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Acute transverse myelitis in childhood

Center-based analysis of 47 cases

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ABSTRACT Objective: To relate clinical characteristics associated with acute transverse myelitis (ATM) in children with functional outcomes at follow-up. **Methods:** We identified 47 patients for whom ATM occurred under the age of 18 years. Chart analysis, clinical evaluation, and administration of functional measures were completed. **Results:** The age at onset clustered between ages 0 to 2 and 5 to 17. Febrile illness had occurred in 47% and vaccination in 28%. Major disability at the nadir of the clinical course was noted. Eighty-nine percent were unable to walk, required assisted ventilation, or both. At a median of 3.2 years after acute illness, 43% were unable to walk 30 ft and 21% required a walker or other support, 68% experienced urinary urgency, 50% required bladder catheterization, 54% were troubled by persistent dysesthesias, and 75% had numbness. Factors associated with a better functional outcome included older age at time of diagnosis, shorter time to diagnosis, lower sensory and anatomic levels of spinal injury, absence of T1 hypointensity on spinal MRI obtained during the acute period, lack of white blood cells in the CSF, and fewer affected spinal cord segments. Neither rapid progression to maximum impairment in less than 1 day nor any antecedent illness, immunization, or trauma was associated with a worse outcome. **Conclusion:** Persisting disability was present in many children with acute transverse myelitis. Urinary problems and sensory symptoms were the most common issues. Age at onset below 3 years was associated with worse functional outcomes. **NEUROLOGY 2007;68:1474-1480**

Acute transverse myelitis (ATM) is a rare disorder with about 1,400 new cases diagnosed in the United States per year.^{1,2} In approximately 20%, the acute illness occurs at younger than 18 years.³

Diagnostic criteria and a classification scheme for ATM were recently established by the Transverse Myelitis Consortium Working Group.⁴ The diagnosis requires both the presence of spinal cord inflammation, as defined by CSF pleocytosis, elevated CSF IgG index, or gadolinium enhancement on a spinal MRI, and the absence of an identified CNS infection. The diagnosis also requires exclusion of acute myelopathy secondary to a known underlying disease and from compressive myelopathies. Depending on the series, 6 to 43% of patients with ATM develop signs and symptoms sufficient to make the diagnosis of multiple sclerosis (MS), 8 to 16.5% manifest features of a systemic mixed connective tissue disorder, and up to 5% are found to have localized nonpyogenic infection of the spinal cord^{1,2,5} (Johns Hopkins Transverse Myelitis Center [JHTMC] case series). Idiopathic ATM accounts for about 10 to 45% of all cases of ATM.^{1,2,6-10}

We evaluated a large cohort of patients under age 18 who developed ATM. This cohort was evaluated and treated at a tertiary referral center. Information is provided on antecedent factors, acute clinical and paraclinical features, and functional and ambulatory outcome measures at the time of onset of ATM and at follow-up and treatment. This study qualified for institutional review board exemption (under 45 CFR 46.101 [b]⁴ on 20 September 2001 [protocol number 01-09-20-16e]).

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METHODS Case selection and data collection. All patients evaluated at the JHTMC between January 2000 and February 2004 who met established criteria for acute or remote transverse myelitis under age 18 were included.⁴ Patients with disease-associated ATM were included. All information collected was coded to protect confidentiality and entered into SPSS 11.5.0 for analysis.

Retrospective clinical data were collected from chart review and from the history obtained at the time of evaluation at the JHTMC. This included demographic items (age at onset, sex, geography), antecedent factors (immunizations, infectious disease, trauma), description of the acute illness (onset of first neurologic symptom, time to nadir, time to diagnosis, acute symptoms), bladder function, and reported sensory symptoms. Vaccinations within 30 days of onset of ATM were confirmed by review of medical records. Laboratory data collected included the extent and type of spinal cord lesions seen on MRI, CSF white blood cell (WBC) counts, and protein. Treatment variables assessed included use of IV or oral corticosteroids, IV immunoglobulins, acyclovir, and plasmapheresis.

