Role of anesthesiologist in ex utero intrapartum treatment procedure: A case and review of anesthetic management

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Abstract

The ex utero intrapartum treatment (EXIT) procedure is a rare form of perinatal resuscitation. It is basically a bridge therapy between partial delivery of the child and stabilization of its cardiorespiratory functions. This procedure has multiple anesthetic challenges including maternal anesthesia, maintenance of uteroplacental flow, tocolysis till the neonate is stabilized, management of postpartum hemorrhage, fetal, and neonatal anesthesia. This review also describes a case of cervical teratoma in fetus, for which the EXIT was performed in our institute. In addition to the case description, multiple concerns specific for EXIT procedure are discussed in this review.

Keywords: Cervical teratoma, ex utero intrapartum treatment, tocolysis, uteroplacental blood flow

Introduction

Large neck mass in the fetus has the potential for causing airway obstruction and fetal demise after delivery of the newborn.[1] Ex utero intrapartum treatment (EXIT) is the name given to a clinical procedure where a fetus with antenatally diagnosed life-threatening airway or pulmonary abnormalities is oxygenated through an attached placenta during delivery by cesarean section till the airway is secured and/or extracorporeal membrane oxygenator (ECMO) is established. The first EXIT was reported by Norris et al. as perinatal surgery in the year 1989.[2]

The EXIT procedure presents unique and multiple anesthetic challenges. First, unlike a standard cesarean section, the conduct of anesthesia during this procedure requires uterine tocolysis to prevent intrapartum placental separation despite a surgically open uterus.[3] Second, the steps need to be taken to prevent postpartum hemorrhage (PPH) or aggressive management if it does occur after the neonate is separated. EXIT procedure has been reviewed by many authors, and a case of cervical cystic hygroma with cord around the neck has been reported from India.[4,5] We describe the successful anesthetic management of an EXIT procedure for a fetus with antenatally diagnosed large anterior neck teratoma and present the literature review on perioperative management of such cases.

Case Report

Permission for publication of the case details for research purpose was obtained from the patient. A 32-year-old third gravida at 35-week gestation weighing 70 kg was referred to our institution for peri-partum management when routine obstetric ultrasound revealed a large neck mass in the fetus. She was detected to be hypothyroid in the first trimester and...
was on levothyroxine 100 µg/day. Recent thyroid function tests were normal. There were no other medical or obstetric comorbidities in the mother.

The antenatal ultrasound revealed a 10.1 × 8.2 cm solid cystic anterior neck mass in the fetus and polyhydramnios. The trachea could not be visualized. However, fetal lungs appeared normal. Magnetic resonance imaging (MRI) of the fetus showed solid cystic mass consistent with teratoma, with intrathoracic extension. The fetal cervical spine was hyper-extended due to the mass [Figure 1].

As the trachea was not visualized in the preoperative ultrasound, failure to secure the neonatal airway was anticipated and hence EXIT procedure followed by tracheal intubation or tracheostomy was planned. A multidisciplinary team consisting of obstetricians, anesthesiologists, pediatric surgeons, otorhinolaryngologists, and neonatologists were assembled.

Preoperatively, the patient was explained about the need for the procedure, its outcome, and possible complications. Logistical issues included arrangement of the operating room (OR) and allocation of duty to each specialty. The main neonatal issue was how to secure the airway, for which plan A was a direct conventional laryngoscopy/rigid bronchoscopy at delivery of the fetal head, failing which plan B was to be activated, which was to attempt to secure the neonatal airway with the neonate kept on a Mayo stand, still connected to the placenta which was to serve as a cardiopulmonary bypass circuit for fetal oxygenation. Plan C was to perform a tracheostomy.

Standard aspiration prophylaxis was administered to the mother an hour before the procedure. The OR was warmed and was equipped with two sets of anesthetic workstations, suction apparatus, nurses’ trolley, and electrocautery. In addition, a neonatal resuscitation trolley with a radiant warmer was set up. The schematic representation of our OR arrangement is shown in Figure 2.

