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Spinal cord anomalies in children with anorectal malformations: Ultrasound is a good screening test

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ABSTRACT

Purpose: The purpose of this study is to correlate spinal ultrasound (US) and magnetic resonance imaging (MRI) findings in patients with anorectal malformations (ARMs).
Methods: A retrospective analysis of records was performed for children with ARM presenting to two major pediatric hospitals between 2009 and 2017. The primary outcome analyzed was detection of spinal cord anomalies. Spinal US was performed up to 4 months and MRI within the first year of life. The conus medullaris was considered normal if it had a tapering contour and terminated at or above the Lumbar 2-3 disk space.
Results: One hundred ninety-three patients with ARM presented during the study period with a slight male preponderance (108, 56%). Spinal imaging was performed in 157(82%) - 137(87%) had US, 64(41%) had MRI and 44 (28%) had both. Of the 44 who had both; US was abnormal in 25 children-confirmed by MRI in 20 (80%). US was normal in 17 children- MRI showed a filum cyst in 1 and a lipoma in 2 children and was inconclusive in 2 children ($p<0.001$). All who required surgery except one child, were reported on spinal US to have a low lying cord, borderline low cord or tethered cord ($p<.05$). No child who was reported to have a normal spinal US required de-tethering at a later stage. Spinal US had an overall sensitivity of 91% and specificity of 75% compared to MRI for detecting spinal cord anomalies in children with ARM
Conclusions: Spinal US performed in a tertiary pediatric imaging department was a good screening test for spinal cord anomalies in children with ARM. The finding of a low, borderline low or tethered cord on US mandates an MRI to confirm the findings and correlates with the need for operative correction of spinal cord tethering.
Study type: Clinical research paper.
Level of evidence: 2.

1. Introduction

Anorectal malformations (ARMs) are rare congenital anomalies with an incidence of 1 in 3000 live births [1]. Approximately 60% of ARMs are associated with congenital anomalies involving other systems or with chromosomal aberrations [2]. The presence of spinal cord anomalies is reported in 26 to 60 % children with ARM [2,3]. These can range from clinically insignificant variations such as filum cysts and ventriculus terminalis to clinically significant tethered cord and also rarer associations such as lipomeningocele, spinal lipoma, meningo(myelo)cele, diastematomyelia. Consequently, most centers recommend screening all children born with ARM with a spinal ultrasound (US) soon after birth - followed by magnetic resonance imaging (MRI) within the first year in the select few with abnormal findings on US [4]. Recently there is an increase in use of MRI as first line imaging to screen for spinal cord anomalies, with increased incidence of anomalies reported [3]. MRI has been reported to have higher detection rate of spinal anomalies [3,4] but this has not translated into increased rates of surgical intervention [4–6]. The significance of those anomalies missed by US is therefore uncertain.

The definition of tethered cord syndrome (TCS) has evolved from an anatomical description of the position of the cord to a physiological increased tension on the spinal cord leading to symptoms and signs of sensory and motor neuron dysfunction manifest as bladder and bowel symptoms [7]. In a child with ARM, the clinical picture is further complicated by the disturbed pelvic neurology and anatomy associated with the ARM and sequelae of its surgical correction. The potential overlap of symptomatology has led to a lack of consensus among pediatric

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surgeons and neurosurgeons regarding the need for and timing of operative intervention in asymptomatic children with radiological evidence of cord tethering. Despite the rising trend in detection rates of spinal cord anomalies generally, the incidence of TCS requiring operation has remained constant at 9–10% [3,6,8]. The challenge lies in determining the most appropriate screening of children with ARM to identify the select few who are at risk of future neurological deterioration and would therefore benefit from detethering.

In this multicenter study we aim to evaluate the association of spinal anomalies with ARM, the effectiveness of spinal US and MRI in detecting spinal cord anomalies and spectrum of findings on US which may be of significance in the development of TCS.