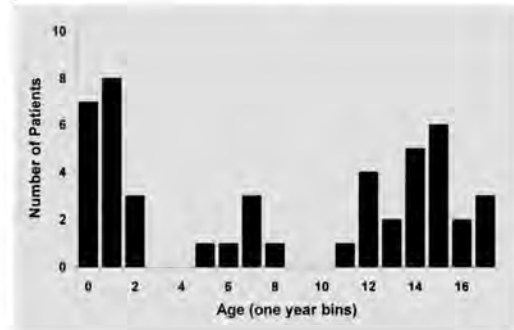
Assessment of function. Ambulatory ability was assessed at the time of presentation to the JHTMC using all retrospective information available from the functional nadir of the acute illness if that had passed. Patients were assigned an ordinal scale score according to an adaptation of the Hughes Functional Disability Scale (HFDS; 0 = normal, 1 = minor symptoms, fully capable of manual work, 2 = able to walk more than 30 ft without assistance, 3 = able to walk more than 30 ft with assistance, 4 = bed bound/wheel chair bound, 5 = requires assisted ventilation, 6 = death).¹¹ Functional independence following the acute phase of illness was assessed using the WeeFIM for children.¹² For those who were older than age 18 at follow-up, the adult FIM was used to assess functional independence.¹³ This follow-up information was collected at an average of 8.0 years (CI: 4.5 to 11.9 years) following the acute onset of disease.

The FIM and the WeeFIM are instruments that measure functional performance of daily skills in 18 separate domains including self-care, toileting, mobility, transfers, communication, cognition, and social interaction. The 18 content items are scored from 1 to 7 based on the individual's level of independence in performing the skill.

Summary data for level of independence at follow-up for each ability area were calculated by grouping patients into three groups, complete dependence, modified dependence, and independence, based on the need for assistance determined by standard rating criteria for the WeeFIM and FIM. WeeFIM and FIM scores at follow-up were then summed into the three domains of activities of daily living (ADL), continence, and mobility. In addition, because younger children are not expected to be completely independent with all activities, all scores were transformed into functional quotients (FQs) based on normative data for each item.

Statistical analysis. The data were analyzed using multiple regression models. Functional outcome was examined using the summed FQ scores for ADL, mobility, and continence. The following predictor variables were examined: age at onset, season of onset, preceding immunization, preceding trauma, the combination of both immunization and trauma, treatment modality, time to nadir, and time to diagnosis. Because of the skewed nature of the distribution of some data, discrete variables were calculated for extent of lesion (zero to three, four to seven, or greater than seven involved segments), CSF pleocytosis (none vs

Figure 1 Distribution of age at onset of acute transverse myelitis



abnormal), rostral border of the sensory level based on exam, and rostral border of the lesion based on MRI (cervical level vs thoracic or lower). In addition, log-transformed values of CSF white blood cells were used for analysis of distribution. Spearman rho correlations were performed between the score on the HFDS at the time of diagnosis and functional outcome scores at the time of follow-up.

Factors that predicted functional outcomes were examined for three domains (ADL, continence, mobility) and for the total WeeFIM and FIM scores at follow-up, using multiple regression. All regression models were first run using raw score ratings from the WeeFIM and FIM as the outcome variable and controlling for age in the regression models. The regressions were then rerun using functional quotients as the outcome variable to control for age. As the significance of predictor variables was the same using both methods, only the FQ analyses are reported for simplicity.

RESULTS Patients included. We studied 47 patients with an acute onset of transverse myelitis at younger than 18 years. Eighty-nine percent (42/47) of the patients had monophasic idiopathic transverse myelitis, two patients had recurrent TM, and three patients had TM that was later identified to be associated with another disease, specifically neuromyelitis optica, acute disseminated encephalomyelitis, and systemic lupus erythematosus. In one case MS was diagnosed at a later time. There were two deaths in this cohort during the interval of follow-up, both due to respiratory failure associated with a very high cervical cord lesion. Seven of the subjects were evaluated at the JHTMC as adults at an average of 35 years following their acute illness as children. The data from the acute phase on these seven cases are not complete.

