Intraoperative neurophysiological monitoring in patients undergoing tethered cord surgery after fetal myelomeningocele repair

Clinical article

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Object. Fetal myelomeningocele closure has been shown to be advantageous in a number of areas. In this study, the authors report on neural function in patients who had previously undergone fetal myelomeningocele repair and returned to the authors’ institution for further surgery that included intraoperative neurophysiological monitoring.

Methods. The authors retrospectively reviewed data obtained in 6 cases involving patients who underwent fetal myelomeningocele repair and later returned to their institution for spinal cord untethering. (In 4 of the 6 cases, the patients also underwent removal of a dermoid cyst [3 cases] or removal of an epidermoid cyst [1 case] during the untethering procedure.) Records and imaging studies were reviewed to identify the anatomical level of the myelomeningocele as well as the functional status of each patient. Stimulated electromyography (EMG) and transcranial motor evoked potential (tcMEP) recordings obtained during surgery were reviewed to assess the functional integrity of the nerve roots and spinal cord.

Results. During reexploration, all patients had reproducible signals at or below their anatomical level on stimulated EMG and tcMEP recordings. Corresponding to these findings, prior to tethering, all patients had antigravity muscle function below their anatomical level.

Conclusions. All 6 patients had lower-extremity function and neurophysiological monitoring recording signals at or below their anatomical level. These cases provide direct evidence of spinal cord and nerve root conductivity and functionality below the anatomical level of the myelomeningocele, further supporting that neurological status improves with fetal repair.

Key Words • electromyography • fetal surgery • intraoperative monitoring • motor evoked potentials • myelomeningocele • craniofacial

Myelomeningocele is a severe form of spina bifida characterized by failure of closure of the neural tube.28 Patients with this condition have long-term disability associated with structural brain abnormalities, bowel and bladder dysfunction, and paralysis below the spinal cord level of the lesion. Serial imaging studies of patients with myelomeningocele have demonstrated progression in a number of areas as these children develop in the womb.16,25 Early experimental studies on animal models and then in patients supported a “two-hit” hypothesis that the paralysis in patients with myelomeningocele results from the congenital myelodysplasia and from spinal cord injury from the intrauterine environment.7,8,10,11,18–20,26

Prenatal myelomeningocele closure was first successfully performed in patients in 1997.1,30 This procedure resulted in improvement in a number of clinical variables, including a decreased shunt requirement and a decreased incidence of hindbrain herniation.5,6,27,32–34 Some patients also had improved lower-extremity function.13
In 2011 the results of the Management of Myelomeningocele Study (MOMS) were published. This study was a randomized trial comparing outcomes after prenatal versus postnatal myelomeningocele closure. Among other variables this study compared the need for a shunt, the rate of hindbrain herniation, and motor function in patients. The investigators found a reduced need for a shunt and a reduction in the rate of hindbrain herniation. Regarding motor function, children who had undergone prenatal myelomeningocele repair were more likely to have a level of function 2 or more levels better than expected and were more likely to be able to ambulate at 30 months of age.

Spinal cord retethering has been well documented in patients with myelomeningocele with late progressive decline in function. Intraoperative neurophysiological monitoring (IONM) is used as an adjunct to prevent iatrogenic neurological injury across the entire spectrum of spinal surgeries. Particularly relevant here is the use of IONM during spinal cord untethering. Recording of compound muscle action potentials (CMAPs) elicited in response to direct bipolar stimulation of spinal nerve roots (stimulated electromyography [EMG]) has proven valuable for identifying nerve root location and verifying functional neural integrity. The more recent advent and use of transcranial motor evoked potential (tcMEP) monitoring has added further information about the integrity of the corticospinal tracts including alpha motor neurons and motor spinal nerve roots. Accordingly, these IONM modalities can provide objective evidence of the extent of neural function relative to the anatomical level of a myelomeningocele.

For this study we analyzed a subset of cases involving patients who had undergone fetal myelomeningocele repair at our institution and returned for spinal cord untethering. Using the intraoperative neurophysiological monitoring data from the untethering surgery, we set out to investigate and document the neurophysiological conductivity and functionality of the spinal cord and nerve roots distal to the anatomical defect in these patients as a further means of investigating lower-extremity function.

