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Midgestational Fetal Procedures

Prenatal Repair of an Open Neural Tube Defect

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A 26-year-old G1P0 with a gestational age of 23 4/7 weeks presents with an open neural tube defect (NTD), namely a myelomeningocele (MMC) extending from L3 to S1. She does not have any other comorbidities. She has been seen by the maternal fetal medicine team. There is a single male fetus with an amniocentesis with a normal 46 XY karyotype. A fetal ultrasound shows some degree of hindbrain herniation compatible with a Chiari II malformation with mild hydrocephalus and normal ankle motion. The placenta is posterior with a normal amount of amniotic fluid and an estimated fetal weight of 590 grams. A psychosocial evaluation considers the patient an appropriate candidate for a prenatal repair of an NTD.

What Is an Open Neural Tube Defect and What Are Its Physiologic Effects?

Open neural tube defects (NTDs) are a group of congenital defects that occur due to failure to close the neural tube. This leads to the exposure of neural tissue to the amniotic fluid with subsequent neurodegeneration due to the persistent exposure. This exposure leads to neuronal cell death and loss of axonal connections. The most common form of open NTDs is a MMC in which the spinal cord is exposed and may be covered by the meningeal sac. This most commonly occurs in thoracolumbar, lumbar, and lumbosacral areas. The open defect leads to abnormal neurologic function at and below the level of the lesion with subsequent sensory and motor deficits such as neurogenic bowel and bladder dysfunction. More severe forms of open NTD are incompatible with life. Spinal dysraphism, such as spina bifida and tethered cord, refers to a NTD in which normal skin covers the underline of the lesion.

What Is the Incidence of NTDs and What Are the Causes?

NTDs have an approximate worldwide incidence of 1 in every 1,000 pregnancies. Although the incidence of most open NTDs is higher in females, MMC defects have an equal incidence in males and females. The causes of NTDs are multifactorial. Most of the cases are sporadic. A genetic predisposition is present in some cases with the involvement of genes that regulate folate metabolism. Environmental issues such as low folate levels or the presence of diabetes or prenatal exposure to valproic acid prenatally increases the incidence. Although some markers such as maternal alpha fetoprotein can be useful as diagnostic screening, pre-natal ultrasound during the first trimester is the gold standard to confirm the diagnosis.

What Anomalies Are Associated with NTDs

NTDs are frequently associated with other abnormalities such as skeletal, genitourinary, and gastrointestinal abnormalities. The most common associated defect with prenatal progression of a MMC is the development of a Chiari type II malformation with hindbrain herniation and hydrocephalus. This prenatal progression to a Chiari type II malformation occurs in 75% of cases and requires a VP shunt in most cases. Neurogenic bladder is also significant with 83% of patients requiring intermittent catheterization. Postnatal orthopedic repairs may also be necessary for congenital taloequinovarus (CTEV). Given the multiple medical problems, these patients require a multidisciplinary approach to management.

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What Public Health Intervention Has Been Important for the Prevention of NTDs?

A worldwide primary prevention campaign has been implemented with the supplemental administration of folate to reduce the incidence of NTD. Women planning a pregnancy receive 0.4 mg of folic acid per day and women with a high risk of NTD receive 4–5 mg a day. The underlying mechanism of the preventive effect of folic acid is related to DNA replication to facilitate cell proliferation, as well as DNA methylation involving gene expression. It is estimated that even with appropriate pre-gestational administration NTDs still occur in 0.7–0.8 cases per 1,000 pregnancies.

What Are the Surgical Options for the Repair of Open NTDs?

There are three approaches to surgical management: open fetal surgery, endoscopic/fetoscopic surgery, and postnatal repair of the NTD. Parents should receive detailed information about the pros and cons of the different approaches based on the best evidence to facilitate the decision-making process. The open fetal surgery involves a transverse (Pfannenstiel) or vertical incision with the performance of a hysterotomy with fetal exposure of the defect and closure of the defect under direct visualization. The fetoscopic repair requires the exteriorization of the uterus without the performance of a hysterotomy. Instead two ports are inserted into the uterus and the amniotic fluid is partially replaced by insufflated CO_2. The postnatal repair occurs in the first 24 hours after birth to decrease the risks of infection into the central nervous system. Postnatal care requires frequent monitoring with head ultrasounds to detect worsening hydrocephalus given the high frequency of these patients requiring cerebrospinal shunting.

What Are Important Considerations During the Preanesthetic Evaluation for Patients Undergoing Prenatal Repair of an NTD?