Demographic features and risk factors. The distribution of age at time of onset is bimodal (figure 1). There appears to be at least two peaks of incidence. One is narrow involving toddlers under age 3 and a second is broader ranging between ages 5 and 17 with increasing frequency in older ages. Males and females are equally affected, with a ratio of 1.04.

An infectious disease, defined by two recorded oral temperatures above 101.5 °F, two recorded serum WBC elevations above 11,000 cells/mm³, or positive PCR or serologic studies preceding the onset of neurologic symptoms, was reported in 47% of cases (22/47). This occurred at an average of 11 ± 10 days (mean ± SD) prior to first neurologic symptom. Twenty-eight percent of cases (13/47) had a confirmed immunization or allergy shot within 30 days (mean 14 ± 7 days, mean ± SD) of the first symptom of ATM. Vaccines given were polio (three cases), measles–mumps–rubella,³ hepatitis B,² diphtheria–tetanus–pertussis,² influenzae,² varicella,¹ small pox,¹ Japanese B encephalitis,¹ *Haemophilus influenzae*,¹ and allergy shots.¹ Two patients received a combination of three vaccinations. In eight cases, both antecedent immunization and illness were reported. Antecedent trauma, usually a twist or fall, was described in 13% of cases (6/47) at an average of 8 days before the onset of acute neurologic symptoms.

Identified treatment modalities included IV steroids in 70% (32/46) cases, IV immunoglobulin in 33% (15/46), oral steroids in 28% (13/46), plasmapheresis in 15% (7/46), and acyclovir in 11% (5/46). Twelve patients reported none of the above treatments. Most of these patients had ATM in the more distant past before high-dose steroid treatment of acute CNS inflammatory disorders became common.

Acute clinical characteristics. The mean time from the onset of acute symptoms to functional nadir was about 2 days in these children; 68.2% of cases were assigned a diagnosis of TM within 7 days of the onset of symptoms. Ninety-one percent of subjects (40/44) described sensory loss or numbness in the initial phase of ATM. Eighty-nine percent (42/47) reported weakness, 85% (40/47) urinary dysfunction, and 75% (30/40) reported pain. Eighty-nine percent (42/47) were bed bound/wheel chair bound or required assisted ventilation during the initial phase of ATM.

The rostral border of clinical sensory loss was cervical in 25% (9/36), thoracic in 53% (19/36), lumbar in 5% (2/36), sacral in 3% (1/36), and unclear in 14% (5/36) of the investigated cohort.

Acute MRI and CSF characteristics. MRI of the spinal cord was obtained in 38 cases. T2 signal abnormalities were identified at cervical levels in 50% of these cases (19/38) and at thoracic levels in 40% (15/38). One patient had multifocal lesions, one had a single sacral level lesion, one had conus level lesion, and one had T2 abnormalities involving the entire spinal cord. Two patients had a normal spine MRI. The findings on T1 signal imaging were reported in 21 cases. A hypointense lesion was identified in 38%

(8/21). Gadolinium infusion demonstrated lesion enhancement on T1-weighted images in 74% (26/35) of cases. The rostral–caudal extent of the lesions measured on spine MRI ranged from one vertebral segment to the entire spinal cord in one patient. The average number of segments spanned was six segments.

