Anesthetic Management of a Patient Undergoing an Ex Utero Intrapartum Treatment (EXIT) Procedure: A Case Report

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The ex utero intrapartum treatment (EXIT) procedure involves partial delivery of the fetus with the fetal-placental circulation maintained. This allows for management of the obstructed fetal airway via direct laryngoscopy, bronchoscopy, tracheostomy, or surgical intervention. These complex and often challenging procedures have been performed about 100 times in the United States to date. Recent advances in prenatal diagnosis of fetal congenital malformations, in particular, abnormalities involving the fetal airway, have allowed for the development of the EXIT strategy to convert potentially catastrophic situations during fetal delivery to a controlled environment. Indications for the EXIT procedure have expanded to a variety of congenital abnormalities, including fetal neck masses, lung or mediastinal tumors, congenital high airway obstruction syndrome, conjoined twin separation, and acute respiratory distress syndrome requiring transitioning from EXIT to extracorporeal membrane oxygen transitioning.

Various considerations must be managed by the anesthesia provider during the EXIT procedure to ensure positive maternal and fetal outcomes. Careful attention to achieving adequate uterine relaxation, maintaining maternal blood pressure, avoiding placental abruption, prioritizing fetal airway establishment, and providing return of uterine tone when indicated are examples of these considerations. In this case report, a parturient presented for an EXIT procedure secondary to fetal cystic hygroma.

Keywords: Anesthesia, difficult fetal airway, EXIT procedure, ex utero intrapartum treatment, fetal congenital malformations.
hygroma or teratoma diagnosed at 24 weeks' gestation. The parturient was currently at 37 weeks' gestation and denied all drug and food allergies. Her prior surgical history was for knee repair, with no adverse anesthetic outcomes reported. She reported no alcohol, tobacco, or recreational drug use. The medical history was unremarkable. Prenatal vitamins were the only medications that this patient said she took. The parturient was referred to the admitting facility by her obstetrician following routine fetal ultrasound, during which a neck mass was observed.

A follow-up MRI (magnetic resonance imaging) was completed at 30 weeks' gestation. The result revealed a multicystic mass in the right side of the fetus' neck that extended posteriorly to the cervical spine, anteriorly into the mediastinum, and into the right hemithorax. The mass caused fetal heart displacement to the left, and penetrated the subcutaneous prethoracic bony chest. Hydrops was present. The mass had increased in size from that in the original ultrasound. The trachea appeared patent. Amniotic fluid was adequate, and no other abnormalities were seen.

Anticipating potential difficulty in establishing the newborn's airway at birth, collaboration between the anesthesia providers, obstetricians, neonatologists, pediatric surgeons, and nursing staff occurred. A specific and detailed EXIT operative protocol was created and was given to all participating healthcare providers involved in this case. A researched-based fetal airway management algorithm was included in the protocol (Figure 1). Room layout, specific personnel, and equipment positions were mapped out for each phase of this procedure, consisting of a cesarean delivery, establishment of the newborn airway by the neonatologist, and establishment of the newborn airway by the pediatric surgeon if necessary. Two mock trials of this procedure were performed 6 weeks and 1 week before the surgery was scheduled.

Results of the preoperative examination revealed an awake and cooperative parturient breathing room air with oxygen saturation at 99%. The patient’s heart rate was 86/min, and blood pressure was 118/65 mm Hg. Airway assessment revealed a Mallampati 3 airway with full range of motion. Lactated Ringer’s infusion existed via a right-hand 18-gauge peripheral intravenous (IV) line initiated in the preoperative holding area. A second 18-gauge peripheral IV line was heparin locked in the left hand. One 500-mL bolus was administered before the patient entered the operating room. Pregnancy with concomitant physical changes indicated that this patient had an ASA physical status class III.