2. Methods

2.1. Patients

This retrospective analysis includes all children with ARM operated at the Children's Hospital at Westmead and Sydney Children's hospital at Randwick in New South Wales, Australia over the nine year period 2009 to 2017. Patients were identified by an electronic search of the prospective hospital data base. The primary outcome analyzed was spinal cord anomaly. Explanatory variables included the type of ARM, associated anomalies and findings from imaging of the spine. The ARMs were classified according to the Krickenbeck International classification [9]. Associated anomalies included chromosomal, inherited and those in the VACTERL association – vertebral, cardiac, trachea-esophageal, renal and limb. Vertebral anomalies refer to bony abnormalities visible on plain x-ray. A separate analysis correlating spinal US and MRI findings was performed

2.2. Screening for associated anomalies and spinal cord anomalies

The practice at both institutions is to screen all neonates with ARM for associated anomalies and TCS. Babies undergo clinical examination as well plain x-ray of the spine, renal ultrasound and cardiac echo. Spinal cord anomalies was screened for using spinal US. This is possible up to 4 months of age [7]. All ultrasound images were evaluated and reported by a pediatric radiologist. MRI was performed in those with abnormal findings or those in whom the opportunity for early US screening was missed at around 1 year of age. All MRI images were evaluated and reported by a pediatric neuroradiologist, who was not blinded to the spinal US findings. All patients with abnormal US were seen by a pediatric neurosurgeon and followed up in a multispecialty clinic.

The conus medullaris was considered normal if it had a tapering contour and terminated at or above the Lumbar 2–3 disk space [10,11]. A cut off of <2 mm was considered normal thickness of the filum terminale. Evidence of decreased movement of the nerve roots with low lying conus was considered as a tethered cord. Other evidence of spinal dysraphism such as lipomeningocele, spinal lipoma, meningo (myelo)cele, diastematomyelia, vertebral anomalies were noted. Filum cysts and ventriculus terminalis were also noted but considered variations of normal [10].

2.3. Statistical analysis

Descriptive statistics for all variables were calculated, with results expressed as percentage (%) or as median with Interquartile range (IQR). A two-tailed *P* value was performed using the Student's *t* test for continuous variables and Chi-square test with or without Yates correction for categorical variables. A $p<0.05$ was considered as statistically significant. Sensitivity, specificity, along with positive and negative predictive values of spinal US were calculated using MRI as the gold standard. The data was analyzed using GraphPad Quickcalcs (CA, USA http://www.graphpad.com/quickcalcs/)

2.4. Ethics and funding

This study was approved by the Sydney Children's Hospital Network Human Ethics Research Committee (LNR/18/SCHN/210). No funding was required for this study.

3. Results

3.1. Population characteristics and associated anomalies

Population characteristics are summarized in Table 1. A total of 193 children were treated for ARM in the study period. There was a slight male preponderance (n = 108, 56%). Perineal fistula was the commonest type of ARM, accounting for approximately one third of cases. It was also the commonest in boys (40%) while vestibular fistula was the commonest type in girls, accounting for over half of cases ($p<.05$). Associated anomalies were seen in 73% children, most of which were in the VACTERL association. Four children (2%) had associated Currarino syndrome and 12 (6%) had chromosomal anomalies including Trisomy 21, 47XX, Kabuki syndrome, Turner's syndrome, Cats eye syndrome and Jacobson's syndrome. Vertebral anomalies visible on plain x-ray were present in 31% children and were significantly more common in common in girls (40% vs 25%, $p<.05$). In girls, vertebral anomalies were most commonly associated with vestibular anus (36%) and in boys with ureteral fistula (24%).

Spinal anomalies detected by US/MRI were seen in both high and low anomalies and were commonest with Cloaca in girls(50%) and urethral fistulae in boys(35%). A statistically significant difference was however only found in children with perineal fistulae.

3.2. Spinal imaging

Fig. 1 represents the diagnostic flow chart and management of the 193 children. Thirty-five (18%) did not have any form of spinal screening and one child did not have reports and images available for review. Of the remaining 157 (82%), 137 (87%) had spinal US, 64 (41%) had MRI, and 44 (28%) had both.

One hundred of 137 (73%) spinal ultrasounds were normal. 17 of these went on to MRI, 14 (82%) of which were normal. The remaining three had minor abnormalities - one showed a filum cyst and two had lipoma of the cord. None of the three underwent operation and none demonstrated any neurological deterioration at a median follow up of 5 years (10, 5 and 4 years respectively).

Two children went on to MRI because the spinal US was not interpretable. Results showed a normal cord in one child and a prominent central canal in the other – the latter has had no neurological symptoms develop at five years follow-up.

Thirty-five (26%) had abnormal ultrasound (Fig. 2a), 25 of whom

Table 1
Population characteristics.

