Assessment and Management of the Parturient Carrying a Fetus With Myelomeningocele: Part 1

PREANESTHETIC ASSESSMENT

Dr. Elizabeth A.M. Frost, who is the editor of this continuing medical education series, is clinical professor of anesthesiology at the Icahn School of Medicine at Mount Sinai in New York City. She is the author of Clinical Anesthesia in Neurosurgery (Butterworth-Heinemann, Boston) and numerous articles. Dr. Frost is past president of the Anesthesia History Association and former editor of the journal of the New York State Society of Anesthesiologists, Sphere. She is also editor of the book series based on this CME program, Preanesthetic Assessment, Volumes 1 through 3 (Birkhäuser, Boston) and 4 through 6 (McMahon Publishing, New York City).

A Course of Study for AMA PRA Category 1 Credit™ Read this article, reflect on the information presented, then go online (www.mssm.procampus.net) and complete the lesson post-test and course evaluation before July 31, 2017. (CME credit is not valid past this date.) You must achieve a score of 80% or better to earn CME credit.

Time to Complete Activity: 2 hours Release Date: August 1, 2016 Termination Date: July 31, 2017

Accreditation Statement

The Icahn School of Medicine at Mount Sinai is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit Designation Statement

The Icahn School of Medicine at Mount Sinai designates this enduring material for a maximum of 2.0 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Dr. Frost is past president of the Anesthesia History Association and former editor of the journal of the New York State Society of Anesthesiologists, Sphere. She is also editor of the book series based on this CME program, Preanesthetic Assessment, Volumes 1 through 3 (Birkhäuser, Boston) and 4 through 6 (McMahon Publishing, New York City).

It is the policy of the Icahn School of Medicine at Mount Sinai to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. Presenters must also make a meaningful disclosure to the audience of their discussions of unapproved or unapproved drugs or devices. This information will be available as part of the course material.

Visit www.mssm.procampus.net today for instant online processing of your CME post-test and evaluation form. There is a registration fee of $15 for this non-industry-supported activity. For assistance with technical problems, including questions about navigating the website, call toll-free customer service at (888) 345-6788 or send an email to Customer.Support@ProCEO.com. For inquiries about course content only, send an email to ram.roth@mssm.edu.

Ram Roth, MD, is director of PreAnesthetic Assessment Online and assistant professor of anesthesiology at the Icahn School of Medicine at Mount Sinai, New York, New York.

LEARNING OBJECTIVES

After completion of this activity, the reader should be able to:

1. Identify the first surgical procedure performed in utero on a human fetus
2. List the risk factors for MMC
3. Describe the neurologic deficits associated with MMC
4. Describe the current standard of care to prevent ongoing deterioration of MMC
5. Explain both components of the two-hit hypothesis for MMC pathogenesis
6. Describe the risks associated with prenatal MMC repair
7. Provide a plan for the anesthetic requirements for fetal surgery
8. Compare the primary and secondary outcomes of the MOMS (Management of MMC Study) trial
9. Evaluate the external validity of the MOMS trial to fetal care centers outside of the study protocol
10. Differentiate the indication for prenatal MMC repair from the indication for surgical intervention of a life-threatening condition
The fetus of a healthy, 19-year-old nulliparous woman was diagnosed with spina bifida after routine prenatal ultrasonography was performed at 21 weeks’ gestation. Her obstetrician referred her to a fetal care center where she underwent preoperative evaluation for prenatal MMC repair. Joined by her fiancé, she met with the obstetric and pediatric anesthesia team. As the discussion led to maternal and fetal risks of general anesthesia, the patient grew tearful, stating, “I don’t think I can go through with this surgery.” Her fiancé explained that he desired prenatal neurosurgical repair, as a family friend had read about its benefits online. Unable to console her, he turned to the anesthesia team and asked, “She can’t refuse a surgery that would allow my son to walk, can she?”

INTRODUCTION

The first in utero procedure performed on a human fetus was an open vesicostomy for urinary tract obstruction resulting in bilateral hydronephrosis in 1981. Michael Harrison, MD, and his colleagues at the University of California, San Francisco, later founded the first fetal treatment center in the United States, and the subspecialty of fetal surgery took hold. In utero animal models and subsequent prenatal human procedures revealed that the progression of potentially devastating congenital malformations was a dynamic process that might be reversed. Thirty-five years later, only a few indications justify in utero surgical intervention (eg, spina bifida, congenital pulmonary malformations, sacrococcygeal teratomas, and congenital diaphragmatic hernia). These procedures are sometimes only possible as open fetal surgery, requiring maternal laparotomy and hysterotomy performed in a manner similar to cesarean delivery. The fetus is exposed, partially removed while maintaining uteroplacental perfusion, and then returned to the uterus at the completion of surgery. The uterus and abdominal wall are closed for the continuation of gestation until a scheduled surgical delivery. Absorbable staples seal amniotic membranes to the myometrium, minimizing blood loss—in contrast to metal staples—without compromising future fertility. Minimally invasive procedures (eg, fetal endoscopic laser ablation of the placental anastomotic vessels for twin-to-twin transfusion syndrome) are performed under real-time fetoscopic video and ultrasonographic guidance. Uterine access is achieved via smaller incisions to accommodate trocars, needles, and fetoscopes.

