Do Not Forget the Spine MRI in Children With Arthrogryposis Multiplex Congenita: High Prevalence of Tethered Spinal Cord and Preliminary Clinical Findings Following Detethering

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Background: Arthrogryposis multiplex congenita (AMC) encompasses congenital conditions with joint contractures in 2 or more joints. Patients with AMC may have scoliosis and neural axis malformations. The study aimed to determine the prevalence of tethered spinal cord (TSC), characterized by a low-lying conus medullaris, and secondarily, present preliminary findings following surgical untethering in children with AMC.

Methods: Patients 18 years of age and younger with a diagnosis of AMC and a spine MRI were identified. The presence of a TSC was defined as a low-lying conus with termination at or below the lower third of the L2 vertebral body. A pediatric neurosurgeon and a pediatric orthopaedic surgeon independently reviewed MRIs. The medical records of patients with AMC who underwent untethering were examined to evaluate preoperative and postoperative clinical findings. The prevalence of TSC in our AMC patients was compared with published normative data using χ^2 analysis.

Results: Forty-two of 105 AMC patients (40%) had TSCs. There was a greater percentage of patients with AMC and a TSC compared with the unaffected population ($P < 0.0001$). Sixteen patients underwent detethering through filum terminale sectioning. Nine patients had preoperative neurological deficits in addition to their AMC. There were no postoperative complications. All patients had improvement in their bowel and bladder symptoms within 3 months after their detethering procedure.

Conclusions: TSC is more prevalent in the pediatric population with AMC compared with those without AMC. MRI is recommended for all patients with AMC due to its high prevalence. Although not a benign procedure, surgical detethering may have potential benefits for children with AMC.

Level of Evidence: Level IV—therapeutic study.

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Arthrogryposis multiplex congenita (AMC) is a clinical finding defined as joint contractures in 2 or more areas of a patient's body and can be associated with various syndromes, either in a myopathic or neuropathic form. Multiple factors, including genetics and environment, play a role in the development of these contractures.[1] AMC is known to occur in up to 1 of every 3300 live births.[2] Spinal deformity affects ~23% of individuals with AMC and is 10 times higher than the unaffected population.[3,4] Nevertheless, there is a lack of data regarding the spinal neural elements in this population.

A tethered spinal cord (TSC) is a condition characterized by an abnormal attachment of the spinal cord within the vertebral column. Clinically, a TSC may cause gradual neurological issues due to mechanical torsion and ischemia in the distal spinal cord.[5] This may present as motor-sensory deficits, contractures, and bladder and bowel complications. Patients with AMC have contractures of the extremities, delays in development, and difficulty with bowel/bladder training; this warrants consideration of additional etiologies of these clinical findings, namely a TSC. If a low-lying conus medullaris is found on advanced imaging [eg, magnetic resonance imaging (MRI)] (Fig. 1), the diagnosis of TSC is confirmed and surgical detethering, through sectioning of the filum terminale, is recommended to the family.[6,7]

The primary purpose of this paper is to describe the prevalence of TSC in the pediatric population with AMC and compare it to the unaffected pediatric population. The secondary purpose is to review the preoperative and postoperative clinical findings of children with AMC following detethering. We hypothesize that children with AMC have a higher prevalence of TSC compared with those without AMC and that patients who underwent detethering have improvements in their clinical findings.