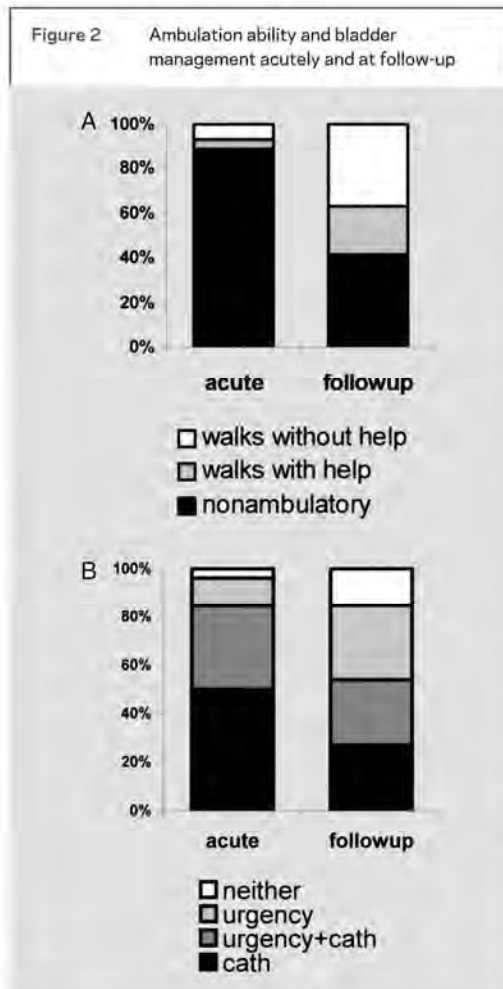
An elevated CSF WBC was apparent in 50% (17/34) of patients, with a mean WBC count of 136 ± 67 cells (range from 6 to 950 cells). An elevated CSF protein level was found in 48% (14/29) of the patients with a mean value of 173 ± 75 g/dL (range 45 to 1,120 g/dL). CSF WBC count and protein were normal in 31% (9/29) patients. Oligoclonal bands and elevated IgG index were reported in less than 5% of the cohort.

Sensory and motor characteristics. Information about sensory symptoms was collected in 38 patients. During the acute phase of illness, positive sensory complaints (burning, tingling, or electric shock sensations) were present in 23, disquieting numbness was apparent in 27, and a combination of the two was reported in 10. Positive sensory phenomenon resolved at follow-up in 52% (12/23), whereas numbness resolved in only 30% (8/27). At follow-up, new sensory complaints that were not part of the acute illness included positive phenomenon in 12 and numbness in 3. At follow-up, a total of 54% (15/28) of patients still experienced positive sensory dysesthesias, and 75% (21/28) reported numbness.

The need for bladder catheterization during the acute phase of illness was 82% (36/44) compared with 50% (22/44) at follow-up. Urinary urgency was reported in 46% (13/28) of patients during the acute phase of illness. This resolved in four of these patients. Seven patients acquired urgency as urinary function improved during the interval of follow-up. Overall, 68% (19/28) of patients experienced urinary urgency at follow-up (figure 2).

Of the 42 patients nonambulatory at the nadir of acute illness, 52% (22/42) were able to walk at least 30 ft with or without the help of a walker or some form of support at the time of follow-up. Acute-illness requirement for ventilator assistance was related to later impairment in ambulation. Only 39% (5/13) of these patients were later able to walk, whereas 59% (17/29) of those patients who were confined to bed during the acute period of illness without ventilator assistance were able to walk. A higher level of sensory impairment or MRI-identified lesion was not related to later walking with or without mechanical aids. Ambulation of 30 ft or more was reported in 66% (6/9) of patients with a cervical sensory level and 42% (8/19) with a thoracic sensory level. This level of ambulation was

(A) Ambulation ability (Hughes Functional Disability Scale) acutely and at follow-up. (B) Bladder management acutely and at follow-up



achieved by 44% (4/9) of patients with a cervical lesion identified on MRI and 58% (7/12) with a lesion on MRI rostrally extending to the thoracic spinal cord. Overall, 36% (17/47) of the patients were able to walk 30 ft independently, and an additional 21% (10/47) required a walker or other form of support to walk more than 30 ft (figure 2).

Functional outcomes. The WeeFIM was used for patients under age 18 and the FIM for those older than 18 at follow-up. The distribution of patients in the

categories of independence, modified dependence, and complete dependence according to their performance in the skill areas of self-care, sphincter control, transfer ability, locomotion, communication, and social cognition is reported in table 1.

At follow-up, the majority of patients had independence in all skill areas with the exception of sphincter control. Locomotion, defined as the ability to walk or use a manual wheelchair for at least 150 ft, was eventually achieved by 67% (22/33). Modified dependence was reported in 30% (10/33) for sphincter control and locomotion, 18% (6/33) for transfers, and 12% (4/33) for self-care. Twenty-four percent (8/33) of patients reported that they were completely dependent for sphincter control. This degree of dependence was reported by 18% (6/33) of patients for performing transfers, 15% (5/33) for self-care activities, and 3% (1/33) for locomotion.

