Ex Utero Intrapartum Treatment Procedure: A Peripartum Management Strategy in Particularly Challenging Cases

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Modern obstetric care continues to improve on the early prenatal detection and diagnosis of many congenital malformations.[1] Prenatally detected malformations affecting the fetal airway or pulmonary function are of particular concern because of the risks incurred at the time of delivery. Resuscitation of these infants at birth can be quite complicated with a significant risk for hypoxia, ischemic brain injury, or even death if the airway cannot be promptly secured. These types of congenital malformations may benefit from an intrapartum strategy to safely secure the airway and reduce the associated risks of delivery and neonatal resuscitation.

Early strategies aimed at reducing the risk of hypoxia associated with the delivery of these patients attempted to maintain the uteroplacental circulation while the obstructed airway was secured and the infant was intubated.[2,3] These early attempts were performed under the assumption that the uteroplacental circulation and gas exchange are maintained by simply keeping the umbilical cord intact. These early case reports made little attempt to prevent normal uterine contraction during the procedure, and in some cases, the fetus was removed entirely from the uterus to instrument the airway. As we now recognize, these maneuvers can lead to rapid loss of uterine volume and cessation of uteroplacental circulation and gas exchange. These approaches may be no better than clamping the umbilical cord and passing the infant off for urgent airway management.

In contrast, the development of the ex utero intrapartum treatment (EXIT) procedure was based on the central principle of controlled uterine hypotonia to preserve the uteroplacental circulation and gas exchange.[4] The EXIT procedure is a technique that has been refined and is now instrumental in the management of complex malformations, particularly of the airway. Growing experience with the EXIT technique in fetal surgery centers that routinely treat these fetuses has demonstrated a high level of maternal and fetal safety that has led to expanded indications for its use.

To illustrate the diverse and growing indications for this perinatal management strategy, we present 4 patients, with approval from the Cincinnati Children's institutional review board (IRB#08-01-03). These 4 patients underwent an EXIT procedure at The Fetal Care Center of Cincinnati (FCC) for the management of 4 quite different congenital malformations.

EXIT-TO-AIRWAY: CERVICAL TERATOMA

A 36-year-old woman gravida 2, para 0-0-1-0, was referred for evaluation of a fetal neck mass and polyhydramnios diagnosed at 21 weeks' gestation. An initial prenatal ultrasound scan revealed a large, complex, mostly cystic, fetal neck mass measuring 5.0 × 6.0 × 6.7 cm, which increased to 9.5 × 10.0 × 11.0 cm within 4 weeks. Her amniotic fluid index (AFI) measured at 28 weeks' gestation was 34 cm (>95th percentile).[5] At this time, an amnioreduction was performed and the patient was referred to the FCC. Two days later, a fetal MRI at the FCC confirmed a large, predominantly right sided, multiseptated cervical mass measuring 9.1 × 13.2 × 14.0 cm with marked displacement of the oropharynx, hypopharynx, and trachea to the left. The fetal lung volume measured 35 cm^3 at 28 weeks' gestation (within 1 standard deviation below the mean for gestational age).[6] There was no evidence of fetal hydrops. Doppler ultrasonography demonstrated moderate vascularity of the cervical mass. Echocardiography revealed normal cardiac anatomy and function. However, an increased combined cardiac output of 587 mL/min/kg (>95th percentile)[7] was noted as a consequence of the vascular cervical teratoma. Karyotype analysis showed a normal 46, XY infant.

The patient was then scheduled for an EXIT procedure at 35 weeks' gestation to allow for increased fetal lung maturity. The patient was also relocated to Cincinnati in the

AFI	Amniotic fluid index	EXIT	Ex utero intrapartum treatment
CDH	Congenital diaphragmatic hernia	FCC	The Fetal Care Center of Cincinnati
CHAOS	Congenital high airway obstruction syndrome	HLHS	Hypoplastic left heart syndrome
ECMO	Extracorporeal membrane oxygenation	MRI	Magnetic resonance imaging

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event, of preterm labor at 32 weeks' gestation. Shortly after relocation, at 32.5 weeks' gestation, the mother experienced premature rupture of membranes and went into active labor. She underwent an emergent EXIT-to-airway procedure, during which the fetus was only partially exteriorized from the uterus to maintain uteroplacental circulation. The airway was assessed by direct laryngoscopy and bronchoscopy, which revealed marked deviation of the airway and compression of the larynx and trachea. Only after relieving the laryngeal compression by placing traction on the cervical teratoma was endotracheal intubation possible (Figure 1; available at www.jpeds.com). The umbilical cord was then clamped after the administration of surfactant and placement of arterial and venous umbilical catheters. The uteroplacental bypass time, as defined by the time from hysterotomy to clamping of the umbilical cord, was 60 minutes. After surgery, the neonate was stabilized on minimal mechanical ventilatory settings. At 3 days of life, the infant underwent resection of the giant cervical teratoma without complication. He was extubated at 6 weeks of age and was discharged to home at 8 weeks of age on bolus gastrostomy tube feeds. The pathology report confirmed the diagnosis of cervical teratoma.