After transfer to the OR, a large bore intravenous (IV) access was secured after local anesthetic (LA) infiltration and routine American Society of Anesthesiologists monitoring were instituted in the mother. A lumbar epidural catheter was placed between the second and third lumbar interspinous levels in sitting position, following which the patient was positioned supine with a pelvic wedge. Left radial artery and right internal jugular vein were cannulated with LA infiltration using ultrasound guidance. Controlled amniocentesis was then performed by the obstetricians under ultrasound guidance and approximately 1 L of liquor was removed, with the patient receiving 100% oxygen at 6 L/min. Anesthesia was induced with fentanyl and thiopentone, and tracheal intubation was facilitated with suxamethonium. Tocolysis was rapidly initiated with high dial settings of desflurane (12%) in 100% oxygen to achieve a minimum alveolar concentration (MAC) of 2. Obstetricians confirmed adequate abdominal and uterine relaxation by palpation and proceeded with skin incision. Nitroglycerin (NTG) infusion at 1 µg/kg/min was infused through the central line to maintain tocolysis. Simultaneously, phenylephrine infusion was started at 25 mcg/min to maintain maternal blood pressure and uteroplacental blood flow.

Uterine incision was made with a harmonic scalpel to prevent blood loss from the relaxed uterine edges. The head and neck of the neonate was delivered, and a Masimo neonatal pulse oximeter was attached which recorded an oxygen saturation (SpO₂) of 64%–66%. Tracheal intubation of the neonate was attempted first with size-zero Miller blade and subsequently with a rigid bronchoscope, both of which were unsuccessful. The neonate, still attached to the placenta, was

![Figure 1: Magnetic resonance imaging done at 22 weeks of gestation showing solid cystic lesion in front of neck](image1)

![Figure 2: Operating room arrangement](image2)
then delivered onto a Mayo stand kept a few inches away from the maternal abdomen and the pulsating cord covered with warm, wet saline-soaked sponges. Atropine (60 µg) was administered intramuscularly to the neonate and IV access was secured with a 24-gauge cannula. Another attempt at intubation was made, which failed due to distorted trachea and hyperextended neck due to the mass. The neonate did not move or grimace during any of the maneuver, indicating adequate anesthetic depth. A unanimous decision was then made for surgical tracheostomy.

Surgical incision was made at the lower margin of the mass, just above the suprasternal notch. There was no fetal response or tachycardia to surgical incision. Neonatal tracheostomy per se is a difficult task and this was further increased by the large and immobile anterior cervical mass. The standard pediatric tracheostomy tube was found to be too short as the trachea was deep and deviated. A 3.0 mm internal diameter endotracheal tube was inserted through what appeared to be the tracheal stoma and connected to a sterile Jackson Rees circuit, but there was no trace of end-tidal carbon dioxide or any visible chest rise after multiple attempts. Throughout these attempts (nearly 60 min), the pulse oximeter showed a SpO₂ reading ranging from 64% to 82% (saturation >30% in a fetus is normal).[6] The tracheostomy had to be abandoned. Direct laryngoscopy was again performed, and as the surgeon lifted the mass away from the neck, a small air bubble started to appear from glottic opening, and tracheal intubation was done. A visible chest rise was now accompanied by a capnograph, appearance of end-tidal desflurane, and increase in SpO₂ to 100%. The fetus did not move at any point of time, and there was no need for extra fetal anesthesia. Figure 3 shows fetus with large mass in front of neck after tracheal intubation.

Following successful neonatal tracheal intubation, termination of tocolysis was announced. NTG and desflurane were discontinued. Oxytocin infusion (20 units in 500 ml normal saline) was started, the umbilical cord clamped, and placenta delivered by controlled traction and uterine massage. Simultaneously, intramuscular methylergometrine 200 µg was administered to the mother to facilitate uterine contraction. These measures were sufficient to ensure satisfactory uterine tone, and further uterotonics were not needed. The total duration of tocolysis was recorded, as 70 min. Nitrous oxide was introduced, and 10 ml of 0.1% bupivacaine with 3 mg morphine was administered through the epidural catheter. Surgery was completed and the mother’s trachea was extubated uneventfully. Total blood loss was 1000 ml. Postoperative course of the mother was uneventful.