There was no significant relationship between season of the year, preceding trauma, preceding immunization, time to nadir, or protein in lumbar puncture to any measure of functional outcome at follow-up.

Normal WBC count in the CSF was associated with a trend for better outcome on the mobility domain in the combined WeeFIM/FIM analysis (mobility FQ 84 vs 64, $p = 0.069$). A greater number of WBC in CSF predicted worse functional mobility outcome ($R^2 = 0.18, p < 0.05$).

Age at onset under age 3 was associated with worse outcome at follow-up in the ADL domain (FQ older age = 91, FQ younger age = 74; $p < 0.05$) and the bowel/bladder control domain (FQ older age = 75, FQ younger age = 50; $p < 0.01$) in the WeeFIM/FIM analysis. Across all ages, younger age at onset was associated with worse bowel/bladder control at follow-up ($R^2 = 0.165, p < 0.019$).

Diagnosis within 7 days of the onset of symptoms was associated with better functional outcome in ADL ($R^2 = 0.165, p < 0.05$) and continence ($R^2 = 0.134, p < 0.05$). Those patients diagnosed within 7 days had an average ADL FQ of 95 (i.e., 95% of typical for age) and an average continence FQ of 77, as opposed to children diagnosed more

than 7 days after the onset of symptoms, who had an average ADL FQ of 76 and continence FQ of 57. Not surprisingly, a higher rostral border of the sensory level of spinal cord injury at the time of diagnosis was predictive of worse ADL outcome (FQ 93 vs 66; $R^2 = 0.225, p < 0.05$).

| Skill Area | Independence, % (n) | Modified dependence, % (n) | Complete dependence, % (n) |
|---------------------|---------------------|----------------------------|----------------------------|
| Self-care | 73 (24/33) | 12 (4/33) | 15 (5/33) |
| Sphincter control | 46 (15/33) | 30 (10/33) | 24 (8/33) |
| Mobility (transfer) | 64 (21/33) | 18 (6/33) | 18 (6/33) |
| Locomotion | 67 (22/33) | 30 (10/33) | 3 (1/33) |
| Communication | 93 (26/28) | 7 (2/28) | — |
| Social cognition | 93 (26/28) | 7 (2/28) | — |

| Ref. no. | JHTMC | 16 | 15 | 14 | 9 |
|--------------------------------|------------|------------|------------|-------------|------------|
| Year of publication | 2007 | 2003 | 1998 | 1986 | 1953 |
| No. | 17 | 24 | 8 | 21 | 25 |
| Collection period, y | 2000-2004 | 1965-1995 | 1993-1996 | 1966-1983 | 1929-1952 |
| Sex, M:F | 1.04 | 0.85 | 1.66 | 0.9 | 0.5 |
| Mean age, y | 8.3 (0-17) | 7 (0-19) | 8.5 (2-15) | 10 (0.6-14) | 8 (0.5-15) |
| Age at onset <3 y, % | 38 | 13 | 12.5 | 10 | 8 |
| Acute phase cervical level, % | 25 | 12 | 0 | 20 | 11 |
| Acute phase thoracic level, % | 53 | 85 | 50 | 75 | 60 |
| Acute phase lumbar level, % | 5 | 0 | 0 | 5 | 26 |
| Acute phase sacral level, % | 3 | 0 | 12.5 | 0 | 0 |
| Acute phase level unclear, % | 14 | 0 | 37.5 | 0 | 0 |
| Acute sphincter dysfunction, % | 85 | 95 | 75 | 85 | 95 |
| Chronic bladder dysfunction, % | 50 | 33 | * | 29 | 38 |
| Deaths | 2 | 1 | 0 | 0 | 1 |
| Abnormal CSF findings, % (n) | 71 (24/34) | 62 (15/24) | 50 (4/8) | 91 (19/21) | 60 (12/20) |
| Abnormal MRI findings, % (n) | 94 (34/36) | 66 (4/6) | 50 (4/8) | ND | ND |

*Insufficient or unavailable information.

JHTMC = Johns Hopkins Transverse Myelitis Center; ND = not done.