Fetal myelomeningocele (MMC) repair originated from animal studies suggesting that intraterine coverage of an MMC lesion could prevent progression of spinal cord destruction and preserve neurologic function at birth. After the first successful open in utero MMC repair was performed in 1997, more than 400 fetuses had undergone the procedure by 2010. Today, prenatal MMC repair represents the most common, and arguably the most clinically relevant, indication for fetal surgery. As the volume of fetal procedures increases with fetal care centers opening across the country, understanding of intrauterine surgical techniques is an important responsibility of modern anesthesiologists. Equally essential is the establishment of fetal center criteria to promote optimal maternal, fetal, and pediatric outcomes as well as ensure short- and long-term patient safety. Finally, members of the multidisciplinary fetal care team must be prepared to adequately counsel women considering fetal procedures with regard to the risks and possible benefits of prenatal surgery.

SPINA BIFIDA

With a global incidence of 1 in 2,000 newborns, spina bifida is one of the world’s most prevalent major malformations at birth and the leading congenital anomaly of the central nervous system compatible with life. The most common and most severe form of spina bifida is MMC, in which the failed closure of the spinal cord (occurring between the third and fourth weeks of gestation) allows exposure of the protruding meninges and other neural elements to amniotic fluid (Figure). The specific etiology of MMC is unknown and likely multifactorial. While history of a previously affected pregnancy with the same partner is the strongest risk factor for MMC, other risk factors include fetal toxin exposure (ie, valproic acid, carbamazepine, cytochalasins, and calcium channel blockers), fetal hyperthermia, pregestational maternal diabetes, and maternal and/or fetal folate deficiency. The reduced incidence of MMC in the United States (3.4/10,000 live births) has been attributed to maternal folic acid supplementation, improved prenatal screening, and the option for pregnancy termination. Diagnosis of MMC can occur as early as the first trimester with detection of elevated maternal serum α-fetoprotein levels and confirmation by high-resolution ultrasound or magnetic resonance imaging. The implementation of routine ultrasonography during the second trimester has increased prenatal diagnoses.
ASSOCIATED COMPLICATIONS OF MMC

The severity of motor and sensory disability characterizing MMC is associated with the vertebral level(s) of the spinal cord lesion. The degree of functional neurologic deficit is often one or more levels higher than the anatomic defect. Damage to the spinal cord and peripheral nerves is usually apparent at birth; however, most infants survive the neonatal period without significant morbidity.

Permanent disabilities include paralysis and loss of sensation below the level of the lesion, bladder and bowel dysfunction (sacral nerve loss), sexual dysfunction, cognitive dysfunction, and tethered spinal cord. The mortality rate of liveborn infants with MMC in the United States is 10% and increases to 25% during the first 25 years of life.

Arnold-Chiari Type II Malformation

All infants born with MMC have an associated Arnold-Chiari type II malformation. This set of conditions includes downward displacement of the medulla, fourth ventricle, and cerebellum into the spinal canal (hindbrain herniation); brain stem anomalies; low-lying venous sinuses; and a small posterior fossa. The severity of motor and cranial nerve deficit and cognitive dysfunction does not correlate with the degree of hindbrain herniation, yet is exacerbated by the adverse effects of hydrocephalus and the need for ventriculoperitoneal (VP) shunting.

Typical signs include weak cry or vocal cord dysfunction, inspiratory wheezing; oromotor dysfunction, including prolonged feeding or aspiration pneumonia due to poor swallowing/absent gag reflex; and central hypoventilation or apnea. Respiratory dysfunction and apnea occur in 45% to 64% of MMC patients and are often identified as the cause of death.