The neonate was stabilized in the Neonatal Intensive Care Unit (NICU) and was operated on the first day of life. The mass was excised, and a formal surgical tracheostomy was done as the recurrent laryngeal nerves were presumably irretrievably injured. The mother and the neonate were discharged home after 15 days. Unfortunately, we came to know that the neonate succumbed to recurrent aspiration and infections at 2 months of age.

**Discussion and Review of Literature**

The EXIT procedure is a resuscitative treatment to secure the airway or circulation in fetus with obstructed airway or severe cardiopulmonary malformations who are unlikely to survive without intervention. There are several subtypes, depending on the indication [Table 1].[6,7]

The EXIT procedure thus provides a bridge to intubation or ECMO. It allows for controlled delivery of the neonate and fetal airway intervention while gas exchange is still taking place at the placenta. The etiology of neck mass causing respiratory distress is multifactorial [Table 2].

Incidence of cervical teratomas is reported to be 1 in 20,000–40,000 live births.[8] Significant airway compression

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**Table 1: Indications of ex utero intrapartum treatment procedure**

| EXIT till   | Examples                                           |
|-------------|----------------------------------------------------|
| Establishment of airway | Cervical teratoma (as in the present case) |
|             | Thyroid goiter                                    |
|             | Laryngeal or tracheal atresia                     |
| Resection of mass lesion | Large thoracic masses                           |
|             | Pericardial or mediastinal teratoma               |
| ECMO establishment | Severe CDH                                        |
| Separation  | Severe cyanotic congenital heart disease           |
|             | Conjoined twins with airway or major cardiovascular communications |

EXIT = Ex utero intrapartum treatment, ECMO = Extracorporeal membrane oxygenation, CDH = Congenital diaphragmatic hernia
Table 2: Neck masses which can cause potential airway obstruction in the neonate at birth

| Branchial cleft cyst | Laryngocele |
|----------------------|-------------|
| Cervical teratoma    | Lipoma      |
| Congenital goiter    | Lymphangioma|
| Cystic hygroma       | Neural tube defects |
| Cystic teratoma      | Neuroblastoma|
| Ectopic thymus       | Thyroid tumors |
| Hamartoma            | Thyroglossal duct cyst |

is common. Undetected or poorly managed cervical teratomas might have adverse outcomes. The fetus in the present case had a large, solid cystic teratoma causing hyperextension of the neck.

EXIT procedure is way different from cesarean section. The basic steps involved in any EXIT procedure are:
1. Maternal anesthesia
2. Controlled maternal amnioreduction
3. Initiation of tocolysis
4. Hysterotomy with continuous amnio-infusion
5. Partial delivery of the neonate
6. Care of the umbilical cord
7. Securing the fetal airway
8. Termination of tocolysis
9. Aggressive management of PPH
10. Transport of neonate to surgery or NICU.

Management of EXIT procedure should be carried out in a tertiary care center where provisions for comprehensive maternal and neonatal intensive care services are available. The multidisciplinary team should meet well before the procedure. Anesthesiologist has a central and multimodal role in the following:
- Providing maternal anesthesia
- Maintaining uteroplacental circulation and maternal hemodynamic stability
- Adequate tocolysis to prevent placental separation
- Fetal anesthesia
- Assisting with primary facilitators in neonatal airway management
- Ensuring return of uterine tone
- Aggressive management of PPH if it occurs
- Providing anesthesia to the newborn for surgery if required.

The anesthesiologist takes a lead role in the allocation of duty to colleagues of different specialties, accommodation of extra equipment and personnel in the OR, and preventing confusion.