	Total N = 193 (100%)	Male N = 108 (52%)	Female N = 85 (48%)	Spinal anomalies on US/MRI	p Value
Krickenbeck classification					
Perineal fistula	62 (31)	42(38)	20(24)	9(15)	<.05
Rectourethral fistula	37 (19)	37(34)	0	13(35)	NS
Rectovesical fistula	5 (3)	5(4)	0	1(20)	NS
Vestibular fistula	46 (24)	0	46(54)	14(30)	NS
Cloaca	4 (2)	0	4(5)	2(50)	NS
No fistula	23 (12)	15(13)	8(9)	2(1)	NS
Anal stenosis	4 (2)	3(3)	1(1)	0	NS
Perineal fistula with anal stenosis	8 (4)	4(3)	4(5)	2(25)	NS
Rare regional variants	4 (2)	2(2)	2(2)	4(100)	<0.005

*A child may have more than one associated anomaly; NA – not applicable; NS – not significant.

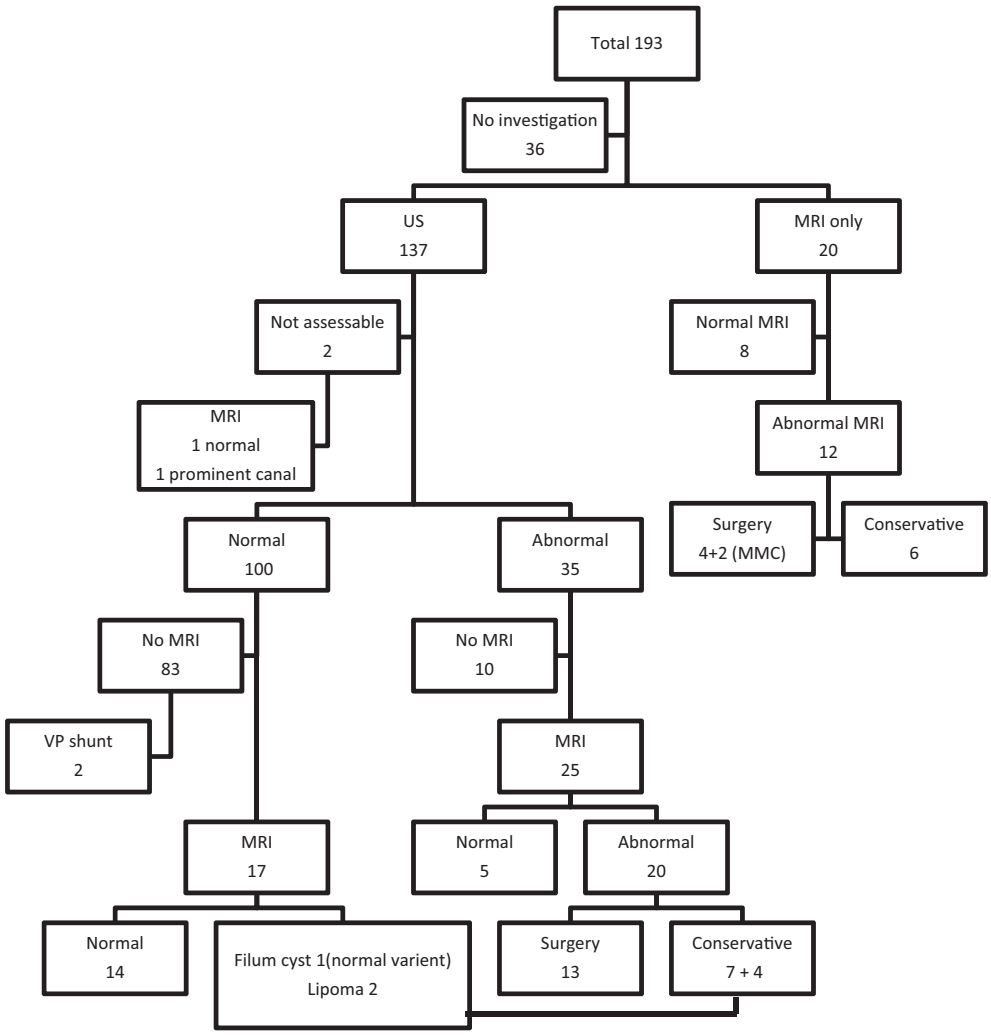


Fig. 1. Diagnostic flow chart.