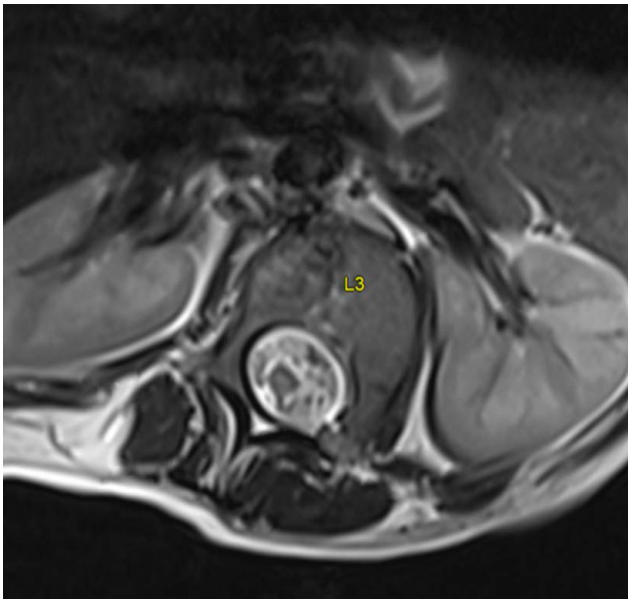

FIGURE 1. Axial T2 MRI showing a low-lying conus medullaris at the L3 vertebral body, signifying a TSC. full color online

METHODS

A retrospective, IRB-approved chart review was performed on all patients seen at the authors' institution from June 2015 to July 2023 with a diagnosis of AMC.[1] Patients were included if they had an MRI at the age of 18 years or before, either from an outside institution or the authors' institution. Patients were also excluded if they had a poor-quality MRI, incomplete MRI (did not have full cervical, thoracic, and lumbar images), or if a myelomeningocele or tumor was found. A subanalysis was performed on patients with AMC who underwent surgical detethering through filum terminale sectioning at the age of 18 years or before. Follow-up for the subanalysis was defined as the date of surgical detethering to the date of the last follow-up before orthopaedic intervention on the lower extremities.

A pediatric neurosurgeon and pediatric orthopaedic surgeon reviewed all MRI studies. The images were acquired with the patient's supine. Axial and sagittal T1, T2, and short tau inversion recovery (STIR) sequences were reviewed as described by Blaaza et al.[8] The vertebral level was determined by counting from C1 down and confirmed by counting up the last lumbar vertebra (identified as the last well-formed vertebral body above the sacrum). The termination level was determined by the point where the conus tapered and demonstrated optimal clarity. The termination level vertebra was subdivided into upper, middle, and lower thirds to accurately describe the level. In instances where termination occurred at an intervertebral disc, the level was identified as that of the corresponding disc. In cases where the surgeons did not initially agree, a consensus was reached through collaboration. A TSC was defined as a conus that terminated at or below the lower third of the L2 vertebral body.[9] Occasional dorsal adherence of the cord, thickened filum, or fatty infiltration was only observed in those cases with a low-lying conus medullaris (Fig. 2).

Descriptive statistics were calculated. A χ^2 test for homogeneity was performed by comparing study data to data published by Blaaza et al[8] with Yates correction. All statistical analysis was performed using GraphPad Prism 10.2.0 (GraphPad Software Inc., San Diego, CA).

RESULTS

In total, 105 patients (52 females and 53 males) were included in the study. The mean age at MRI was 6 years (0 to 17 y). Forty-two patients (40%) had MRI findings of a low-lying conus. Of those with a low-lying conus: 11 (11%) ended at the lower third of L2, 11 (11%) ended at the L2-L3 disc space, 3 (3%) ended at the upper third of L3, 7 (7%) ended at the middle third of L3, 6 (6%) ended at the lower third of L3, 3 (3%) ended at the L3-L4 disc space, and 1

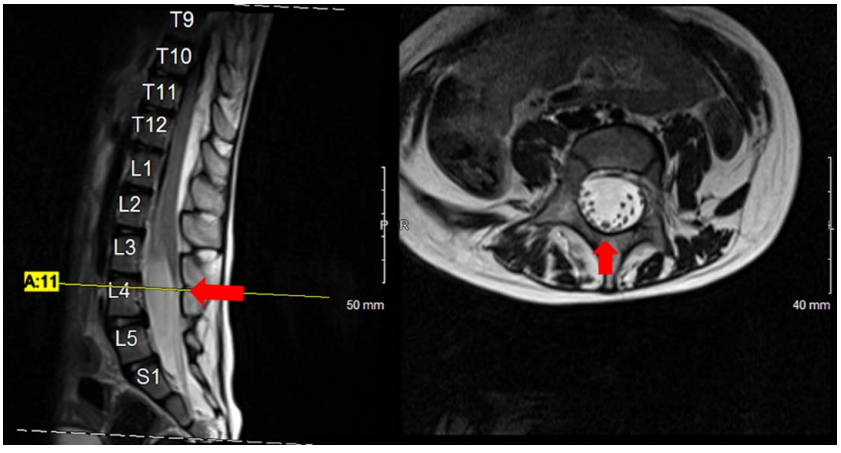

FIGURE 2. Low-lying conus in a 4-year-old patient with knee flexion contractures, urinary incontinence, and constipation. The patient was described as no. 16 in Table 2. Note the dorsal adherence of the spinal cord. The arrows point to the termination of the conus medullaris. full color online