A preoperative laboratory evaluation included a urinalysis, a basic metabolic panel, and a complete blood count, all of which had results within normal physiologic parameters. A hemoglobin level of 12.9 g/dL was noted. The patient was typed and cross-matched with 2 U of packed red blood cells in the operating room, and 4 additional units were placed on hold. The patient received 30 mL of sodium citrate and 2 g of cefazolin IV preoperatively.

When the patient entered the operating room, she was positioned with left uterine displacement, and all standard monitors were placed. Fetal heart tones were 151/min. A radial arterial line was inserted without difficulty using local anesthesia. Subsequently, a rapid-sequence induction with cricoid pressure took place using 100 µg of fentanyl, 370 mg of sodium thiopental, and 120 mg of succinylcholine with atraumatic direct laryngos-
copy. A 6.5-cm endotracheal tube was placed without difficulty. A video laryngoscope (GlideScope, Verathon, Bothell, Washington) and Eschmann catheter were on standby but were not required. General anesthesia was maintained with 2.0% sevoflurane in 100% oxygen. In order to relax the gravid uterus, 40 µg of subcutaneous terbutaline was administered, and a nitroglycerine drip was on standby. Umbilical cord compression was prevented with IV lactated Ringer’s infusion via a fluid warmer (Hotline, Smiths Medical, St Paul, Minnesota).

**Figure 1. Operative Protocol: Fetal Airway Management Algorithm**

Abbreviations: MRI, magnetic resonance imaging; EXIT, ex utero intrapartum treatment.
An amnioinfusion technique was administered via the rapid infuser to maintain uterine volume. Maternal blood pressure was supported with 5-mg ephedrine boluses as needed to ensure that the blood pressure decreased no lower than 10% of baseline, with a dopamine drip on standby. Hemoglobin values were assessed via arterial blood gas analysis every 30 minutes. Mechanical ventilation continued throughout the case, with tidal volume, rate, and positive end-expiratory pressure adjusted to normal respiratory parameters.

The fetus was partially delivered from the head to the thorax 14 minutes after skin incision, and fetal pulse oximetry and echocardiograph monitors were placed. The neonatologist suctioned and evaluated the fetus’s airway, followed by a moderately difficult intubation. The neonatologist successfully secured the airway after one attempt using a Miller size 0 laryngoscope blade and a 2.5-cm uncuffed endotracheal tube. Confirmation of endotracheal tube placement was made via lung auscultation and pulse oximetry. Moderate fetal movement was observed during the intubation that likely complicated this process. The fetus did not receive additional medications before intubation, but fentanyl, midazolam (Versed), and vecuronium were prepared for intramuscular injection had the neonatologist believed this was necessary to augment fetal anesthesia. Bronchoscopy equipment was available but not used. Pediatric surgical intervention was available but not required. With the neonate’s airway secured, the anesthesia team began methods to prevent uterine atony.

The fetal cord was clamped, and the entire neonate was delivered at 21 minutes after skin incision, with the fetal heart rate and oxygenation remaining stable (Figure 2). The female neonate weighed 3,510 g and had 1- and 5-minute fetal Apgar scores totaling 9. The neonate remained intubated and was transferred to the neonatal intensive care unit for observation.

After placental delivery, 40 U of oxytocin was infused in conjunction with uterine massage to facilitate adequate uterine contraction. Both methylergonovine maleate and carboprost tromethamine were immediately available but not needed. The patient received fentanyl, 50 µg IV, for intraoperative pain management and was redosed as needed to maintain baseline hemodynamic parameters. Neuromuscular blockade was given after delivery using rocuronium in 20-mg IV boluses to maintain no more than 1 to 2 twitches during train-of-four monitoring.

The EXIT procedure remained uneventful and lasted approximately 91 minutes. Urine output was clear yellow and averaged 150 mL/h. Intravenous crystalloid fluids administered totaled 2,000 mL. Estimated blood loss totaled 800 mL at the end of the case. The patient’s hemoglobin level remained greater than 11.5 g/dL, and no blood transfusions were administered. Maternal systolic blood pressure remained greater than 110 mm Hg throughout the case, with ephedrine doses totaling 15 mg.