went on to MRI. Of these, 20 (80%) were abnormal (Fig. 2b). The US showed a thickened filum in one child and dilated central canal in four children who were found to have normal MRI (n = 5). This compares with the 20 (13%) patients who had MRI only, with no screening US, 12 (60%) of which were abnormal. The reasons for having up front MRI included complex abnormalities on x-ray, Currarino's syndrome and missed opportunity for ultrasound under 4 months of age. The likelihood of having a normal MRI was 40% without prior US and 20% if an abnormality was picked up by US before doing an MRI spine.

3.3. Sensitivity and specificity of spinal US

Both spinal US and MRI were done in 44 children, the sensitivity and specificity of US are presented in Table 2. Lipomeningocele, meningo(myelo)cele and diastematomyelia were not detected in any ultrasound. An US finding of a low lying cord and normal cord showed good corroboration with MRI with a sensitivity of 88 and 89% respectively, and specificity of 82 and 91% respectively. All other abnormal ultrasound findings had high specificity (79–100%) but low sensitivity (25–41%) for predicting the abnormality on MRI.

Spinal US had an overall sensitivity of 91%, specificity of 75%, positive predictive value of 80% and negative predictive value of 88% compared to MRI for the detection of spinal anomalies.

3.4. Surgical intervention and follow-up

The correlation of US findings to neurosurgical intervention is presented in Table 3. Nineteen children (10%) underwent a neurosurgical operation, out of 32 with an abnormal MRI (60%) – 1 child had meningomyelocoele repair, 1 an anterior meningocoele repair and 17 (9%) had laminectomy and de-tethering of cord with or without excision of lipoma.

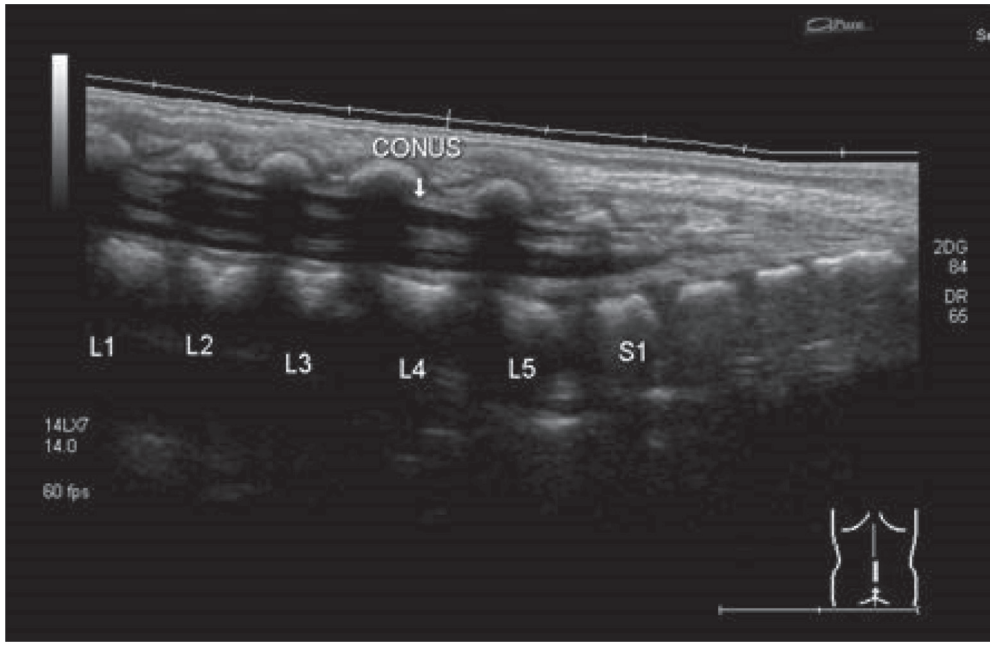
Of the children requiring de-tethering, 13 (76%) were detected on US and confirmed by MRI, 4 (24%) had MRI without US. No child who had a normal spinal US required de-tethering of the cord ($p<0.05$). Of the 13 requiring laminectomy and detethering detected on US, all but one had a low lying cord, borderline low cord or tethered cord detected on ultrasound. The one exception had multiple vertebral anomalies, precluding the assessment of the exact level of the cord on US (the US was however reported abnormal suggesting MRI). A borderline conus, low lying cord or tethered cord on US was significantly associated with the need for neurosurgical intervention ($p<.05$).