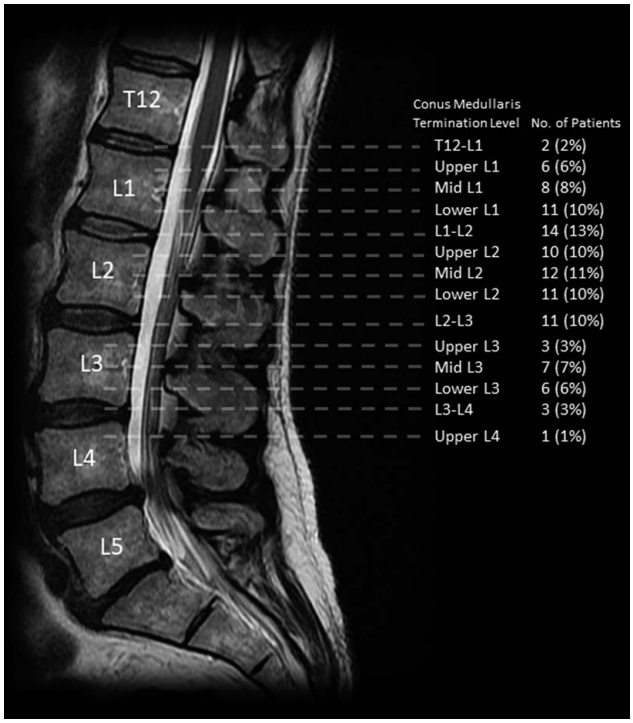

FIGURE 3. Sagittal T2 MRI of a normal spine showing typical conus medullaris termination at L1-L2, alongside the distribution of conus medullaris termination level found in the AMC population from this study.

(1%) ended at the upper third of L4. The distribution of conus medullaris termination levels for all patients in the study is found in Figure 3. Table 1 is the contingency table comparing the level of conus medullaris termination between patients with AMC and normal pediatric population from a previous study by Blaaza et al;[8] the χ^2 statistic with Yates correction was 123.8 ($P < 0.0001$). The prevalence of low-lying conus medullaris in patients with AMC was significantly higher than in patients without AMC.

Sixteen patients (38%) at a mean of 7 years (1 to 17 y) were surgically detethered. The mean follow-up was 6 ± 4.8 months. Preoperatively, 5 patients had bowel issues and 7 patients had bladder issues; all improved after detethering. One patient with scoliosis had improvement of their curve following detethering. Six patients had improved motion or strength in the lower extremities and 8 patients had increased sensation in the lower extremities. Table 2 outlines the preoperative and postoperative clinical conditions for all patients who underwent detethering; the postoperative comments are those provided by family and as documented in the office notes. Despite the low numbers, this study found that patients with Escobar syndrome and ZARD are more frequently found in a TSC condition compared with those without. No postoperative complications were found in this series.

TABLE 1. Contingency Table of Low-lying Conus Medullaris in Normal and AMC Children

	Low-Lying	Normal	Total
AMC	39	66	105
Normal (Blaaza et al)[8]	20	500	520
Total	59	566	625

DISCUSSION

There are over 400 known conditions that have been associated with AMC.[10] Depending on the diagnosis, various body systems can be affected, including the respiratory, gastrointestinal, genitourinary, and central nervous system (CNS). In cases where the CNS is involved, cognitive functions may also be impacted. Mobility, daily activities, and participation levels can vary significantly among individuals.[11] Spinal deformities frequently occur in this population as well.[3] Presumably caused or associated by anterior horn cell defect,[12] the presence of a TSC in pediatric patients with AMC may also contribute to decreased mobility, development of worsening contractures, and issues with the gastrointestinal and genitourinary systems.[1] Ruling out a TSC in the pediatric population with AMC is paramount.