On completion of the procedure, neuromuscular blockade reversal was administered using 4.0 mg of IV neostigmine and 0.6 mg of IV glycopyrrolate. A sustained tetany of 5 seconds was confirmed. Orogastric suctioning occurred, and then an awake extubation to nasal cannula took place once the patient met appropriate criteria for extubation.

The patient was transferred to the obstetric postanesthesia care unit and then admitted to a postpartum inpatient room 3 hours afterward. A debriefing session was held for all participating healthcare providers to review moments of success and identify areas for improvement. In the 24-hour postoperative period, the mother did not demonstrate any signs of increased bleeding, hypotension, or respiratory distress. Three days of inpatient recovery were uneventful, at which time the mother was discharged.

In the 24-hour postoperative period, the newborn’s vital signs, results of arterial blood gas analysis, and respiratory status remained stable. Ultrasound confirmed that the mass was a benign cystic hygroma measuring 13 cm × 6 cm. The neonate was extubated successfully 1 week later in the operating room, and multiple airway access devices were readily available. The neonate was discharged home 11 days after delivery, with instruction to be followed up carefully by her pediatrician.

The cystic hygroma was scheduled to be resected in 2 stages because of its penetration from the base of the skull to the tongue, heart, trachea, and great vessels. The neonate successfully underwent her first operation 29 days after delivery to remove the neck portion of the hygroma. The second part was planned in the following few months provided that no respiratory or cardiac difficulties arose.

**Discussion**

Patients undergoing an EXIT procedure have important
physiologic considerations that anesthesia providers must take into account. Providers not only must understand the large contrast between cesarean delivery and EXIT procedure goals but also must consider the anesthetic implications of the parturient and the fetus. Finally, it is important to recognize the advantages and disadvantages with each anesthesia option and pharmacologic agent available for patients undergoing an EXIT procedure so that the safest plan can be executed (Table 2).

A common misconception is that an EXIT procedure is merely a cesarean delivery. During the EXIT procedure, one important goal is to achieve a state of uterine hypotonia to maintain uteroplacental circulation using deep general anesthesia. This is markedly different from a normal cesarean delivery in which a regional technique is preferred and the goal is to maximize uterine tone to prevent postpartum hemorrhage. Another objective of the EXIT procedure is to achieve a surgical level of fetal anesthesia while preventing cardiac depression. In contrast, a goal of cesarean delivery is to minimize diffusion of anesthetic agents to the fetus. Finally, in an EXIT procedure there is no need to limit skin incision to delivery time, and the fetus is partially delivered with maintenance of placental support until the airway is secured. The longest reported placental support duration in a successful EXIT procedure lasted approximately 150 minutes. In a cesarean delivery, skin incision to delivery time is as quick as possible, the entire fetus is delivered, and the umbilical cord is cut immediately.

The EXIT procedure, like any other form of obstetric surgery, involves the treatment of 2 patients: the parturient and her baby. For this reason, it is recommended to have 2 anesthesia providers to divide these responsibilities. The risks associated with the parturient undergoing general anesthesia are still applicable during the EXIT procedure and include the increased chance for aspiration, the decrease in uterine artery perfusion and hypotension with supine positioning, and decreased functional residual capacity. Thus, a rapid-sequence induction with left uterine displacement is still required when administering general anesthesia to these patients. Also, these parturients are at increased risk of uterine atony and maternal hemorrhage. Therefore, the literature recommends having multiple pharmacologic agents to increase uterine tone in the operating room, including oxytocin, methylergonovine maleate, and carboprost tromethamine. The patient should have blood immediately accessible if hemorrhage ensues, and monitoring of hemoglobin levels will help guide transfusion requirements. In this case report, all of these recommendations were adhered to, and although many of these interventions were not required, it was important to be prepared for potential complications that could have easily occurred.

