal MRI 3- Progression of the symptoms within 4 hours-21 days to the peak level (if the patient has symptoms when he wakes up, it is calculated according to the time he is awake) 4- Exclusion of an extraaxial compression by imaging findings.

Exclusion criteria from the study: Cases with a previous diagnosis of demyelinating disease, spinal tumors, or vascular origin were excluded from the cohort.

Modified Rankin scale (3): 0 points: No symptoms, 1 point: No obvious disability. 2 points: Mild disability; unable to carry out all previous activities, but able to look after own affairs without assistance. 3 points: Moderate disability; requiring some help, but able to walk without assistance. 4 points: Severe disability; unable to walk unaided and unable to look after own bodily needs without assistance. 5 points: Very severe disability; Bedridden, incontinence and in need of constant care and attention. 6 points: Death.

Statistical analysis: Chi-square test was used to compare categorical variables, and Kolmogorov-Smirnov test was used to determine whether the distribution of data was normal. In the comparison of the two groups, Student-T test was used in case of normal distribution and Mann-Whitney U test was used in case of non-normal distribution.

Results:

The median age at presentation and follow-up time were 8.9-years, and 18-months, respectively. The etiological causes were idiopathic (73.6%), demyelinating (21.2%), and infectious diseases (4.1%) (Table 1). The clinical findings of the patients were summarized in Table 2.

The HRS group had statistically significant six clinical and immunologic parameters for an unfavorable outcome (Table 3); (1) higher m-RS at admission (p<0.003), (2) increased neutrophil-lymphocyte ratio (NLR) (p=0.013), (3) higher rate of seropositivity of a recent infection (p=0.018), (4) high rate of CMV IgM positivity (p=0.012), (5) lower lymphocyte count (p=0.01) and (6) a higher prevalence of hypoactivity of deep tendon reflexes (DTR) on admission (p=0.028) (Figure 1). However, the rate of patients given intravenous methylprednisolone (IVMP) as initial treatment was lower (p=0.024) in the HRS group (Table 3).

Variable	(Mean ± SD, or n,%)
Age at admission	8.9±4.3 (1.1-17.9)
Gender (n,%)	
Male	99 (51.3%)
Female	94 (48.7%)
Length of hospital stay (days)	21.7±27
Follow-up period (months)	24.5±21.6
Number of episodes	1.1±0.37
Duration of symptoms before admission (days)	6.8±10.4
Time to peak symptom (days)	4.8±4.79
History of infection	
Respiratory	90 (46.6%)
Gastrointestinal	22 (11.4%)
Vaccination history	11 (5.7%)
Final diagnosis	
Idiopathic	125 (64.8%)
Neuroinflammatory	37 (19.2%)
Infectious	8 (4.1%)
Symptoms	
Weakness	183 (94.8%)
Sensory	82 (42.3%)
Pain	83 (43%)
Back pain	26 (13.5%)
Sphincter involvement	74 (38.3%)
m-Rankin score at admission	3.6±1.3
m-Rankin score at discharge	2.4±1.4
m-Rankin score-1 year	1.1±1.37
Latest m-Rankin score	0.94±1.26
Recurrence	14 (7.3%)

Table 1. Demographic characteristics, features in the history, and Rankin scores at presentation and follow-up, in the patients.

Variable	n	%
Motor involvement		
Paraparesis	85	49.7
Tetraparesis	52	30.4
Monoparezi	22	12.9
Symetric involvement	93	54.4
DTR		
Hypoactive	43	31.2
Hyperactive	57	41.3
Normoactive	38	27.5
Loss/decrease in abdominal skin reflex	91	54.8
Spasticity	11	6.4
Pathological reflexes	62	36.3
Sensory finding	107	62.6
Paresthesia	72	42.1
Dysesthesia	31	18.2
Sensory level	37	22.6
Urgency	4	2.3
Urinary incontinence	41	24
Globe vesical	50	29.2

Table 2. Clinical findings of the patients.

Variable (mean ± SD or n/total)	m-Rankin score < 3	m-Rankin score ≥ 3	*p* value
n	125	24	
Age at presentation (y)	8.5±4	9.9±4.9	>0.05
Female /male ratio	62/63: 0.98	10/14: 0.71	>0.05
Symptom duration before admission (days)	5.8±7.1 median 3	7.5±11.4 median 2	>0.05
Time to nadir (days)	4.7±3.9 median 3	5.26±5.7 median 2	>0.05
Initial Rankin score	3.4±1.2 median 4	4.25±1.2 median 5	0.001
Rankin score at discharge	2±1.1 median 2	4.2±0.9 median 4	<0.001
Lymphocyte count (x10^3/μL)	2.77±1.67 Median 2.37	2±1.1 Median 1.8	0.010
Neutrophil to lymphocyte ratio	3.8±6.8 median 2.1	5.2±4.4 median 4.1	0.013
Idiopatic type (n/total)	87/120, 72.5%	20/22 (90.9%)	0.065
DTR hypoactivity	47/123, 38.2%	15/24 (62.5%)	0.028
History of infection (n/total)	80/127, 63%	11/24, (45.8%)	>0.05
IgM positivity of recent infection	13/95 (13.7%)	7/18 (38.9%)	0.018
Positive nfectious antibodies	CMV (n=1), Mycoplasma (n=6), Lyme (n=3), EBV (n=2), HSV (n=1)	CMV (n=3) Mycoplasma (n=2) Covid-19 (n=1) Salmonella (n=1)	-
IgM positivity of CMV	1/84 (1.2%)	3/16 (18.8%)	0.012
Initial therapy IVMP / IVIG IVMP (%)	102/18 İVMP (85%)	14/8 İVMP (63.6%)	0.024
Prognosis			
Unassisted walking	123/125 (98.4%)	13/23, (43.5%)	<0.001
Bedridden	3/125 (2.4%)	8/23 (%34.8)	<0.001
Motor deficit	31/125 (24.4%)	19/24 (79.2%)	<0.001
Sensory deficit	11/125 (8.7%)	6/24 (25%)	0.032
Sphincter involvement	19/125 (15%)	7/24 (29.2%)	0.091

Table 3. Comparison of the groups of patients with the final Rankin score ≥3 and <3 at follow-up.

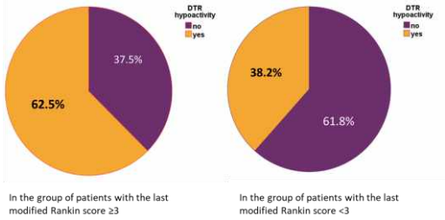

Figure 1. DTR hypoactivity at admission was significantly higher in patients with the most recent modified Rankin score ≥3 (p=0.028).

Conclusions:

Certain immunologic parameters (increased NLR and lower lymphocyte count) might be considered unfavorable outcome parameters for children with ATM. These findings indicate increased inflammation.(4) In our study, increased seropositivity related with recent infection and CMV, in the group with high Rankin score, suggests that virulent microorganisms may have a role in increased inflammation.

Acute TM may be initially misdiagnosed as Guillain Barre syndrome in severe patients, because of more frequent DTR hypoactivity. However, early IVMP treatment is important in terms of good prognosis.

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