This is the first study to evaluate the presence of TSC in patients with AMC. Since not all outside MRIs had radiologist readings available in the system, agreement of the readings in this study was done between the pediatric neurosurgeon and pediatric orthopaedic surgeon. This study found that 40% of pediatric patients diagnosed with AMC affecting the lower extremities have a TSC. As part of the care of patients in this population, we recommend an MRI of the entire neural axis in childhood to rule out a TSC. While there are some risks to consider when sedating young patients for an MRI,[13] the high prevalence and potential morbidity of delayed appropriate care for TSC have led to routine MRI becoming a standard practice at our center for children with AMC.

Despite being mentioned in various reports,[14–16] there is a lack of data in the literature concerning the prevalence of TSC in the pediatric population with AMC. Typically, the conus medullaris terminates at the L1-L2 disc space.[7] The definition of a low-lying conus medullaris in this study was at or below the lower third of the L2 vertebral and based on previously published data.[8,9] This study found a significantly higher proportion of patients with a low-lying conus medullaris compared with the unaffected population,[8] with 40% exhibiting a low-lying conus (Fig. 4).

In addition to determining the prevalence of TSC in pediatric patients with AMCs, a subanalysis reviewed preliminary results of detethering in this population. In this study, 5 patients had constipation as a complaint before the detethering procedure. Within 3 months of detethering, all had qualitatively improved. Constipation coexists with urinary incontinence, and the treatment of underlying constipation usually also results in the improvement of incontinence.[17,18] Rosen et al[19] found that only 9% of children with spinal cord abnormalities experienced intractable constipation, with TSC being the most prevalent association. This study had 7 patients with urinary complaints and all 7 also qualitatively improved

TABLE 2. Preoperative and Postoperative Conditions of Arthrogryposis Patients Who Underwent Spinal Cord Detethering

No.	Sex	Age at surgery	CM level	Preoperative	Postoperative	Notes
1	M	2	Lower L2	Scoliosis, bilateral hip, and knee flexion deformities, bilateral cavovarus foot deformities	Improved scoliosis (without orthopaedic intervention)	
2	F	2	Lower L2	Decreased sensation to bowel/bladder, constipation	Increased sensation to bowel/bladder, less constipation	
3	M	1	Lower L2	Constipation, core muscle imbalance	Resolved constipation, improved strength in his lower extremities, sitting more upright	
4	M	1	Lower L2	Congenitally dislocated knees , bilateral clubfeet, lower extremity weakness	Improved leg movement, reacts more when parents tickle his feet	
5	F	7	L2-L3	Bilateral knee flexion contracture, clubfeet, decreased sensation in the toes and feet	Improved sensation in the toes and feet	
6	F	15	L2-L3	Restrictive lung disease, kyphoscoliosis	Stable condition	ZARD (ZC4H2 mutation)
7	M	14	L2-L3	Bilateral equinovarus, hip dislocations	Increased lower extremity strength, more ticklish	Larsen's
8	M	17	L2-L3	Has sensation and is not incontinent but getting more difficult to urinate	Return of bowel/bladder function, increased sensation and movement in both legs	
9	F	12	L2-L3	Multiple contracture	Loosened contracture	
10	F	4	L2-L3	Neurogenic bladder	Neurogenic bladder resolved, improved gait, improved sensation to feet	Escobar
11	F	5	Upper L3	Urinary dribbling	Dribbling has almost completely resolved	Escobar
12	M	7	Mid L3	Occasional bowel accidents, urinary accidents at night, numbness, tingling	Less frequent bowel incontinent episodes, no urinary accidents, less numbness and tingling in lower extremities	
13	F	4	Lower L3	Constipation, urinary accidents	Bowel/bladder sensation	
14	F	10	Lower L3	Bilateral hip flexion contractures, knee contractures, vertical talus	Improved lower extremity movement and sensation	Escobar
15	F	2	L3-4	Constipation, decreased sensation	Decreased constipation, increased sensation	
16	F	4	Upper L4	Knee flexion contractures, urinary incontinence, constipation	Decreased incontinence, decreased constipation	Escobar

The postoperative column is obtained from subjective reports from patients and families.