Support of the fetus during the EXIT procedure depends on preservation of uteroplacental gas exchange. Uterine artery blood flow is affected by maternal systemic blood pressure; therefore, maintenance of this pressure within 10% of baseline is crucial to ensure adequate fetal oxygenation, especially during the EXIT procedure. These facts provide the rationale for placing an arterial line before the induction of anesthesia in order to monitor maternal blood pressure more frequently than a noninvasive cuff can achieve (Table 3). The literature reports a variety of methods for increasing maternal blood pressure when indicated. Marwan and Crombleholme recommend ephedrine because it acts selectively on the mother’s peripheral vascular resistance and spares the placental circulation. Chang and Kuczkowski encourage the use of dopamine infusion, as it is easily titratable, improves blood flow to the kidneys and viscera, and presumably increases uterine flow. In other case reports, phenylephrine has been successfully used. In this case report, ephedrine was used with dopamine drip on standby in case continued hypotension had occurred. The anesthesia providers attributed the lack of prolonged hypotension to the relatively lower dose of volatile agent used for this type of procedure. Maintenance of uterine volume is also important to prevent uterine contraction and is accomplished by avoiding complete delivery of the fetus and by the use of amnioinfusion. A rapid infusion device is preferred to prevent cord compression and likely decreased the vasoressor requirements in this case report.

As mentioned earlier, uterine hypotonia to maintain uteroplacental circulation is a primary goal during the anesthetic management of a patient requiring the EXIT procedure. The recommendation of high concentrations of potent inhalational agents of at least 2.0 minimum alveolar concentration (MAC) has historically been encouraged for this effect but is of controversy in more recent literature. With the use of adjunct uterine

<table>
<thead>
<tr>
<th>Indication</th>
<th>Pharmacologic agent</th>
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<tr>
<td>Decrease uterine tone</td>
<td>Volatile agent, nitroglycerin, indomethacin, and/or terbutaline</td>
</tr>
<tr>
<td>Maintain blood pressure</td>
<td>Ephedrine, dopamine, and/or phenylephrine</td>
</tr>
<tr>
<td>Promote adequate fetal anesthesia</td>
<td>Fentanyl, vecuronium, rocuronium, and/or ketamine</td>
</tr>
<tr>
<td>Increase uterine tone</td>
<td>Oxytocin, methylergonovine maleate, and/or carboprost tromethamine</td>
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Table 2. Recommended Drugs for EXIT Procedure
Abbreviation: EXIT, ex utero intrapartum treatment.
relaxants, it appears as though 0.5 to 1.0 MAC can be used with equivalent uterine relaxation, while avoiding the cardiovascular depressive effects of high concentrations of inhalation agents. In multiple case reports, a nitroglycerin bolus was given immediately before uterine incision, followed by a continuous drip, with successful relaxation achieved. Benefits reported for nitroglycerin use included its high potency, easy titration, and short duration. Castillo et al administered indomethacin preoperatively, which has the additional benefit of preventing prostaglandin-mediated increases in placental resistance as well as decreasing uterine tone. Finally, uterine relaxation can be enhanced with tocolytics such as terbutaline, as in this case report; however, providers must be cautious of the potential for effects lasting up to 4 hours, which could encourage maternal hemorrhage after fetal delivery.

In this case report, the neonatologist was designated with the responsibility to secure the fetus’s airway. In the literature, however, this is not always the scenario, and the anesthesia team also must be prepared to secure the airway during an EXIT procedure. The most important aspect of fetal airway management during an EXIT procedure is preparedness for every contingency. This is why an airway algorithm must be established with all providers informed of their role in this process. Also, if fetal movement is complicating the intubation process or inhibiting pulse oximetry readings, intramuscular fentanyl, vecuronium, rocuronium, and ketamine have all been reported as successful adjuncts to promoting adequate fetal anesthesia. This may be a common challenge during the EXIT procedure as it takes approximately 1 hour for fetal volatile concentrations to reach 70% of maternal levels. The literature encourages the use of armored endotracheal tubes, as they can prevent the collapse of an unsupported tube secondary to mass compression.

