

## C A S E R E P O R T

# The Ex-utero intrapartum treatment (EXIT) procedure: case report of a multidisciplinary team approach

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**Abstract.** *Background and aim of the work:* The EXIT-to-airway procedure is aimed to provide the time required to secure airways when an extrinsic or intrinsic fetal mass raise concerns about airways control at delivery. Due to the rarity of the procedure, we aim to provide a summary of the appropriate prenatal planning by a multidisciplinary team. *Methods:* Report of a case of EXIT-to-airway procedure. *Results:* A 30 years-old woman, G2P1 with previous cesarean section, was referred to our Unit at 34 gestational weeks due to a fetal cervical mass of 7cm. An EXIT-to-airways procedure was performed by a multidisciplinary team after accurate preoperative planning and the practice simulations. The partial fetal extraction and the amnioinfusion of pre-heated saline were used to prevent fetal complications. The use of supplemental intravenous anesthesia with remifentanyl and better control of uterine tone with nitroglycerin allowed reducing the exposure to volatile halogen for both the mother and the fetus. The accurate preoperative planning and the practice simulations allowed us to perform the treatment safely in urgency due to the onset of spontaneous labor at 37 weeks and 6 days. *Conclusions:* The strong cooperation among specialists, accurate prenatal planning, and adopting all the required procedures and precautions are of paramount importance to successfully perform the EXIT-to-airway procedure.

**Keywords:** EXIT procedure, cesarean section, fetus, multidisciplinary management, case report.

## Introduction

The ex utero intrapartum treatment (EXIT) procedure is a technique that allows maintaining the uteroplacental circulation during lifesaving surgery/procedures aimed to establish the cardiopulmonary function in the fetus (1). After the successful application for the management of the airway obstruction determined by the fetal surgery for severe congenital diaphragmatic hernia (CDH), the EXIT procedure has been implemented for any congenital anomaly

that impedes the immediate neonatal resuscitation (1). With the growing number of indications, the EXIT procedure received different declinations based on the final objective of the lifesaving surgery, such as EXIT-to-airway, EXIT-to-resection, EXIT-to-extracorporeal membrane oxygenation (ECMO), and EXIT-to-separation. The EXIT-to-airway is aimed to establish the patency of the airways in case of severe micrognathia, obstructing mass, or tracheal balloon; EXIT-to-resection is aimed to restore the anatomic volume in case of neck, thoracic or mediastinal mass;

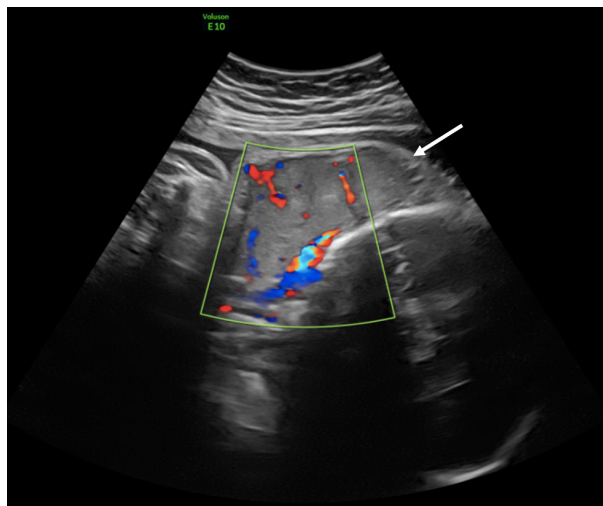
ECMO is required to establish the extracorporeal circulation with membrane oxygenation; the EXIT-to-separation is adopted in conjoined twins (1–3).

The appropriate prenatal planning is an essential element underlining a successful EXIT procedure, which should be performed by the same multidisciplinary team that will be involved. The preoperative imaging workup, the planning of the proper neonatal positioning, and the development of standardized communication among the team members are essential elements, particularly considering the rarity of the procedure. All these factors act around the key point, which is the maintenance of the uteroplacental circulation during the lifesaving surgery/procedures, balancing between the uterine relaxation and the hemorrhage risk. With the aim to highlight all these components of this multidisciplinary surgical approach, here we report a case of an EXIT-to-airway procedure performed to manage a cervical mass in a fetus delivered at 38 gestational weeks.

## Case report

### *The patient*

A 30 years-old woman, G2P1 with previous cesarean section, was referred to our Obstetrics and Gynecologic Unit at 34 gestational weeks due to a fetal cervical mass identified at ultrasounds. The in-patient evaluation with 2D and 3D ultrasound scan confirmed a solid non-homogeneous mass with a maximum diameter of 7cm suggestive for mesenchymal origin with large feeding vessels (Fig. 1). The further investigation by magnetic resonance (MR) imaging located in detail the mass on the lateral right side of the neck, infiltrating the homolateral parapharyngeal space and extending posteriorly to the dorsal cervical region (Fig. 2). The MR investigation of the fetus allowed excluding a skeletal or neurological involvement but confirmed the large feeding vessels identified at the ultrasound scan. There was not polyhydramnios, signs of hyperexpanded lungs, a flattened diaphragm, or clear evidence of anatomic compressions. Further investigation by fetal echocardiography excluded cardiovascular malformations. After the hospital admission, the cervical



**Figure 1.** 2D ultrasound scan showing the solid non-homogeneous mass of 7cm in maximum diameter involving the lateral right side of the neck of the fetus (white arrow). The color doppler allows identifying the vascularization pattern characterized by the presence of a large vessel.

mass was followed up every 48 hours by ultrasound to monitor the fetal status and identify possible changes in size, especially considering the vascular component of the mass.