Hydrocephalus

Hydrocephalus occurs in approximately 85% of thoracolumbar, lumbar, and lumbosacral MMC patients. Eighty percent to 90% of children developing this condition require diversion of cerebrospinal fluid (CSF) to the peritoneal cavity via VP shunting to prevent additional damage to the brain and brain stem. Ventriculoperitoneal shunting requires lifelong surveillance after frequent surgical revision for failure or infection. Children who require VP shunting for hydrocephalus are more likely to demonstrate learning disabilities and lower average IQ. Complications related to VP shunts represent a significant cause of neonatal death.
Continuing Medical Education

TREATMENT

Postnatal Surgical MMC Closure

Surgical closure of the neural tube defect within the first few days (48-72 hours) of life is identified as the current standard of care to prevent further deterioration associated with MMC.5 This procedure does not improve neurological function.16 The mortality rate stays around 10% and increases to 35% in infants demonstrating symptoms of Chiari type II malformation.10 The mean age of survival for MMC patients after postnatal surgical closure is 30 years.4

Prenatal MMC Repair

The rationale for prenatal MMC repair emerged from a large body of compelling experimental and clinical evidence revealing the two-hit pathogenesis of the disease.9,20 Histologic analysis found that exposed fetal spinal cord tissue appeared intact during early gestation—after the initial hit of failed neural tube closure—but showed worsening deterioration after the second hit of prolonged exposure to the intrauterine environment.21 Progressive development of central and peripheral nervous system damage also was supported by sequential fetal ultrasonography detecting loss of lower limb movement and visualization of worsening hindbrain herniation occurring later in gestation.22

Reports of early open prenatal MMC repair procedures described reversal of hindbrain herniation in almost all fetuses, reducing the need for a VP shunt by 50%.23,24 Further studies versus historical controls confirmed reversibility of hindbrain herniation along with favorable alteration in head size, brainstem function, motor function of the lower extremities, and neurodevelopmental parameters.2 These improvements were suspected to be associated with the timing of surgery during a period of greater plasticity in nervous system development, allowing accelerated repair and regeneration in addition to reduced amniotic fluid exposure of neural tissue.25

Statistically significant differences in hydrocephalus were seen after surgery was performed at a younger gestational age (≤25 weeks); this improvement was not seen after surgery during later gestation.26 The decreased rate of VP shunt placement in the prenatal surgical group was attributed to the reduced rates of hindbrain herniation and improved flow of CSF.4

Not surprisingly, early data also revealed increased maternal and fetal complications associated with preterm labor and delivery. Pregnancy complications related to fetal surgery include oligohydramnios, chorioamnion separation, placental abruption, and premature rupture of membranes.2 Total uterine relaxation for open fetal surgery is accomplished through deep general anesthesia, exposing both the woman and fetus to the risks of maternal airway management (eg, hypoxia, aspiration) and high concentrations of volatile agents (eg, hypotension, hypothermia, hemorrhage, decreased fetal myocardium and acidosis, and possible neuronal apoptosis). Invasive monitoring is indicated.

In addition to the surgical delivery after intrauterine MMC repair, all women undergoing prenatal surgery also are counseled that subsequent pregnancies should allow a recommended 2-year minimum interval between deliveries and require cesarean delivery to optimize obstetric outcomes.5,8 Without confirmation of the claimed benefits and risk assessment of a randomized controlled trial, comparisons between infants treated in utero and historical controls were subject to substantial bias.4

MANAGEMENT OF MMC STUDY

Dubbed the “most influential milestone study ever conducted in the history of fetal surgery,”2 the MOMS (Management of MMC Study) trial4 was a randomized controlled trial to compare the safety and efficacy of prenatal MMC repair with those of standard postnatal surgical closure. Enrollment was restricted to 3 maternal-fetal surgery centers in the United States. A total of 183 women with the prenatal diagnosis of MMC located between levels T1 and S1 and with evidence of hindbrain herniation were randomly assigned to either standard postnatal or prenatal surgery (between 19 and 25.9 weeks gestation).

Based on the results of the 158 patients whose children were evaluated at 12 months of age, the primary outcome of VP shunt placement occurred in 40% of the prenatal and 82% of the postnatal group. In each group, 2 perinatal deaths occurred. The prenatal surgery group demonstrated higher composite scores for mental development and improved motor function at 30 months. Prenatal surgery also resulted in improvement of secondary outcome hindbrain herniation.

At 12 months, 36% of the infants in the prenatal surgery group had no evidence of hindbrain herniation, versus 4% of the postnatal group. Furthermore, the prenatal group demonstrated lower rates of moderate or severe hindbrain herniation (25% vs. 67%).

Prenatal MMC repair also was associated with an increased risk for complications. The average gestational age at delivery was 34.1 weeks for the prenatal group, with 13% born before 30 weeks, compared with 37.3 weeks gestational age for the postnatal group, and none born before 30 weeks.