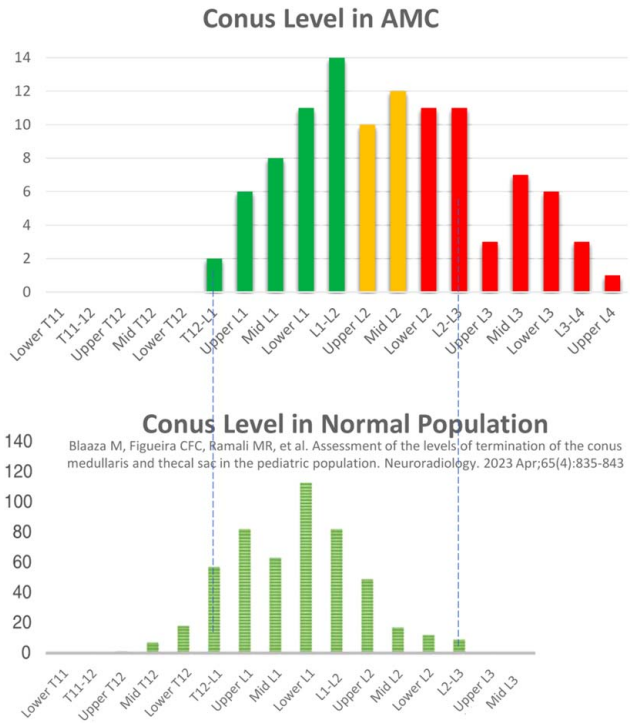

FIGURE 4. Conus level in pediatric population with AMC compared with the normal pediatric population. full color online

following filum terminale sectioning. We did not distinguish between treatments for myogenic and neurogenic AMC, as our preliminary findings suggest that even myogenic conditions, such as Larsen syndrome and Escobar syndrome, also show positive outcomes following detethering. In addition, not all patients with evidence of TSC underwent detethering. This was due to: (1) family preference as detethering is not a benign procedure and (2) the pediatric neurosurgeon did not join our practice until recently so they were previously referred to outside surgeons and follow-up on those patients is limited.

About spinal deformities, surgical detethering has been shown to spontaneously improve scoliosis or at least halt its progression. In a study involving 27 pediatric patients presenting with symptomatic TSC-associated scoliosis, McGirt et al[20] demonstrated that patients with Risser Grades 3 to 5 and Cobb angles <40 degrees did not experience curve progression after undergoing TSC release. Furthermore, Yamada et al[21] observed that all TSC patients with some (mild to severe) degree of scoliosis experienced subsidence to various extents after detethering procedures. Similar phenomenon was observed by Chern et al[22] in which among 14 patients with scoliosis and TSC, 5 patients' curves stabilized and 2 patients had their spinal alignment improved after detethering. Interestingly, a small multicenter study showed that younger age at detethering, not curve size, was linked to lower scoliosis progression.[23] In the present study, we observed 1 patient who had improvement of his curve and pelvic obliquity without any bracing or orthopaedic intervention after the detethering procedure (Fig. 5).

Similarly, in the limbs, the incidence of clubfoot deformity recurrence was found to be higher among subjects who had a TSC release post-tenotomy (56%) as compared with pretenotomy (0%).[24] One long-term study in 114 patients with myelomeningocele found that within 3 months after TSC release, their spasticity improved by 63%, motor function improved in 70%, and gait improved in 79% of patients who underwent detethering procedures.[25] In this series, 5 patients had improved strength/motion of their