Patient selection is critical given the potential maternal risks and the potential benefits of the procedure to the fetus. The first consideration is for maternal safety such that serious and uncompensated comorbidities preclude the performance of a fetal procedure. During the physical examination, emphasis must include the evaluation of the airway and the examination of the spine.

The description of the NTD and the surgical fetal planning has evolved. Therefore, it is important to review the studies preoperatively including fetal ultrasonography and fetal MRI. Specific points of utility to the anesthesiologist include the extension of the NTD defect, the dynamic evaluation of the motor function of the lower extremities, any associated fetal anomalies, the estimated fetal weight, the presence of a Chiari II malformation, the presence and severity of hydrocephalus, and the placenta location. Any important associated fetal anomalies or abnormal karyotype precludes fetal intervention. Another important consideration during the preoperative evaluation is a multidisciplinary approach that includes members of the fetal maternal team, a neonatologist, a neurosurgeon, a pediatric anesthesiologist with experience in fetal surgery, a pediatric surgeon, operating room nurses, and a social worker.

What Are the Advantages and Disadvantages of Proceeding with a Prenatal Repair of the NTD?

The landmark study of prenatal closure versus postnatal closure was the Management of MMC Study (MOMS). The primary outcome was the fetal or neonatal mortality and the need for the placement of cerebrospinal shunt by twelve months of age. Secondary outcomes include the evaluation of motor function and mental development in a follow up at 30 months of age. The study was prematurely discontinued due to better outcomes in the prenatal repair group. The results showed a 50% reduction in the need to perform a ventriculo-peritoneal (VP) shunt (40% vs. 82%), decreased incidence of the progression towards a Chiari II malformation at a 30-month follow up, and improvement in the neurologic function and ambulation in those undergoing prenatal closure. Although the prenatal closure provides all the advantages mentioned above, the prenatal closure group had a higher incidence of maternal complications such as preterm deliveries (mean gestational age 34.1 weeks vs. 37.3 weeks), uterine dehiscence at delivery and mandatory surgical delivery with current

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and subsequent pregnancies. Long-term outcomes (greater than 30 months) are still unknown. A follow up of the MOMS trial (MOMS 2) is expected in children at the ages of 6–10 years of age.

What Are the Potential Benefits of the Fetoscopic Approach?

It is important to realize that the endoscopic approach for the prenatal repair of a NTD is still experimental. It is a promising technique given the potential reduction in the short- and long-term maternal complications. Potential benefits of the fetoscopic approach include a decreased incidence of preterm deliveries and reduced newborn complications by allowing a vaginal delivery as well as reduced maternal complications associated with hysterotomy. Concerns with the fetoscopic surgery are longer surgical time, the need for further surgery after birth due to cerebrospinal fluid leak and the risk of fetal acidosis secondary to the insufflation of CO_2. Current studies have not shown indirect evidence of fetal acidosis (mainly looking at fetal heart rate as a marker of fetal distress) due to the insufflation of CO_2. An early study comparing the fetoscopic closure versus the open approach showed some concerns due to a longer operative time, higher need for postnatal reoperation rate (28% vs. 2.5%) with similar shunt rate, and perinatal mortality. A more recent report involving more experience and standardized technique reports a lower incidence of reoperation after birth due to cerebrospinal leak, greater gestational age at birth. Further prospective studies with longer follow ups are necessary to establish the role of the fetoscopic repair of NTDs and the safety of CO_2 insufflation, as well as long-term neurodevelopmental outcomes.

What General Perioperative Obstetric Anesthetic Considerations Are Necessary in Patients Undergoing a Prenatal Repair of an NTD?

Principles of anesthesia care for the obstetric patient apply during the performance of the second trimester closure of a NTD. Preinduction, this includes antiaspiration prophylaxis with an H2 receptor antagonist and metoclopramide. Obstetric airway changes require complete airway evaluation with the use of smaller endotracheal tubes and further preparation to manage a potential difficult airway. A three minute pre-oxygenation is mandatory given the decrease in the functional residual capacity (FRC) and the increased oxygen consumption. A rapid sequence induction is performed given the risks of aspiration. Appropriate sniffing position is critical to facilitate the intubation of these patients. Intraoperative mechanical ventilation should be titrated to maintain a maternal physiologic $PaCO_2$ of 32–35 mmHg. Aortocaval compression usually starts after 20 weeks of gestation due to the mechanical effects of the uterus while lying supine with subsequent decrease in the venous return, causing hypotension and compromising the uteroplacental perfusion. Therefore, placement of a wedge to facilitate a left uterine displacement is crucial. Given the procoagulant state during pregnancy, sequential compression devices should be placed on the lower extremities.

