The Spectrum of Myelopathies in Children: Beyond Idiopathic Transverse Myelitis

Laura S. Munoz MD[1], Eliza Gordon-Lipkin MD[1,2], Paula Barreras MD[1], Sergio Gómez[1], Wendy Piedra[3], Maria Jimena Castañeda-Valderrama MD[1], Anusha Yeshokumar MD[3], Maureen Mealy[1], Olwen Murphy MD[1], Michael Levy MD PhD[1], Daniel Becker MD[1], Scott Newsome MD[1], Carlos A. Pardo MD[1]

[1]Johns Hopkins University School of Medicine & Johns Hopkins Transverse Myelitis Center, Baltimore, MD; [2]Kennedy Krieger Institute, Baltimore, MD; [3]Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD

BACKGROUND

- Pediatric idiopathic transverse myelitis (ITM) accounts for 20% of the cases of inflammatory myelopathy in children. In the United States, the incidence is 1-8 cases per million people per year.
- ITM is clinically indistinguishable from other myelopathies. The differentiation between inflammatory or non-inflammatory myelopathies in children is important for better treatment outcomes and prognosis.

OBJECTIVE

To investigate the differential diagnosis of pediatric myelopathy at the Johns Hopkins Transverse Myelitis Center (JHTMC).

METHODS

- Retrospective review of patients under 21-years-of-age seen at the Johns Hopkins Transverse Myelitis Center with a diagnosis of myelopathy between 2015-2017 was performed.
- Temporal profile of symptoms, clinical presentation, cerebrospinal fluid (CSF) analysis and etiological diagnosis were reviewed.
- Comparative analysis of clinical features between non-inflammatory and inflammatory myelopathies was completed.
- Categorical variables were summarized in frequencies and compared using x^2 or Fisher exact test. Comparison of two medians was done using Mann-Whitney U test.

RESULTS

Table 1. Demographic characteristics in 55 children with myelopathy

Characteristic		Characteristic	
Total	**55 (100)**	Motor delay, n (%)	0 (0)
Age, median [IQR], years	11 [3-15]	Language delay, n (%)	2 (4)
Gender, male, n (%)	31 (56)	Autoimmune disorder*, n (%)	1 (2)
Ratio male:female	1.3:1	Asthma, n (%)	5 (9)
Ethnicity, Caucasian, n (%)	36 (66)	Overweight (BMI > 25), n (%)	2 (4)
Ethnicity, African-American, n (%)	10 (18)	Obesity (BMI>30), n (%)	5 (9)
Birth history, full term, n (%)	47 (86)	Substance abuse, n (%)	1 (2)
Immunization status, up to date, n (%)	46 (84)		

* Hashimoto's thyroiditis

Figure 1. Age at presentation in 55 children with myelopathy. The distribution shows a bimodal (orange columns) pattern with the highest prevalence at 0 and 13 years of age.

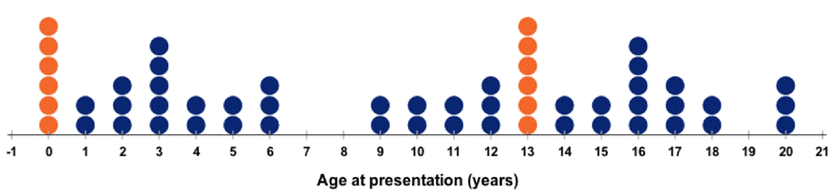


Figure 2: Diagnostic categories in 55 pediatric patients with myelopathy. Most of the patients presented with infectious (para-infectious and post-infectious) myelopathies (n=23, 42%), followed by vascular (n=15, 27%), autoimmune demyelinating (n=13, 24%) (including ITM (n=3), neuromyelitis optica (NMO) spectrum (n=3), multiple sclerosis (n=7)) and of uncertain etiology (n=4, 7%). Etiological diagnosis was based on the criteria of the expert neurologist.