Similarly, lower level of the rostral border of the lesion on MRI was also associated with better outcome for both ADL and mobility. Children with thoracic or lower level lesions had an average ADL FQ of 89 and an average mobility FQ of 81 compared with children with higher lesions, who had an average ADL FQ of 62 and an average mobility FQ of 51 ($R^2 = 0.25$, $p < 0.05$). The extent of the MRI lesion at diagnosis (number of segments involved) was also predictive of outcome, with fewer involved segments being associated with better outcome for ADL and mobility ($R^2 = 0.17$, $p < 0.05$ and $R^2 = 0.26$, $p < 0.05$). T1 hypointensity was associated with worse scores on the HFDS at follow-up (Mann-Whitney U $p < 0.05$) and a trend toward worse continence outcome (FQ 83 vs 54, $p = 0.057$).

Patient scores on the HFDS at nadir were correlated with functional outcome at follow-up across all three domains (ADL $\rho = 0.61$, $p < 0.001$; continence $\rho = 0.57$, $p < 0.01$; mobility $\rho = 0.72$, $p < 0.001$).

Although length of time to follow-up was not statistically related to better outcomes, there was a trend for improvement in WeeFIM/FIM scores for mobility ($p = 0.052$) and ADL skills ($p = 0.063$).

Evaluation of treatment modalities did not show an advantage of one treatment method over another. The patients who did not receive treatment tended to have better functional outcomes for ADL (FQ 99 vs 77, $p < 0.05$) and mobility (FQ 88 vs 66, $p < 0.05$). They were the patients who had consider-

ably longer follow-up times (277 vs 41 months, $p < 0.001$). Their average HFDS on presentation was 3.83 compared with 4.17 for the group that reported treatment, suggesting that this group was less severely impaired than the group that did receive therapy; however, this difference was not significant. One specific treatment, oral steroids, was associated with a better functional outcome in the area of mobility (FQ = 95 vs 55, $p < 0.001$).

DISCUSSION This largest reported single case series of patients with ATM concentrates upon individuals with diagnosis by newly established criteria, in a single academic referral center, over an interval of 4 years. Previous case series, including 8 to 25 cases each accrued at single centers over mostly longer intervals of 4 to 25 years (table 2),^{9,14-16} were similar to the current series in age at presentation, initial symptoms, and initial course. Other features of these case series are more difficult to compare, owing to the nonspecific and descriptive nature of previously reported outcomes, as, for example, regarding sensory findings, MRI features, continence, or the amount of assistance required for ambulation.¹³ This study is the first to use common validated measures of functional outcome.¹¹⁻¹³ Other factors limiting comparison include potential biases in ascertainment related to severity of presentation, length of time in which cases were collected, and the absence of modern diagnostic criteria requiring a surrogate marker of spinal inflammation.

An unexpected feature of this case series is an apparent bimodal age distribution at time of presentation. A substantial peak, comprising 38% of the total, was under age 3, in contrast to a combined 10% of those in all previous studies combined.^{9,14,16} Whether this group represents a different form of ATM or a developmentally regulated vulnerability to otherwise typical ATM cannot be discerned from these data. This group of children, however, clearly has greater long-term disability as a consequence of their illness and requires further investigation.

The report of an immunization being given within 30 days of onset of ATM in 28% of our cases was initially viewed as surprising. However, the large fraction of younger children affected, the current recommended vaccination schedule for children, and the lack of any single vaccine association within this group all undermine a potential causal link between vaccination and ATM. In addition, no significant relationship between a preceding illness, immunization, or trauma and worse outcome was noted.

The rapidity of progression of symptoms did not predict a worse outcome. This suggests that deterioration in clinical status during the first 24 hours after presentation should not be used by itself as a negative prognostic factor. This is in contrast to the findings reported by other authors.^{14,16}

We observed normal CSF WBC counts in 50% of cases. This is similar to findings reported in other case series of 38 and 52%.^{14,16} Normal CSF WBC count in our series was associated with better outcome in mobility. The predictive value of this finding was not reported in other studies.^{14,16}

Consistent with previous reports,^{14,16,17} impaired bladder control is the most common long-term neurologic deficit following ATM. Recovery of motor function within 20 days of presentation has been associated with a more favorable prognosis for less severe urinary sequelae.¹⁸ In our cohort, we found a strong correlation between Hughes scale at presentation and WeeFIM/FIM bowel and bladder control at follow-up.