Describe the Perioperative Care of the Patient Undergoing a Second Trimester Repair of an NTD

Intraoperative management of the patient undergoing a prenatal closure of a NTD starts with the placement of a high lumbar/low thoracic epidural catheter to manage pain upon emergence as well as to provide postoperative analgesia. Maternal cross-matched blood as well as O Rh negative irradiated leukocyte reduced blood for the fetus should be available before proceeding with the induction of anesthesia. The operating room temperature should be raised to 26.6°C to avoid maternal and fetal hypothermia. Once the surgical field is prepped and draped and all the surgical equipment is ready, general anesthesia is induced. Close monitoring and optimization of the uteroplacental perfusion requires placement of an arterial line. Appropriate large bore IV access is necessary to administer fluids and to transfuse if necessary. Judicious management of fluids is extremely important, if possible limiting the total administration of intravenous crystalloids to less than 1 liter.

In order to provide optimal conditions during the closure of a NTD (open or fetoscopic), the fetus is administered atropine (20 mcg/kg), fentanyl (5–20 mcg/kg), and vecuronium (0.2–0.4 mg/kg) intramuscularly. During the open repair of a NTD, the exposure of the fetus must be limited to preserve fetal temperature. Replacement of amniotic fluid

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losses during the open repair is generally done with warm lactated Ringer's solution. Fetal monitoring during the prenatal closure of a NTD is performed by echocardiography with the frequent evaluation of fetal HR, contractility, and volume status. Another useful parameter of monitoring is the umbilical artery flow since absent or reverse diastolic flow may indicate significant fetal distress. If fetal distress is detected during the prenatal closure of a NTD, a rapid sequence of events is necessary to provide in utero fetal resuscitation. Placenta abruption, maternal hemorrhage, or umbilical cord compression should be excluded. Preservation of uteroplacental perfusion must be guaranteed along with preservation of uterine relaxation. Maternal MAP is increased by 15–20% of the preoperative values, aortocaval compression syndrome is avoided, maternal normothermia maintained, and oxygen delivery maximized. If fetal distress persists, administration of IM epinephrine in doses of 1–10 mcg/kg should be considered. In rare instances fetal transfusion may be necessary. Knowing that the fetal estimated total blood volume during the second trimester is 110 mL/kg facilitates calculation of fetal blood transfusion volume. If the fetal distress persists despite all the interventions, delivery with postnatal resuscitation by a neonatology team should be considered in a viable fetus.

An important consideration is the maintenance and preservation of uterine relaxation most commonly provided with the administration of volatile anesthetics. There is a direct correlation between MAC and uterine relaxation. However, higher MAC leads to significant maternal vasodilation and myocardial depression with resultant fetal acidosis. Previous studies looking at the effects of the administration of volatile anesthetics suggest that limiting exposure to volatile anesthetics until uterine manipulation for a hysterotomy can provide better hemodynamics, better preservation of fetal myocardial function, less fetal bradycardia, and better fetal acid base status. Some authors suggest administering total intravenous anesthesia of propofol and remifentanil and switching to volatile anesthetics immediately prior to the performance of the hysterotomy. Coadjuvants and alternative options to provide muscle relaxation include nitroglycerin (bolus of 50–100 mcg followed by a continuous infusion of 0.5–1 mcg/kg/min up to 20 mcg/kg/min), magnesium sulfate (bolus of 4–6 g followed by a continuous infusion of 1–2 g/hour), and subcutaneous administration of 0.25 mg terbutaline.

For vasopressor therapy, phenylephrine has been shown to be the first line therapy given the limited transfer through the placenta with limited effect on fetal acid base status. For the preservation of uteroplacental perfusion, the maternal MAP must be equal to or greater than 65 mmHg of the blood pressure or maintenance within 10% of the preoperative values. The uteroplacental flow lacks autoregulation and is dependent on the uterine perfusion pressure.

Once the closure of a NTD is completed, the amniotic fluid is replaced, and the uterine incision is closed. In the case of fetoscopic procedures, warm lactated Ringer's solution replaces the CO_2 that was previously insufflated. Local anesthetic is administered through the epidural catheter prior to emergence. The patient is extubated under conditions of complete reversal of neuromuscular blockade, being awake, and meeting extubation criteria including appropriate pain control.

Suggested Reading

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