While the higher rate of preterm delivery in the prenatal group resulted in lower average birth weight and increased rates of neonatal respiratory distress syndrome, rates of adverse neonatal outcomes—including other complications of prematurity—were similar between both groups. Infants in the prenatal group underwent more procedures for tethered spinal cord.
Maternal complications in the prenatal group included higher rates of pulmonary edema, wound dehiscence or uterine scar thinning, and transfusion at delivery.

Introduced as a 10-year study, the MOMS trial started in 2003 and was prematurely stopped upon the recommendation of an independent data and safety monitoring committee, based on positive comparative outcomes criteria. Whether the results of the MOMS trial are reproducible at fetal care centers outside of those involved in the study is a matter of controversy. Only 15% of the women desiring fetal intervention met the strict criteria of the MOMS trial, including a maternal age of 18 years or older, a body mass index (BMI) less than 35 kg/m², and an otherwise normal fetal karyotype (Table). In all cases, a multidisciplinary team of experts adhered to a standardized protocol.

Follow-up of both patient groups continues in order to determine whether early benefits persist and to assess the effect of prenatal intervention on bowel and bladder continence, sexual function, and mental capacity.

**MANAGEMENT OF THE CASE PRESENTED**

The obstetric anesthesiologist gently explained to the patient and her fiancé that their appointment with the anesthesia team was only one component of a preoperative evaluation process, concluding, “No decision about a fetal surgical procedure will be made today.” She and the pediatric anesthesiologist permitted the patient and her fiancé a few moments alone in the conference room before returning at the patient’s request to continue the discussion.

The anesthesia teams described the anesthetic plan to permit deep uterine relaxation during the prenatal MMC repair and how the medications involved would increase her risk of postoperative nausea and vomiting and blood transfusion. They answered the patient’s questions regarding how the patient and the fetus would be continuously monitored throughout the MMC repair and following surgery.

The patient and her fiancé returned for their next scheduled prenatal counseling appointment the following day. At that point, they asked again to meet with the obstetrician, neonatologist and anesthesiologist. After considerable discussion, the mother agreed to surgery. It was scheduled for the following week.

In the preoperative holding area on the morning of the procedure, a lumbar epidural catheter was placed, tested and capped. Sodium bicarbonate solution was given per os to reduce risk for aspiration pneumonitis. Rectal indomethacin was administered for prophylactic tocolysis. The patient was transported to the operating room where she was placed in left-lateral tilt and routine monitors were initiated.

A rapid sequence induction was performed, followed by the placement of a radial arterial line and gradual deepening of the inhaled anesthetic to greater than 2 minimum alveolar concentration (MAC). Mean maternal arterial pressure was maintained via titration of continuous phenylephrine infusion while IV fluid administration was restricted to less than 2 L. Fetal heart rate and oxygen saturation were monitored via fetal pulse oximetry and continuous fetal echocardiography. At the start of uterine closure, tocolysis was achieved with magnesium sulfate (loading dose over 20 minutes, followed by continuous infusion).

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singleton pregnancy</td>
</tr>
<tr>
<td>Myelomeningocele with upper boundary located between thoracic level 1 and sacral level 1</td>
</tr>
<tr>
<td>Evidence of hindbrain herniation</td>
</tr>
<tr>
<td>Gestational age of 19.0-25.9 wk at time of randomization</td>
</tr>
<tr>
<td>Normal karyotype</td>
</tr>
<tr>
<td>US residency</td>
</tr>
<tr>
<td>Maternal age of ≥ 18 y</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal anomaly unrelated to myelomeningocele</td>
</tr>
<tr>
<td>Severe kyphosis</td>
</tr>
<tr>
<td>Body mass index ≥ 35 kg/m²</td>
</tr>
<tr>
<td>Placental abruption</td>
</tr>
<tr>
<td>Contraindication to surgery</td>
</tr>
<tr>
<td>Previous hysterotomy in the active uterine segment</td>
</tr>
<tr>
<td>Risk for preterm birth</td>
</tr>
<tr>
<td>Short cervix</td>
</tr>
<tr>
<td>History of preterm birth</td>
</tr>
</tbody>
</table>
The patient was weaned from the volatile agent as the epidural was incrementally dosed for postoperative pain control. The neuromuscular blockade was fully reversed and the patient’s trachea was extubated. She was transferred to the PACU in stable condition.

In Part 2 of this lesson, available as lesson 50 at ProCEO.com, the moral and legal implications of intrauterine repair will be discussed, as well as how patients and their significant others might be counseled.