Both general as well as regional anesthesia have been used for maternal management during EXIT. General anesthesia involves endotracheal intubation and maintaining a deep level of inhalational anesthesia, which results in the reduction of uterine tone (tocolysis). Optimal tocolysis is one of the cornerstones of EXIT as the fetal survival depends on an intact uteroplacental circulation. All inhalational agents used for general anesthesia are excellent tocolytics. Anesthetic depth is initially kept at 1 MAC and subsequently stepped up to 2–3 MAC guided by uterine tone estimation by the obstetricians. It is also important to maintain uterine volume to prevent placental separation, and this is accomplished by continuous amniinfusion with warm saline, and only partial delivery of the neonate. All inhalational agents ranging from halothane to desflurane have been successfully used for EXIT. Desflurane was most commonly used by Lin et al. (61 of the 65 cases).

The depth of tocolysis induced by inhalational agents obviates the need for IV tocolytics, which are associated with hypotension requiring vasopressors. We used desflurane for two reasons: sympathetic stimulation inherent to desflurane would be useful to prevent hypotension; low blood–gas partition coefficient of desflurane would allow more rapid titration and thus the ability to control uterine tone better, and also allows rapid elimination during reversal. Remifentanil total IV anesthesia (TIVA) is also reported in literature.

A few case reports have been published describing the use of neuraxial anesthesia for EXIT. George et al. and Fink et al. used combined spinal epidural for anesthesia and NTG for tocolysis. Gagnon et al. used epidural anesthesia, while subarachnoid block was used by Henry et al. Intrathecal catheter and NTG bolus have been reported in literature by Benonis and Habib.

Neuraxial anesthesia alone may result in significant maternal anxiety and/or discomfort, necessitating the use of sedation. Fink et al. also added remifentanil infusion to this technique and stated that it resulted in adequate analgesia in the fetus, permitting laryngoscopy. However, the author/s noted “respiratory depression” and “sedation” in two parturients, one of whom was morbidly obese (body mass index >46 kg/m²). In our opinion, this may not be ideal, given the major nature of the procedure and propensity for maternal blood loss. Further, in the majority of these reports, the mother required pressor support and the newborn required intramuscular anesthesia and/or relaxant for intubation. Oliveira et al. recommend that neuraxial anesthesia in parturients involved in EXIT may be used if GA is contraindicated, for any reason.

Among other pharmacological agents, NTG, terbutaline, indomethacin, and magnesium sulfate have all been effectively used for tocolysis. They are especially required if the mother has been administered...
neuraxial anesthesia. NTG infusion at 10–100 µg/min produces profound tocolysis. The speed of onset and the efficacy of NTG effect are not equaled by other classes of available tocolytic drugs such as betamimetics or magnesium sulfate. In the experience of O’Grady in 22 patients, maternal complications were infrequently observed.\[30\] The drug appears to have no direct adverse effects on the fetus. NTG doses of >400 µg/min are associated with hypotension and cardiovascular instability. Unlike vital organs which regulate their blood supply at various blood pressures, uteroplacental blood flow is not autoregulated. Both a fall in mean arterial pressure (MAP) and an increase in uterine vascular resistance can impair utero-placental blood flow and cause fetal compromise. Commonly, phenylephrine has been used to maintain MAP\[20\]. MAP is ideally targeted within 20% of baseline value to avoid precipitous fall in uterine blood flow.\[7\]

\[
\text{Uterine blood flow} = \frac{\text{Uterine arterial pressure} - \text{Uterine venous pressure}}{\text{Uterine vascular resistance}}
\]

Special care needs to be exercised while performing the hysterotomy, as the myometrium is rendered hypotonic during tocolysis, which may result in severe bleeding, excessive blood loss, maternal hemodynamic instability, and interference with management of the fetus. Coagulating instruments such as the harmonic scalpel are very useful in this regard, which were used in the present case. However, Butwick \textit{et al.}\[12\] described profound maternal hemorrhage during EXIT performed using 2% sevoflurane, despite the use of the harmonic scalpel, necessitating abandonment of the procedure. The fetus was mask ventilated till bronchoscopy could be done. In the majority of cases of EXIT, however, blood loss was well within 1500 ml avoiding the need for transfusion.

We placed an epidural catheter to facilitate good postoperative analgesia. Intrathecal morphine\[17\] in low doses (100–150 µg) has also been used for maternal analgesia. Analgesia deserves special attention since the procedure takes longer than a standard caesarean section with more visceral manipulation.

