FETAL MYELOMENINGOCELE REPAIR

Surgical Specialty:	Fetal Surgery/Maternal Fetal Medicine
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Background:

- General Considerations[1-6]
  - Fetal surgery offers the unique opportunity for in-utero treatment of congenital conditions, with otherwise significant morbidity and mortality.
  - Fetal surgery can be either open (for example, in-utero lung mass excision) or minimally invasive (for example, laser therapy for twin-twin transfusion syndrome), or ex-utero intrapartum treatment (EXIT) procedures.
  - The anesthetic management depends on the type of fetal intervention planned, surgical approach, and patient comorbidities.
  - Minimally invasive fetal interventions can be done with the mother under sedation and local anesthetic infiltration or neuraxial anesthesia. For open fetal surgeries and EXIT procedures, the mother typically receives general anesthesia with neuraxial anesthesia.
  - Myelomeningocele (MMC) is the most common indication for mid-gestation in-utero surgery where a laparotomy is first performed to expose the uterus and then the fetal MMC defect is closed via a hysterotomy (open repair) vs. a fetoscopic approach. This case guide will focus on the anesthetic management for open fetal surgery for MMC repair.
  - In MMC patients who undergo prenatal repair, there is reduced long-term disease morbidity. However, there is an increased risk of preterm labor and delivery.
  - Due to the benefits of prenatal MMC repair, the American College of Obstetrics & Gynecology recommends offering in-utero surgery for women with pregnancies complicated by fetal MMC.[6]

- Patient Considerations
  - Disease Specific Considerations[1]
    - MMC is an open neural tube defect (NTD) with both the spinal cord and meninges exposed through a skin defect.
    - Neural tube defects occur due to a failure of fusion of the neural tube in the third week of development around the twentieth day. This failure affects the development of the brain, spinal cord, meninges, and vertebral bodies.
    - The goal of prenatal intervention for MMC is to decrease the overall disease morbidity and mortality by decreasing the length of exposure to the neurotoxic uterine environment and reducing hindbrain herniation.

        - Disabilities associated with MMC include bladder and bowel incontinence, limb weakness, paralysis, deformity, and loss of sensation.
        - Traditionally, MMCs are repaired postnatally within the first 2 to 3 days of life. The goal of surgery is to untether the spinal cord from the surrounding skin and close the tissue defect in multiple layers with the final layer being skin closure.
        - Fetuses who have undergone prenatal repair have a decreased risk of hydrocephalus and improved lower extremity function compared with the standard postnatal repair after birth.
        - Diagnosis can be made accurately as early as 18 weeks of gestation, and almost always prior to 23 weeks of gestation. Testing involves a combination of maternal serum alpha-fetoprotein screening at 15-18 weeks, high-resolution obstetrical ultrasonography, amniocentesis, and in some cases, fetal magnetic resonance imaging (MRI).

- Associated Comorbidities/Syndromes
        - Chiari II malformation - the hallmark change is the caudal displacement of the cerebellar vermis, 4th ventricle, and brainstem through an enlarged foramen magnum.[8, 11]
        - Hydrocephalus

Anesthetic Planning:

- Pre-Anesthetic Evaluation
    - Maternal history and physical exam
    - Review fetal imaging studies (ultrasound, MRI) and obtain estimated fetal weight to prepare fetal medications.
    - Participate in a multi-disciplinary team meeting with the patient and her family to discuss the risks, benefits, alternatives, and anticipated postoperative course.
    - Plan for general anesthesia with epidural analgesia
    - Additional labs/tests indicated during work-up
        - CBC, Type & Cross-match blood for the mother.
    - Discussions to have with surgeon/family
        - Code Status of mother: Typically, full code
        - Code Status of the fetus: Discuss the options to deliver and resuscitate or not, full code vs. Do Not Resuscitate (DNR) depending on the gestational age and patient wishes.
        - ECMO Candidate: N/A

- Specific or Unique Room Set-up Requirements
    - Airway: General Endotracheal Intubation
    - Drugs/Infusions
        - Maternal medications: midazolam, lidocaine, propofol, succinylcholine, rocuronium or vecuronium, fentanyl, phenylephrine, ephedrine, ondansetron, dexamethasone, neostigmine, glycopyrrolate, volatile anesthetic, +/- nitroglycerin.
        - Maternal infusions: Propofol, remifentanil, phenylephrine, magnesium sulfate, +/- nitroglycerin.
        - Maternal epidural medications: Bupivacaine 0.25% or ropivacaine 0.2% for epidural bolus, preservative-free morphine, epidural infusion (local anesthetic of choice + opioid).

        - Fetal Intramuscular (IM) medications include:
            - In one syringe, "Fetal cocktail": Vecuronium 0.2 mg/kg (or rocuronium 2 mg/kg) + fentanyl 10-20 mcg/kg + atropine 20 mcg/kg x 4 syringes
            - Epinephrine 10 mcg/kg X 2 syringes
            - Epinephrine 1 mcg/kg X 2 syringes
            - Atropine 20 mcg/kg X 2 syringes
            - Draw medications up and transfer them to the scrub technician in a sterile fashion to be used on the sterile field.

    - Monitors/Access:
        - Mother – American Society of Anesthesiologists (ASA) standard monitors; 2 large-bore peripheral venous lines, +/-arterial line, Foley catheter
        - Fetal well-being monitor - Fetal heart rate (FHR) is used as an indicator and fetal bradycardia (<100 bpm) is managed pharmacologically, and when needed chest compressions are performed. Intermittent measurement of FHR is conducted using Doppler ultrasound.

    - Blood Availability:
        - Cross-matched blood for the mother and irradiated, leukocyte-reduced, O-negative blood for the fetus.