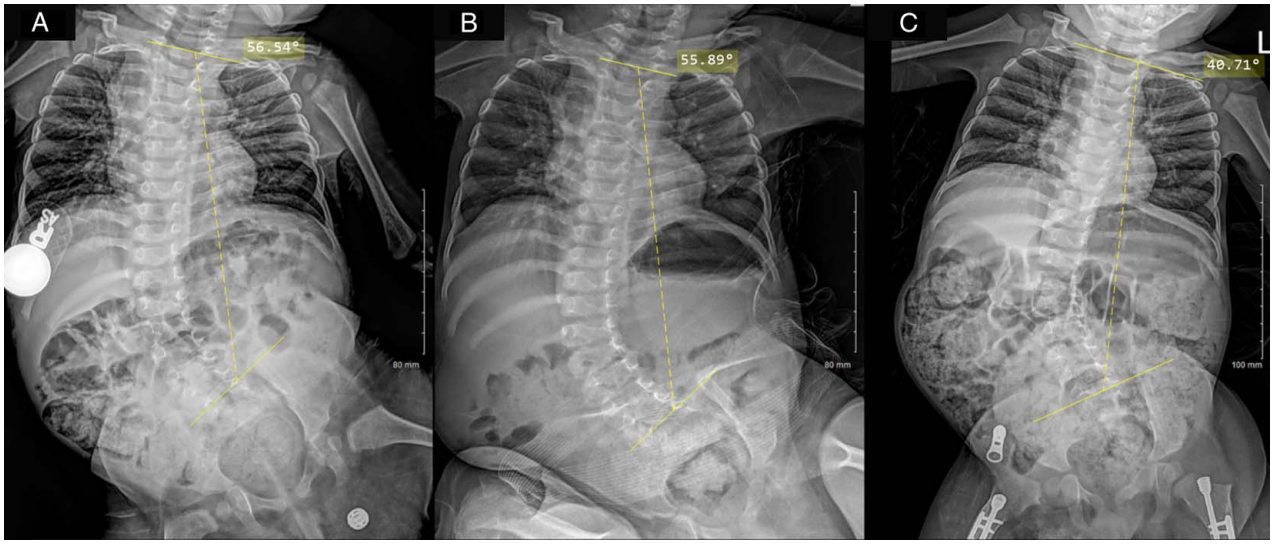

FIGURE 5. A 2-year-old boy had improvement of his scoliosis and pelvic obliquity after detethering 6 months prior, without bracing or any other orthopaedic intervention for his spine. His conus medullaris terminated at the inferior margin of the L2 vertebral body. A, On the first visit. B, Four months before detethering C, On the latest visit, 6 months postdetethering. The patient was described as no. 1 in Table 2. full color online

lower extremities following surgery. In addition, 1 patient had preoperative truncal muscle weakness and was able to sit more upright following detethering.

The subanalysis of patients undergoing detethering found no associated complications; however, detethering is not a completely benign procedure. This study is in concordance with recent studies concerning the safety of the procedure, even for TSC patients exhibiting minimal symptoms.[6] A recent study by Pan et al[26] involving 340 patients has also shown that detethering is safe and has a low secondary retethering rate of 1% compared with 12% in detethering done for spinal dysraphism.

This study has limitations. Many patients in the study were referred to our institution for operative procedures on their upper and lower limbs. This suggests a bias of more severely affected patients with AMC, and the prevalence in the population with AMC at large may be less than what is reported. The findings presented in the subanalysis for detethering are preliminary. All data was found retrospectively in the medical record, and no standardized functional outcome data was available.[27] As aforementioned, many of the findings are qualitative and may be affected by recall bias from the family or patient. Furthermore, the follow-up time is relatively short. To mitigate the confounding effect of subsequent orthopaedic intervention for contractures, the duration of follow-up extended only until the limbs underwent reconstruction. This study also lacks a control group; however, in the authors' experience, TSC release is beneficial in improving, or at least halting the progression of neurological, urological, and orthopaedic functioning in children born with AMC. Future studies would be improved with standardized functional and clinical outcomes and a comparative cohort.

CONCLUSION

There is a higher prevalence of TSC in children with AMC as illustrated by a low-lying conus medullaris, highlighting the importance of obtaining an MRI of the spine in children with AMC. Detethering can improve bowel and bladder symptoms as well as associated orthopaedic conditions in these patients. Further study is needed to deepen understanding of this condition and its treatment in patients with AMC.

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