**Methods**

A retrospective chart review was conducted for all patients who had fetal repair of a myelomeningocele performed at the Children’s Hospital of Philadelphia (prior to MOMS) and later returned for additional surgery for spinal cord untethering. At the time of repeat surgery for untethering, multimodality intraoperative neurophysiological monitoring consisting of spontaneous and stimulated EMG and tcMEP and posterior tibial nerve somatosensory evoked potential (SSEP) recordings was performed as per the standard of care for spinal cord untethering at the Children’s Hospital of Philadelphia.

All neuromonitoring was accomplished with one of two 16-channel neurophysiology workstations (Axon Epoch XP, Axon Systems; Nicolet Endeavor, Viassys Healthcare). EMG and tcMEP monitoring was performed with a 10-channel recording from 5 bipolar subdermal needle electrode pairs inserted into the left and right adductor, quadriceps, tibialis anterior, gastrocnemius, and external anal sphincter muscles. This electrode montage provided adequate nerve root coverage from the L2–S4 segments. At times, a sixth recording channel from rectus abdominis–iliopsoas muscle combinations was added when it was necessary to monitor T12–L1 nerve roots.

For stimulated EMG monitoring, a sterile, hand-held concentric bipolar stimulus was used for neural depolarization. The stimulus was a 50- to 100-μsec square-wave electric pulse delivered at a rate of 3.1 pulses per second at progressively increasing intensity levels until either a CMAP was recorded from the respective myotome or the level reached or exceeded 10 mA, suggesting the absence of functional neural elements.

Transcranial motor evoked potentials were recorded bilaterally from the same myotomes used to record EMG. These myogenic responses were elicited using a commercially available transcranial electrical stimulator (Digitimer D185, Digitimer Corp.), that delivered a brief (50 μsec), high voltage (250–500 V) anodal pulse train (number of pulses 2–5, interstimulus interval 1–3 msec) between 2 subdermal needle electrodes inserted subcutaneously over motor cortex regions C1 and C2 (International 10–20 system). Stimulation parameters of output voltage, number of pulses in the stimulus train, and interstimulus interval were all optimized to elicit maximal response amplitudes for each individual patient.

Subcortical posterior tibial nerve SSEPs were elicited in response to a 300-μsec square-wave electrical pulse. Stimulation intensity levels ranged from 25 to 30 mA, with intensity selected to achieve response amplitude within the asymptotic portion of the SSEP intensity versus amplitude curve for each individual patient. Cortical potentials were recorded from subdermal needle electrodes (Rochester Electro-Medical, Inc.; Axon Systems, Inc.) placed over the surface of the second or third cervical vertebra and referenced to Fpz (forehead) (International 10–20 system).

Both the initial fetal repair of the myelomeningocele and the surgical untethering were performed by a single senior surgeon (L.N.S.), while all of the IONM was carried out by a board-certified surgical neurophysiologist. The intraoperative neurophysiological records were reviewed to assess the lumbosacral nerve root signals. Hospital and office records as well as available radiographic images were analyzed to assess the anatomical level of the myelomeningocele and the functional status. Neuro-motor functional level was determined by the best functional myotome as documented in the medical record by a specialist physical therapist. Muscle strength was graded on the Medical Research Council (MRC) scale. A muscle strength score of at least 3/5 in the lower extremity was required for a myotome level to be assigned. For patients with different neuromotor levels on the left and right, the higher (worse) level was assigned. Testing was performed on all children who could follow commands and actively participate in the testing process. For newborns, clinical observation was used to determine which muscle groups were functional.

Anatomical level by ultrasound was defined as the first level with abnormal-appearing posterior elements.
The MRI defect was defined as the first level with loss of posterior elements. On radiographs, the anatomical level was considered to be the first level noted to have widening of the interpedicular space.

Results

Six patients were identified and reviewed for the study. These 6 patients represent all of the patients who underwent fetal repair and returned to the Children’s Hospital of Philadelphia for untethering. Fetal repair was performed in these patients at 21–25 weeks’ gestation (mean 23 weeks). At the time of tethered cord surgery, the patients were 6 months, 15 months, and 2, 3, 4, and 5 years of age. Indications for tethered cord surgery included: 1) worsening of gait/loss of foot function, 2) increasing back and leg pain, and 3) significant lesion progression (Fig. 1). Four of the 6 patients had an untethering with removal of a lesion—3 patients with dermoid cysts and 1 with an epidermoid cyst. The 2 remaining patients had untethering performed without a discrete lesion. At the time of surgery, the general impression of the senior surgeon was that the nerve roots appeared to have a more normal appearance than is often seen at or below the level of a myelomeningocele (Fig. 2).