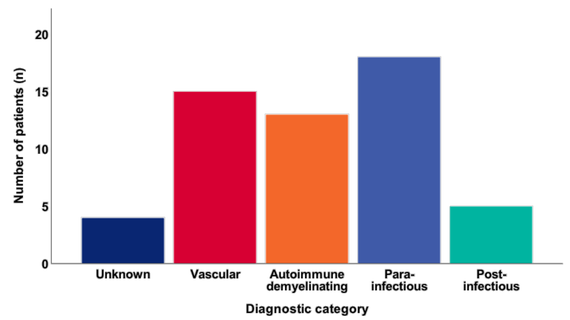
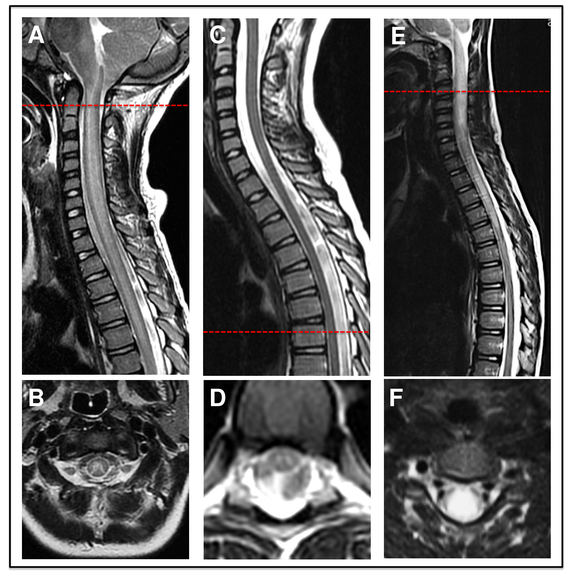


Table 2. Comparative analysis of clinical features between non-inflammatory and inflammatory myelopathies in 51 children. Inflammatory myelopathies included infectious, post-infectious and autoimmune demyelinating myelopathies. Vascular myelopathies corresponded to non-inflammatory myelopathies. Myelopathies of uncertain etiology were excluded from the comparative analysis.

Characteristic	Overall	Non-inflammatory	Inflammatory	p value
Total	**51 (100)**	15 (29)	36 (71)	
Age, median [IQR], years	11 [3-16]	11 [0-14]	12 [4-16]	0.9
Gender, male, n (%)	27 (53)	7 (48)	20 (56)	0.76
Prodromal infection, n (%)	27 (53)	4 (28)	**23 (64)**	0.03
Preceding trauma, n (%)	4 (8)	3 (20)	1 (3)	0.07
Clinical findings				
Hyperacute temporal profile (<6 hours to nadir), n (%)	21 (41)	**10 (68)**	11 (31)	0.03
Motor symptoms at onset, n (%)	43 (84)	15 (100)	28 (78)	0.09
Sensory symptoms at onset, n (%)	33 (65)	9 (60)	24 (67)	0.75
Sphincter dysfunction at onset, n (%)	16 (31)	**10 (67)**	6 (17)	0.001
Cranial nerve involvement, n (%)	16 (31)	0 (0)	**16 (44)**	0.002
Weakness, lower extremity, n (%)	38 (75)	**15 (100)**	23 (64)	0.006
Symmetric involvement, n (%)	30 (59)	**15 (100)**	15 (42)	<0.001
Sensory involvement, n (%)	19 (37)	9 (60)	10 (29)	0.06
Spinal fluid analysis				
Pleocytosis >5 WBC/ul, n (%)	29/40 (73)	3/8 (38)	**26/32 (81)**	0.03
Protein >45 mg/dl, n (%)	17/36 (47)	2/5 (40)	15/31 (48)	1

Figure 3. Illustrative magnetic resonance imaging (MRI) of three children presenting with myelopathy.



(A-B) Six-year-old female with sudden onset of flaccid quadriparesis secondary to acute flaccid myelitis. (A) Sagittal T2-weighted (T2W) MRI sequence demonstrates a longitudinally extensive T2W hyperintensity throughout the spinal cord with associated edema. (B) Axial view shows predominant gray matter involvement.

(C-D) Twelve-year-old male with sudden onset of back pain followed by paraplegia due to a spinal cord infarction. (C) Sagittal T2W MRI shows a longitudinally extensive T2 hyperintensity involving the thoracic cord. (D) Anterior horn involvement is demonstrated on the axial view.

(E-F) Eleven-year-old female with a 2-week-course of lower extremity numbness and weakness found to have anti-AQP4 seropositive Neuromyelitis Optica. (E) T2W MRI shows a longitudinally extensive T2 hyperintensity with cervical and thoracic involvement associated with cord expansion (F). Patchy enhancement was present in the cervical cord (not shown).

CONCLUSIONS

- Though inflammatory myelopathies were the most commonly seen, only three (5%) cases were diagnosed with ITM.
- In contrast to what is described in the literature, in our series almost a third of the patients were suspected to have a myelopathy secondary to an ischemic event.
- Distinctive clinical and laboratory findings at presentation are of value when distinguishing inflammatory vs. non-inflammatory myelopathies in children.
- Clinicians must be aware of the broad spectrum of differential diagnosis of myelopathies in children.

ACKOWLEDGMENTS

We would like to acknowledge the individuals and their families who participated in this study through their generous contribution of their time and effort. This research is supported by the Bart McLean Fund for Neuro-immunology Research and the Johns Hopkins Project Restore.