After securing the airway, it is vital to confirm the position of the endotracheal tube using flexible bronchoscopy, especially in patients with cervical and mediastinal masses. Eschertzhuber et al report a case in which bronchoscopy was ineffective as a means for correct placement secondary to secretions. These authors used capnography and achieved a successful outcome. Another case report discusses the use of carbon dioxide devices as a means of confirming an endotracheal tube with questionable efficacy due to continuous uteroplacental circulation. In this case report, fetal movement was noted and could have been reduced had intervention occurred. In addition, an armored endotracheal tube, capnography, and bronchoscopy were not used, which could have resulted in an adverse outcome.

The literature on the EXIT procedure frequently discusses the debate between using regional anesthesia vs a general anesthesia technique. General anesthesia is associated with a higher maternal morbidity and mortality rate due to failed intubation and aspiration of gastric contents. Also general anesthesia uses volatile agents that can depress both maternal and fetal cardiac function. Neuraxial anesthesia is the anesthetic approach of choice in normal cesarean deliveries and provides greater patient satisfaction because of the mother’s ability to witness the newborn’s birth. Many drawbacks to the regional technique during an EXIT procedure have been reported, including increased risk of severe hypotension, increased fetal movement requiring adjunct anesthetics, and the possibility of the mother witnessing fetal demise. To date, it appears as though general anesthesia is still recommended, with adequate preparation for a difficult airway or aspiration incident, and decreased volatile agent administered.

### Conclusion
During an EXIT procedure, anesthesia providers become one aspect of a multidisciplinary team that must work together to achieve the common goal of a positive outcome for mother and child. An organized approach to planning, practicing, and implementing a surgical agenda should occur to ensure that every circumstance can be handled safely. Providing general anesthesia during an EXIT procedure is a critical time for providers, who must consider many aspects of the procedure in order to safely manage maternal and newborn anesthesia. It is imperative that the contrast between cesarean delivery and EXIT procedure is known as well as that a heightened awareness is maintained for maternal hemorrhage and difficult airway. Also, ensuring that maternal blood pressure and uterine volume are adequate is vital to the preservation of uteroplacental gas exchange. Furthermore, uterine atony, a systematic approach to fetal airway establishment, and general anesthesia are recommended by the literature to facilitate this surgical procedure.

### Table 3. Recommended Equipment for EXIT Procedure

<table>
<thead>
<tr>
<th>Patient</th>
<th>Equipment</th>
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<tbody>
<tr>
<td>Parturient</td>
<td>Arterial line, multiple peripheral intravenous lines, rapid infusion device, fluid warming device, laryngoscopes, endotracheal tubes, difficult airway equipment</td>
</tr>
<tr>
<td>Neonate</td>
<td>Fetal ultrasound, pulse oximetry, suction equipment, laryngoscopes, armored endotracheal tubes, stethoscope, flexible bronchoscope, capnography monitor</td>
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Abbreviation: EXIT, ex utero intrapartum treatment.
volatile agents, tocolytics, and uterine hypertonic medications is of great importance.2,3,6

Although EXIT procedures are rare, recent advances in the antenatal diagnosis of fetal congenital malformations of the airway could increase the incidence of this challenging surgery because it has been shown to improve perinatal outcomes.3-5,12 It is also important to recognize fetal airway compromise quickly when no prenatal care has been received, and to adopt some of the EXIT principles in order to successfully establish the newborn’s airway.6 Furthermore, the limited literature regarding anesthesia management during EXIT procedures should be expanded, as it is currently restricted to a collection of case reports with empirical suggestions. Anesthesia during an EXIT procedure is manageable, even in difficult cases, provided that all medical, surgical, and anesthesia obstacles are recognized and evaluated for best practice methods.

REFERENCES

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