    - PICU Bed Availability (if indicated) – N/A

    - Other Indicated Resources (e.g., ECMO standby) – N/A

Intraoperative Considerations:

- General
    - The major anesthetic considerations during open fetal surgeries include:
        - Maintaining uteroplacental blood flow and maternal hemodynamics by avoiding hypotension, hypoxia, and acidosis.
        - Achieving profound uterine relaxation before hysterotomy and maintaining uterine hypotonia until uterine closure.
        - Minimizing fetal cardiac dysfunction.

- Preoperative epidural
    - Typically, a low thoracic or high lumbar epidural is placed preoperatively and used postoperatively for analgesia. Preoperatively, only a test dose is administered and the epidural is not bolused secondary to concerns of intraoperative hemodynamic instability.

- Aspiration prophylaxis medications (ranitidine and Bicitra) should be administered preoperatively.

- Induction and intubation
    - Adequate preoxygenation should be performed and rapid desaturation should be anticipated secondary to reduced functional residual capacity.
    - Difficult airway management should be anticipated secondary to pregnancy and a smaller (6.5 or 7.0 cuffed) endotracheal tube should be used.
    - A rapid sequence induction should be performed with IV propofol, fentanyl, lidocaine, and succinylcholine or rocuronium.

- Maintenance
  - Some centers use a supplemental intravenous anesthesia technique that involves using propofol and remifentanil infusions for maintenance of general anesthesia and turning on the volatile anesthetic right before the hysterotomy.
  - Other centers use volatile agents for maintenance and increase the concentration of volatile anesthetic agent (sevoflurane is preferred at the author's institution) (often 2-3 minimum alveolar concentration) to obtain adequate uterine relaxation prior to hysterotomy.

- Positioning – Supine with left uterine displacement to avoid hypotension secondary to aortocaval compression.

- Hemodynamic/Physiologic goals
  - Hypotension should be promptly treated with ephedrine and/or phenylephrine. Some institutions use nitroglycerine to assist with uterine relaxation.
  - Fetal anesthesia is achieved through the placental transfer of volatile anesthetics/opioids and direct intramuscular administration of opioids and muscle relaxants.
  - The intramuscular fetal cocktail is given and re-dosed every 45 to 60 minutes until the end of fetal surgery (institution-dependent). Some centers administer the fetal cocktail only once or twice during the surgery.
  - Continual intraoperative monitoring of the fetus is performed via real-time echocardiography.
  - Intra-operative fluid administration should be limited to approximately 500-1000cc crystalloids because there is a concern for maternal pulmonary edema which may occur as a result of magnesium sulfate administration.
  - Magnesium sulfate potentiates non-depolarizing neuromuscular blockers; therefore, the level of neuromuscular blockade should be closely monitored.

- Tocolysis is a central tenet of open fetal surgery and multiple agents are used perioperatively.
  - Indomethacin (oral or rectal) is administered preoperatively and continued postoperatively for 1 or 2 doses.
  - Magnesium sulfate- typically, a 6-gram IV loading dose is given following induction, and a 2-3 gram/hour infusion is continued until 24-48 hours postoperatively.
  - Intraoperatively, volatile anesthetic agents are commonly used for uterine tocolysis. Often, high doses (2-3 minimum alveolar concentration) are needed and constant communication with the surgeon is critical to maintain complete uterine relaxation.
  - Postoperatively, nifedipine is used for the remainder of the index pregnancy.

- Surgical Considerations (such as neuromonitoring, muscle relaxation, anticipated blood loss)
  - Prenatal surgery typically occurs between 19 and 26 weeks of gestation.[8]
  - The goal of surgery is to create a water-tight closure and protect the neural tissue.
  - To maintain uterine volume after hysterotomy, an amnioinfusion of warm crystalloid is used by the surgeons. For fetoscopic MMC repair, warm humidified carbon dioxide is insufflated into the uterine cavity.

- Emergence/Disposition:

  - After uterine closure, the epidural is bolused with local anesthetic (bupivacaine 0.25% or ropivacaine 0.2%). Some centers also administer an epidural bolus of preservative-free morphine.
  - Strategies for postoperative nausea and vomiting prophylaxis include dexamethasone, ondansetron, and scopolamine patch.
  - Residual neuromuscular blockade is typically reversed with neostigmine and glycopyrrolate and not sugammadex since the patient will remain pregnant after surgery.
  - The patient should be extubated when fully awake and transferred to the recovery room.

- Post-op Care
  - The epidural and magnesium sulfate infusions are typically continued for 24-48 hours postoperatively.
  - Some centers use a wound soaker catheter for postoperative analgesia.
  - The patient is followed for postoperative pain management x 2-3 days, then transitioned to oral acetaminophen/hydrocodone or acetaminophen/oxycodone.
  - Postoperative deep vein thrombosis prophylaxis is critical since the patient is on bed rest while on magnesium sulfate infusion.
  - Fetal echocardiography should be performed postoperatively to check for fetal ductal closure since indomethacin is commonly used.

Case-Specific Complications/Pitfalls

Despite the beneficial effects of fetal intervention, women are subject to an increased risk of preterm labor and delivery, with up to 38% rate of spontaneous labor[7,9]. Some of the other complications include [5,7]:

- Pulmonary edema (6%)
- Oligohydramnios (21%)
- Chorioamniotic separation (26%)
- Placental abruption (6%)
- Partial or complete uterine scar dehiscence noted at the time of delivery (35%)
- Maternal transfusion requirement at delivery (9%)

Preterm labor and delivery could be due to manipulation of the gravid uterus, fetal surgical stimulation, noxious stimuli in the fetus, and inadequate uterine perfusion, among others.[9]

The perioperative team must hold a high clinical suspicion for these possible complications while maintaining extreme vigilance and preparation.

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