Fetal airway may be extremely difficult to secure, as was in this case. Tracheostomy may also be challenging or impossible due to distortion by tumor. Case series of EXIT procedures involving cervical teratomas and their airway management is shown in Table 3.

Backup plans for securing the airway should be in place. These include and are not limited to fiberoptic bronchoscopy\[34\] and retrograde intubation.\[31\] Many algorithms for fetal airway management are reported in literature [Figure 4].

Fetal monitoring includes observing the color of the neonate, cord pulsations, precordial stethoscope, fetal scalp electrodes,\[35\] umbilical cord blood gases,\[17,36\] continuous fetal Doppler,

![Figure 4: Fetal airway management algorithm: adapted from Marwan et al. (2006)](image)

| Author          | Year | Cervical teratomas of total number of EXIT | Intubation | Tracheostomy | Other        |
|-----------------|------|-------------------------------------------|------------|--------------|--------------|
| Liechty \textit{et al.}\[19\] | 1997 | 5/5                                       | 4          | 1            | -            |
| Mychaliska \textit{et al.}\[18\] | 1997 | 2/8                                       | 1          | 1            | -            |
| Bouchard \textit{et al.}\[20\] | 2002 | 13/31                                     | 7          | 5            | Abandoned    |
| Hirose \textit{et al.}\[28\] | 2004 | 5/52                                      | 1          | 3            | Resection 1  |
| Lazar \textit{et al.}\[32\] | 2011 | 14/24                                     | 1          | 1            | Bronchoscopy 12 |
| Laje \textit{et al.}\[33\] | 2012 | 17/87                                     | 12         | 5            | -            |
| Lin \textit{et al.}\[20\] | 2016 | 12/65                                     | NA         | NA           | NA           |

\textit{EXIT}=Ex utero intrapartum treatment, \textit{NA}=Not available

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**Table 3: Large series of ex utero intrapartum treatment procedures described in literature**

| Author          | Year | Cervical teratomas of total number of EXIT | Intubation | Tracheostomy | Other        |
|-----------------|------|-------------------------------------------|------------|--------------|--------------|
| Liechty \textit{et al.}\[19\] | 1997 | 5/5                                       | 4          | 1            | -            |
| Mychaliska \textit{et al.}\[18\] | 1997 | 2/8                                       | 1          | 1            | -            |
| Bouchard \textit{et al.}\[20\] | 2002 | 13/31                                     | 7          | 5            | Abandoned    |
| Hirose \textit{et al.}\[28\] | 2004 | 5/52                                      | 1          | 3            | Resection 1  |
| Lazar \textit{et al.}\[32\] | 2011 | 14/24                                     | 1          | 1            | Bronchoscopy 12 |
| Laje \textit{et al.}\[33\] | 2012 | 17/87                                     | 12         | 5            | -            |
| Lin \textit{et al.}\[20\] | 2016 | 12/65                                     | NA         | NA           | NA           |

\textit{EXIT}=Ex utero intrapartum treatment, \textit{NA}=Not available
Exit surgery. In many series is attributed to pulmonary hypoplasia and respiratory distress syndrome. One series described fetal mortality as 15%. [20]

Fetal outcome was not completely favorable in many cases, and included an inability to secure the airway, sepsis, cardiac failure, [22] necrotizing enterocolitis, [11] recurrent tension pneumothorax, [15] laryngotracheomalacia, [34] neurologic deficit, [32] bleeding into the airway, [25] and death. Death in many series is attributed to pulmonary hypoplasia and respiratory distress syndrome. One series described fetal mortality as 15%. [20]

EXIT is not the end; most of the newborns succumb to ignorance of the caretakers. In many cases, the child requires a long-term tracheostomy, and there is a need for multiple surgeries.

Conclusion
Mortality without EXIT in cervical teratoma is >60%, and EXIT is a safe and effective way of delivering fetuses with obstructed airway. EXIT needs orchestrated teamwork and planning for successful outcomes.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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