At the time of chart review, all patients were ambulatory with pre-tethering neuromotor functional levels of L-5 or S-1. Anatomical levels across all evaluated imaging modalities as well as pre-tethering neuromotor functional levels are presented in Table 1. As far as imaging modalities are concerned, there were some differences noted across modalities, most notably in Case 3. Of note, with one exception the neuromotor functional level was consistently below the anatomical level for all patients across all imaging modalities. The exception was Case 6; in this patient, the MRI defect level was the same as the functional level. As of this writing, the modality most predictive of the functional level is currently under investigation, and there is no standard in the literature. For consistency in this study, we chose to use prenatal ultrasound as our modality for assessing anatomical level, as it is commonly cited and was the most uniformly obtained.

At the time of surgery, stimulated EMG and tcMEP recordings were suggestive of robust lumbosacral spinal nerve root function at or below the level of the myelomeningocele (Figs. 3 and 4). Although they were recorded at the time of surgery, SSEP data did not yield any additional information in this patient population. A summary of the neurophysiological data comparing the presence of signals for both stimulated EMG and tcMEP with the anatomical level is depicted in Fig. 5. All patients who underwent fetal repair had signals below their anatomical level. As some patients had weak, inconsistent signals that may not be consistent with normal function at some levels, the lowest level with consistent, reproducible neurophysiological responses across both modalities was noted as well (Fig. 6). Five of the patients had functional signals definitively below the anatomical level. One patient had functional signals at or slightly below the anatomical level (L-3 in a patient with an L2–3 anatomical level). No patient demonstrated loss of signals above the anatomical level.

Our patients who undergo postnatal myelomeningocele repair typically do not have significant function below the level of the lesion and uncommonly undergo untethering procedures related to progressive decline or pain. During this study period, one patient who had undergone postnatal myelomeningocele repair presented with a symptomatic tethered cord. This patient had a repair of a low lumbosacral myelomeningocele 2 days after birth with an
MRI level of L-5. At 15 years of age, the patient presented with decreased sensation in his feet and legs and deterioration of his foot and leg function. An untethering procedure was performed. Transcranial MEPs were recorded over the course of surgery from myotomes innervated by the L2–S4 nerve roots (Fig. 7). The tcMEPs demonstrated left versus right amplitude asymmetry at baseline. The responses from the tibialis anterior muscle on the left side were attenuated compared with those on the right, and there were only trace responses from the left gastrocnemius, left abductor hallucis, and bilateral external anal sphincter muscles. Overall, these data are consistent with preexisting left lower-extremity weakness. The data also are suggestive of weakness in muscles innervated by the lower sacral nerve roots.

Discussion

We document here the use of intraoperative monitoring in patients undergoing tethered cord release after fetal myelomeningocele repair. This study provides direct evidence of intact neural pathways below the anatomical level of the myelomeningocele in patients who have undergone fetal repair. All 6 patients in this retrospective study showed both neurophysiological and physical evidence of neural function at and below (1 patient) or below (5 patients) the anatomical level of the myelomeningocele defect as defined by prenatal ultrasound. In 3 cases (Cases 3, 4, and 5), the level of lowest consistent signals mirrored the pre-tethering neuromotor functional level. In 2 cases (Cases 1 and 6), the consistent monitoring signals were below the pre-tethering neuromotor level. As was noted in Figs. 3 and 4, this finding can be explained by the fact that patients may have some demonstrable function but if the strength is not antigravity, that myotome is not included in their functional level. (For example, the patient in Case 6 had good signals at S-1 but was given