The requirement for assistance with transfers (36%) or for self-care activities (27%) at follow-up is not reported in previous studies. Daily living skills remain compromised in many children, and rehabilitation needs are great. Long-term issues that may require attention include skin integrity, hygiene, nutrition, pain, arthritis, constipation, urinary incontinence, and spasticity.³

The persistence or occurrence of uncomfortable sensory phenomena suggests that management of ongoing pain is also an important part of the long-term management of children following ATM.

Chronic sensory findings have been reported in 46% of children with ATM, but whether these reflect disquieting sensations or numbness is not discussed.¹⁶ Early assessment and intervention of dysesthetic or painful symptoms may be necessary to prevent chronic pain in these children. Referral to a comprehensive pain management program would be appropriate depending on the severity of symptoms and the degree to which the child's life is interrupted.

Previously reported cases series in children have not characterized the MRI findings in pediatric ATM to the extent possible in this series. In another case series, MRI abnormalities in four and normal MRI findings in two of six cases are reported.¹⁶ In that series, one child had multifocal lesions in the cervical region and conus medullaris and three had isolated thoracic level lesions. T1 signal abnormality was identified in two of these cases. Our data suggest that MRI lesions often extend over many segments in children rather than the more typical one to three segments in adults. Current MRI techniques appear to be quite sensitive in diagnosing ATM: Thirty-six of 38 cases meeting diagnostic criteria for ATM had abnormal MRI findings.

Features of the initial diagnostic MRI may be of assistance in predicting outcome in children. Our analysis suggested that the location and extent of T2 lesions on MRI were associated with functional skills at follow-up. Not surprisingly, lower thoracic level of involvement results in better performance on tasks that assess function of the upper extremities. MRI confirmed involvement of fewer segments was associated with better outcome in the areas of ADL and mobility. Why the effect of lesion size was not also apparent in the recovery of continence is unclear.

MRI features of T1 hypointensity at the time of diagnosis independently correlated with worse ambulation outcome. In MS, this finding in the brain is thought to indicate more serious axonal loss.¹⁹ The importance of its presence in the spinal cord has not been defined. Although edema of the spinal cord is a potential alternative cause of T1 hypointensity, the observation that T1 hypointensity correlates with poorer prognosis suggests a more ominous pathology such as severe axonal loss and a poorer prognosis.

The effect of specific treatment modality on functional outcome is not clear. Our finding that treatment with IV steroids did not improve outcome contrasts with that of a previous study that reports an association between high-dose IV methylprednisolone treatment and an increased proportion of patients walking independently or achieving full recovery.¹⁶ We found that treatment with oral steroids

was associated with a better outcome in the area of mobility, which contrasts with another previous study that found no improvement in outcome in their steroid-treated group.¹⁴ Despite these conflicting findings regarding outcomes, steroids given either IV or orally remain the standard first-line intervention for treatment of acute inflammatory conditions including ATM. Better outcomes in the group that received no treatment are likely a reflection of the milder course of disease in these individuals and the decision to forego the use of steroids.

Shorter time to diagnosis was associated with better outcomes. This finding requires cautious interpretation because we do not know the relationship between early treatment and subsequent skills. Additional studies should be undertaken to address this issue.

The finding that longer time to follow-up was associated with better outcome for mobility and ADL skills suggests that some functional recovery occurs. This may be related to primary neurologic recovery or may be the result of rehabilitation. Additional longitudinal studies are needed to determine the trajectory of recovery in these patients and to delineate the factors accounting for the improvements.

This is a large cohort of children with ATM in which associations between preceding factors, diagnostic tests, clinical findings at follow-up, and functional skills at follow-up are reported. Limitations include the referral nature of the sample and the wide range of time to follow-up. These observations should be expanded through collaborative programs that involve multiple clinical centers using the recent strict diagnostic criteria. The effects of initial intervention on outcome and the effects of rehabilitation interventions on outcome are two important issues that require further study.

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