Follow up was available for (169) 89% children (median, 3 years; IQR – 1 to 5 years). No child in the nonoperated cohort with or without abnormal imaging had deterioration of neurological symptoms or required surgery.

4. Discussion

Using MRI as the gold standard, this paper confirms the sensitivity and specificity of US for detecting potential TCS in babies with ARM.

a



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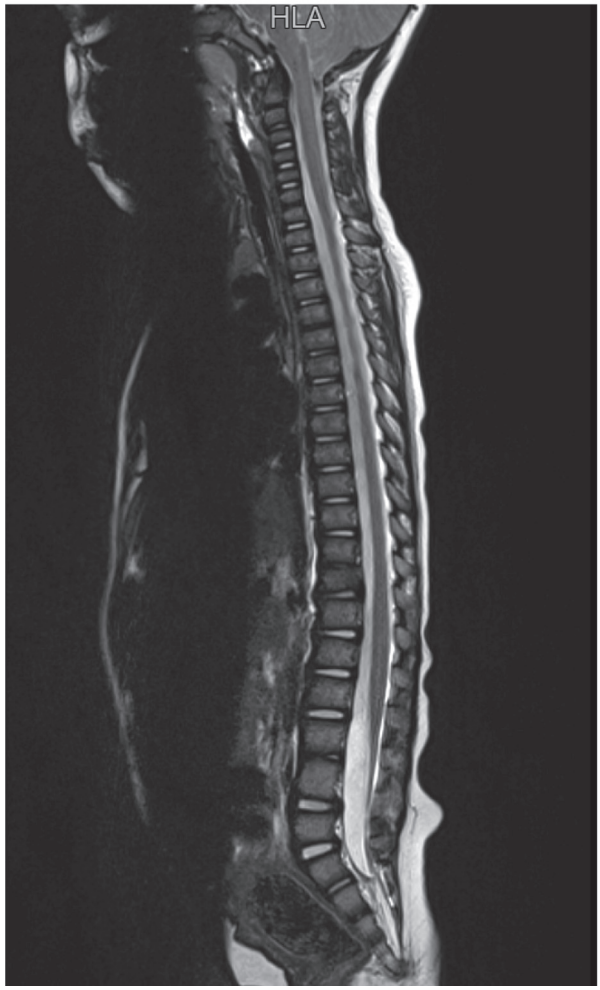

Fig. 2. a) US showing a low lying cord. b) MRI demonstrating a low lying conus.

Table 2
Comparison of spinal US and MRI findings

Spinal US	MRI		Sensitivity(%)	Specificity(%)
	+	-		
Normal cord			89	91
+	8	3		
-	1	32		
Low lying cord			88	82
+	15	5		
-	2	22		
Thickened filum terminale			41	94
+	5	2		
-	7	30		
Tethered cord			36	85
+	4	5		
-	7	28		
Filum cyst			25	79
+	4	6		
-	12	22		
Vertebral anomalies			35	100
+	6	0		
-	11	27		

The challenge in children with ARM and associated spinal cord anomalies is to identify the subgroup of patients who have TCS, those at risk of developing TCS and future neurological deterioration and those that would benefit from neurosurgical intervention. A screening test by definition is performed in asymptomatic population to identify a subgroup that is "at risk". It is not meant to be diagnostic and the identified high risk group would typically need further evaluation [12]. It is applied to a large population and thus needs to be easy to perform, cost effective, easily available and non-invasive [12]. The spinal US in the setting of ARM fulfils all these criteria. In most cases, screening test needs to be benchmarked against a "Gold Standard" test which would be impractical to apply to large numbers. In the case of occult spinal dysraphism, the spinal MRI provides excellent soft tissue definition of the neuromuscular system and is thus considered the gold standard. It is however, not universally available, expensive (three and a half times the cost of the US) and may require sedation or a general anesthetic to obtain the best image. In addition, it should be noted that, while MRI gives very accurate anatomical definition, the correlation with a clinically significant TSC is not certain.