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**TABLE 1: Anatomic myelomeningocele level in prenatal closed patients according to different imaging modalities and pre-tethering neuromotor functional level**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Prenatal Ultrasound</th>
<th>Postnatal MRI Defect</th>
<th>Postnatal MRI Bony Dysplasia</th>
<th>Postnatal Radiograph</th>
<th>Pre-Tethering Motor Functional Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L-4</td>
<td>L-4</td>
<td>L2–3</td>
<td>L-4</td>
<td>L-5</td>
</tr>
<tr>
<td>2</td>
<td>L2–3</td>
<td>L-4</td>
<td>L2–3</td>
<td>NA*</td>
<td>S-1</td>
</tr>
<tr>
<td>3</td>
<td>L-2</td>
<td>T-12</td>
<td>T-11</td>
<td>L-4</td>
<td>L-5</td>
</tr>
<tr>
<td>4</td>
<td>L4–5</td>
<td>L-5</td>
<td>L-4</td>
<td>L-4</td>
<td>S-1</td>
</tr>
<tr>
<td>5</td>
<td>L4–5</td>
<td>L-4</td>
<td>L-3</td>
<td>L-3</td>
<td>S-1</td>
</tr>
<tr>
<td>6</td>
<td>L-4</td>
<td>L-5</td>
<td>L3–4</td>
<td>L-5</td>
<td>L-5</td>
</tr>
</tbody>
</table>

* Radiograph was not available (NA); level was L2–3 based on note.

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**Fig. 3.** A stack display of tcMEPs recorded over the course of surgery in Case 6 (L-4 level) from myotomes innervated by the L-2 through S-4 nerve roots. The first MEP column in each panel represents controls recorded from the intrinsic hand muscles. The following columns represent recordings from the hip adductors, quadriceps, tibialis anterior, gastrocnemius, and anal sphincter, in that order. Note the clear presence of repeatable tcMEPs from external anal sphincter muscles bilaterally (arrows). While responses from the low sacral nerve roots on the right are smaller in amplitude than those on the left, they are clearly present and reproducible nonetheless.
an L-5 neuromotor function level due to a gastrocnemius strength of 2/5 rather than 3 or greater.) In only 1 case (Case 2) was the pre-tethering functional level below the level of consistent signals. In this case, signals were present throughout, but reproducible signals were only found at or slightly below the anatomical level (L-3 in L2–3 level); the pre-tethering neuromotor function level had been approximately 2 levels lower (L-5). As this patient presented for untethering with a worsening gait, a possible explanation for this discrepancy includes decreased signals at the time of surgery due to the functional loss from spinal cord tethering (her function was worse than at the time of physical therapy examination to determine the functional level).

Although not perfectly predictive in all cases, these data suggest that the EMG and tcMEP data can provide an objective measure of function for comparison across patients. The SSEP data, on the other hand, are not felt to be useful for comparison in studies like this one, as SSEPs are based on mixed-nerve conduction rather than specific nerves and tracts like EMG and tcMEPs. Therefore they are less sensitive to focal injury and less able to provide specific localization for comparison.

The presence of function below the anatomical level differs from previous data obtained in patients with postnatally treated myelomeningocele, which suggests that most patients with myelomeningocele function at levels at or above their anatomical level.6,15,24 Previous reports on lower-extremity function in patients who underwent prenatal myelomeningocele repair were inconsistent, some showing improved function and others showing no difference.13,29,31 However, the MOMS trial provided evidence in the form of a randomized trial indicating that fetal surgery does improve motor function.2 We believe this study provides the electrophysiological evidence of neural function below the anatomical level of the myelomeningocele in patients who have undergone fetal repair. This report, along with the MOMS trial, provides further support that fetal surgery provides some protection of the neural elements from exposure to the neurotoxic intrauterine environment.

There are a number of limitations in this study. The conclusions are drawn from a limited and restricted patient sample from before the MOMS trial. Therefore, there may be some element of selection bias to this population that skews the results. It will be important to determine if similar findings with regard to direct multimodality neurophysiological monitoring data are observed in the patients within the MOMS trial, as these patients are being followed in a more controlled and screened environment. Secondly, only 1 patient with postnatal myelomeningocele repair underwent a similar operation at our institution during the same time period for comparison, and we did not have a large sample of age-matched controls for this study. Our patients who have undergone postnatal myelomeningocele repair do not have function below the level of the lesion, and thus we are not able to make direct comparison between prenatal and postnatal closure with respect to neurophysiological testing.

Conclusions

We feel that the results of this study and the larger
MOMS trial provide strong evidence that prenatal closure protects the spinal cord from continued injury in the uterine environment. This study also provides an interesting area of investigation in the MOMS patients as they get older.

Acknowledgments

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Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Jackson, Adzick, Sutton. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Heuer.

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