EXIT-TO-AIRWAY: CHAOS

A 32-year-old woman, gravida 2, para 1-0-0-1, was self-referred to the FCC at 23 weeks' gestation for a pregnancy complicated by multiple congenital anomalies, including a fetal lung anomaly characterized by bilaterally enlarged echogenic lungs. Before her referral, she was misdiagnosed with bilateral congenital pulmonary airway malformations. Further evaluation at the FCC revealed bilaterally enlarged lungs with inversion of both hemidiaphragms and significant distension of the tracheobronchial tree below the larynx, consistent with congenital high airway obstruction syndrome (CHAOS). A 5-mm gap was seen between the distended fluid-filled trachea and the fluid-filled hypopharynx, believed to represent a complete laryngeal atresia. Massive ascites, placentomegaly, polyhydramnios (AFI = 33 cm, >95th percentile), and soft tissue edema were also noted. In addition, a horseshoe kidney and a 2-vessel umbilical cord were seen.

The patient was monitored with weekly ultrasound scanning, which continued to show severe polyhydramnios. At 32 weeks' gestation an improvement in fetal ascites and edema were seen, suggesting a possible spontaneous perforation through the presumed laryngeal atresia. Repeat fetal MRI and ultrasound scanning at 33 weeks' gestation confirmed an improvement in the distention of the tracheobronchial trees of both lungs with normal configuration of the diaphragms. A decrease in soft tissue edema and ascites was also seen, as well as resolution of the placentomegaly (Figure 2; available at www.jpeds.com). Polyhydramnios, however, persisted with an AFI of 38 cm. In an attempt to prolong the pregnancy and allow for additional lung maturity, one course of betamethasone (two 12.5-mg doses given intramuscularly, 24 hours apart) was administered, and an amnioreduction was performed.

Despite these attempts, the following day the patient presented to an outside hospital in active labor. She was airlifted to the FCC and taken to the operating suite for an emergent EXIT-to-airway procedure. While on uteroplacental bypass, the infant underwent laryngoscopy confirming a laryngeal atresia. A tracheostomy tube was then placed successfully and the umbilical cord was divided after 40 minutes of uneventful uteroplacental bypass.

After surgery, the neonate was given surfactant and stabilized on mechanical ventilation. Ventilatory support was weaned over the ensuing months as the diaphragmatic paralysis resolved and the tracheobronchomalacia improved. The patient began tolerating bolus gastrostomy tube feeds and was transferred back to the family's local hospital at 4 months of age. At 2 years of age, the patient underwent a double-stage laryngotracheoplasty for repair of the laryngeal atresia.

EXIT-TO-ECMO: SEVERE CONGENITAL DIAPHRAGMATIC HERNIA

A 30-year-old woman, gravida 3, para 2-0-0-2, was referred to the FCC at 36 weeks' gestation for evaluation of a severe right-sided congenital diaphragmatic hernia. Comprehensive evaluation with ultrafast fetal MRI, fetal echocardiography, and ultrasound scanning confirmed a large right-sided congenital diaphragmatic hernia with the liver, portions of the large intestine, and most of the small intestine herniated into the right hemithorax, causing a shift of mediastinal structures to the left. Severe pulmonary hypoplasia was present with a total lung volume of 14.9 cm^3 and a percent predicted lung volume of only 5.8%, consistent with CDH at the worst end of the spectrum.[6] Polyhydramnios with an AFI of 37 cm was also noted. Chromosomal analysis showed a normal 46, XY karyotype. At 38 weeks' gestation, an EXIT-to-extracorporeal membrane oxygenation (ECMO) procedure was performed with endotracheal intubation of the infant and venoarterial ECMO cannulation during 65 minutes of uteroplacental bypass (Figure 3; available at www.jpeds.com). The patient then made a seamless transition from uteroplacental bypass to ECMO support and was transferred to the neonatal intensive care unit in stable condition.

The infant underwent ECMO decannulation on day of life 12 and repair of right CDH on day of life 27. The patient was successfully extubated at 4 months of age and was discharged to home at 5 months of age while tolerating goal gastrostomy tube feeds and oxygen administered via nasal cannula.

EXIT-TO-AIRWAY: SEVERE MICROGNATHIA

A 36-year-old woman, gravida 6, para 3-0-2-3, was referred for evaluation of her pregnancy complicated by findings of a 2-vessel umbilical cord and an inability to visualize the stomach during her initial ultrasound scan at 21 weeks' gestation. The following week, on consultation at the FCC, ultrasound scanning and fetal MRI confirmed a single umbilical artery and nonvisualization of the stomach and distal esophagus, suspicious for esophageal atresia. Additional find-