Our policy has been for prophylactic de-tethering with radiological evidence of tethered cord. However, there is a lack of consensus on this approach in the literature. Most neurosurgery literature suggests a preference for early prophylactic de-tethering considering neurological deterioration of sensory/motor, orthopedic, bowel and urinary functions is thought to be naturally progressive [6,13]. However, in patients with ARM, the natural history of TCS seems not to be one of progression of symptoms [14]. Retrospective case series suggest neurological outcomes are comparable in children with ARM with or without spinal cord anomalies with non-operative expectant management [14]. Further, de-tethering has been reported to result in 80–100% of improvement in pain and orthopedics symptoms, but with very little improvement in sphincter function, bowel and urodynamic abnormalities which correlate more strongly with the ARM itself [13]. It would take a longitudinal multicenter trial to definitively determine the value of cord detethering in patients with ARM. In the meantime, our view is the relative safety of the procedure in suitably trained hands means we will continue to recommend a proactive approach.

Table 3
Correlation of findings on spinal US to neurological intervention for TCS

US finding	Neurological intervention (n = 17)*	p Value
Normal cord	0	<.05
Filum cyst	1	NS
Vertebral anomalies	3	NS
Borderline conus	1	<.05
Low lying conus	10	<.001
Tethered cord	9	<.05
Syrinx	0	NS
Ventriculus terminalis	2	NS
Prominent central canal	1	NS
Thickened filum	2	NS

* A patient may have more than one finding.

The sensitivity of spinal US in the detection of spinal anomalies was 91% in our study. The false negative results were in one child with a filum cyst and two with lipomas of the cord, none of whom required surgery. There is a wide range of sensitivity from 20% to 86% reported in literature for spinal US [3,8]. This could be attributed to fact that US is a subjective test and results can vary depending on the experience of the sonologist. Further, the lack of agreement on the definitions of 'normal' can affect results. Chern et al. demonstrated that spinal US is fairly accurate in determining the level of the spinal cord [15]. We have found similarly in our study that the finding of a low lying cord is 88% sensitive. Further, all children requiring neurological intervention were reported to have a low, borderline low cord or tethered cord on US. These findings thus flag a high risk group that requires closer neurological follow up with or without neurosurgical intervention. With a screening test it is important to consider the consequences of false negative tests. The risk of missing spinal cord anomalies or tethered cord is mitigated by recommending that all children with ARM have long term follow up in a multi-specialty clinic. This facilitates monitoring neurological function and early detection of symptoms of TCS. Any deterioration in motor, bladder or bowel symptoms prompts re-evaluation for TSC. Conversely, increased detection of spinal cord anomalies by using MRI as a first line may add to the anxiety of parents although no actual treatment is required. It would therefore be a reasonable choice to monitor and follow up children with ARM clinically and subject only the 'at risk' identified by spinal US and symptomatic children to MRI.

The present study is limited by its retrospective nature. In18% children, spinal imaging was not available for review. These children were outborn and referred for definitive surgery for ARM, were "missed" at birth or had outside imaging which could not be reviewed. Further, a 'template' for reporting would ensure that all required information is documented by the person performing the US scan. The disagreement in US and MRI with respect to the terms 'low lying cord', 'borderline low cord' and 'tethered cord' may be attributed to unclear definitions but taken as a whole they were all indicative of the same – a high risk for TCS.

The accuracy of spinal US can be improved by agreement on the definitions of abnormality and the extent of the spine to be screened. Centralization of screening at specialized pediatric centers that have trained personnel doing the spinal US will further improve accuracy. Further, the spinal US provides an excellent opportunity to screen the pelvis for a presacral mass in children with ARM. This is not routinely performed and must be included in the request for spinal US.

5. Conclusion

Spinal US performed in a tertiary pediatric imaging department is a good screening test for spinal cord anomalies in children with ARM. The findings of a low or borderline low cord or tethered cord on US are flags for patients at risk of TCS. MRI can be reserved for children with abnormal findings on US or as otherwise clinically indicated. While neurosurgical intervention where appropriate based on imaging findings may be helpful this must be underpinned by long-term follow-up by a multi-specialty team who, in partnership with the child and family, can help ensure bowel and bladder functional outcomes are optimal.

Ethical approval

This study was approved by the Sydney Children's Hospital Network Human Ethics Research Committee (LNR/18/SCHN/210).

Funding

No funding was required for this study.

Declaration of competing interest

The authors declare no conflict of interest.

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