References

Post-Test:

1. The first surgical procedure performed in utero on a human fetus was:
   a. tracheal plugging for congenital diaphragmatic hernia
   b. laser ablation of the placental anastomotic vessels for twin-to-twin transfusion syndrome
   c. open vesicostomy for urinary tract obstruction
   d. EXIT (ex utero intrapartum treatment) procedure for cervical teratoma

2. The strongest risk factor associated with myelomeningocele (MMC) is:
   a. history of a previously affected pregnancy
   b. fetal folate deficiency
   c. pregestational maternal diabetes
   d. fetal toxin exposure

3. The infant mortality rate of liveborn infants with MMC in the United States is:
   a. unknown
   b. 10%
   c. dependent on maternal age
   d. 25%

4. The mean age of survival for MMC patients after postnatal surgical closure is:
   a. about 3 years
   b. 30 years
   c. a normal life span
   d. 60 years

5. Which of the following is not an example of evidence supporting the two-hit pathogenesis of MMC?
   a. Histologic analysis of exposed fetal spinal cord tissue
   b. Worsening hindbrain herniation on sequential fetal ultrasonography
   c. Improved hindbrain herniation after prenatal MMC repair
   d. Reduced amniotic fluid levels after prenatal MMC repair

6. Which of the following is not a risk of prenatal MMC repair?
   a. Preterm labor
   b. Premature rupture of membranes
   c. Placental abruption
   d. Future infertility

7. Total uterine relaxation for fetal surgery is accomplished with:
   a. nondepolarizing neuromuscular blockade
   b. spinal anesthesia
   c. an inhaled halogenated anesthetic agent
   d. lidocaine infusion

8. The MOMS (Management of MMC Study) trial, comparing prenatal surgery with standard postnatal repair, revealed in the fetal repair group:
   a. reduced rates of ventriculoperitoneal shunt placement
   b. reduced perinatal death
   c. reduced rates of repeat surgery for tethered spinal cord
   d. increased rates of moderate to severe hindbrain herniation

9. Compared with the postnatal repair group, the MOMS fetal repair group also demonstrated:
   a. a reduced rate of preterm delivery
   b. lower birth weights
   c. decreased incidence of neonatal respiratory distress syndrome
   d. decreased incidence of transfusion at delivery

10. Which of the following candidates would meet the criteria to enroll in the MOMS trial?
    a. A 17-year-old (body mass index [BMI], 31 kg/m²) carrying a fetus at 20 weeks gestation with an MMC lesion beginning at T2
    b. A 30-year-old (BMI, 28 kg/m²) carrying a fetus at 22 weeks gestation with an MMC lesion at T3 and trisomy 13
    c. A 21-year-old (BMI, 30 kg/m²) carrying a fetus at 24 weeks gestation with an MMC lesion beginning at T2
    d. A 32-year-old (BMI, 36 kg/m²) carrying a fetus at 23 weeks gestation with an MMC lesion beginning at T4
Now Available

Reducing Residual Neuromuscular Blockade Through Monitoring, Communication, Reversal, and Enhanced-recovery Protocols

Release Date: February 1, 2016  
Expiration Date: February 1, 2017

Target Audience
This activity has been designed to meet the educational needs of health care professionals involved in the care of surgical patients.

Educational Objectives
After completing this activity, the participant should be better able to:

1. Recognize the prevalence and degree of morbidity and adverse events associated with residual neuromuscular blockade (RNMB) in patients who have undergone general anesthesia for a surgical procedure.

2. Communicate intraoperative factors effectively to optimize surgical conditions while reducing the incidence of RNMB.

3. Advocate for the consistent use of quantitative monitoring for RNMB.

4. Review the efficacy, safety, and appropriate use of neuromuscular blockade reversal agents.

5. Discuss the role of enhanced recovery protocols in reducing the risk for RNMB.

Accreditation Statement
This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Postgraduate Institute for Medicine and Miller Medical Communications, LLC. The Postgraduate Institute for Medicine is accredited by the ACCME to provide CME for physicians.

Credit Designation
The Postgraduate Institute for Medicine designates this enduring material for a maximum of 1.0 AMA PRA Category 1 Credit™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Disclosure of Conflicts of Interest
Postgraduate Institute for Medicine (PIM) requires instructors, planners, managers and other individuals who are in a position to control the content of this activity to disclose any real or apparent conflict of interest (COI) they may have as related to the content of this activity. All identified COI are thoroughly vetted and resolved according to PIM policy. The existence or absence of COI for everyone in a position to control content will be disclosed to participants prior to the start of each activity.

Access today at www.cmezone.com/IP153