### *The multidisciplinary planning.*

After the confirmation of the cervical mass and the complete imaging workup, a multidisciplinary team composed of obstetricians, neonatologists, pediatric surgeons, otolaryngologists, and the anesthesiologist were identified. The solid nature of the cervical mass, the location, and the size higher than 5cm in maximum diameter raised concerns about airway patency. However, clear evidence of anatomic compressions was not identified (4). Mainly based on the diameter of the mass, an intervention aimed to establish and maintain the patency of the airways immediately after delivery by cesarean section was considered mandatory, and an EXIT-to-airway procedure was planned with the intubation by direct laryngoscopy as the first approach. Because it was not possible to predict which airway intervention would be feasible, an algorithm of specific different procedures following a specific order after the direct laryngoscopy was planned, including



**Figure 2.** Magnetic resonance (MR) imaging showing the fetus and the cervical mass (black and white arrows) in the sagittal (A) and transversal (B) planes. The mass was located mainly in the lateral right side of the neck and was infiltrating the homolateral parapharyngeal space (B). In the sagittal plane (A), the extension of the mass posteriorly to the dorsal cervical region is visible. The MR allowed excluding skeletal or neurological involvement, polyhydramnios, signs of hyperexpanded lungs, a flattened diaphragm, or evidence of anatomic compressions.

video laryngoscopy, rigid bronchoscopy, retrograde intubation, and finally tracheostomy (5). The multidisciplinary team defined all the members in charge to perform the procedure, who subsequently took part in all the subsequent steps. Moreover, this team introduced the planned strategy to the mother with deep counseling.

After patient consent, the team in charge of performing the EXIT-to-airway procedure planned and performed multiple meetings to define all steps. The operative planning was developed, and two simulations were performed. In this scenario, the team defined a specific procedure to activate all the members in the case of emergent delivery both for early onset of labor and fetal distress.

#### *Equipment and anesthesiologic/neontologic considerations*

All the elements required to perform the EXIT-to-airway procedure were organized starting from the standard, elective cesarean section, and additional

required equipment was predisposed in the operative room. Since the decision to perform the EXIT-to-airway procedure, the immediate availability of blood products (red blood cells and plasma) was predisposed for emergent maternal transfusion. Moreover, the operative room personnel and anesthesiologist were instructed to set up the blood cell saver machine for immediate use during the surgery. Regarding the fetus, fluids for resuscitation and amnioinfusion, drugs for additional anesthesia (Rocuronium 0,6 mg, Fentanyl 30 mcg, and Atropine 100 mcg), orotracheal cannula, video-laryngoscope, and bronchoscope were predisposed in the operative room for immediate use. Finally, the position of each team member in the operative room was established and agreed upon by all members during the two simulations.

From the point of view of the anesthesiologist, careful maternal monitoring was essential during the procedure. Continuous electrocardiogram (ECG), arterial access for invasive blood pressure monitoring, pulse oximetry, end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>), and bispectral

(BIS) index to monitor the depth of anesthesia were predisposed and adopted during surgery. The anesthesiologist adopted the general anesthesia with a combination of volatile halogenated agent and intravenous (IV) anesthesia, and the target values during the procedure were SatO<sub>2</sub> 99-100%, EtCO<sub>2</sub> 28-32 mmHg, mean arterial pressure > 70 mmHg, and systolic arterial pressure +/- 10 mmHg of preoperative values (6).

For the fetus, the neonatologists predisposed the intraoperative pulse oximetry having as target the normal fetal oxygen saturation, which ranges between 50% and 70%. It is noteworthy that monitoring is of paramount importance because a value lower than 50% suggests impaired placental perfusion and warrants optimization of maternal blood pressure (1). Moreover, instrumentation for the intraoperative ultrasound and venous umbilical access were predisposed.

#### *The EXIT-to-airway procedure*

Although the EXIT-to-airway procedure was planned at 38+1 weeks of gestation, spontaneous labor started at 37 weeks and 6 days. The procedure was performed in urgency by the same trained multidisciplinary team that planned the procedure. Before entering the operative room, a premedication with Metoclopramide 10 mg IV, Pantoprazole 40 mg IV, and Midazolam 2 mg IV was given. The patient was pre-oxygenated with FiO<sub>2</sub> of 1 for 3 minutes, then rapid induction with Fentanyl 1 mcg/kg, Thiopental 4-6 mg/kg, and Rocuronium 0,6 mg/kg followed by intubation was performed. Supplemental intravenous anesthesia with remifentanyl (0,1 – 0,3 mcg/Kg/min) lowered the required inhalational dose of sevoflurane to a minimum alveolar concentration (MAC) of 1 and provided an adequate maternal depth of anesthesia and uterine relaxation. Before incision, antibiotic prophylaxis was given, and a waiting time of at least 10 minutes was guaranteed for fetal anesthesia transferred across the placenta (7), then nitroglycerin was started (100 mg bolus twice, then 1 mcg/kg/min) to obtain the optimal degree of uterine relaxation, which was assessed by the obstetrician.

The intrabdominal cavity was accessed by Pfannenstiel laparotomy, and after exposure of the lower uterine segment, the hysterotomy was performed.

The preoperative assessment of the placental position allowed us to exclude the placental involvement during the incision. After access to the uterine cavity and the opening of the amniotic membranes, the fetus was partially extracted, exposing only the head and shoulders. After the extraction of the upper portion of the fetus, a Foley catheter was introduced in the amniotic cavity to perform the amnioinfusion of pre-heated saline solution 0,9% to preserve the fetal normothermia and the uterine volume, preventing uterine contractions. After extraction, a fetal pulse oximeter was positioned to monitor the heart rate and blood oxygen saturation continuously.

The fetal positioning was essential to provide the best exposure for airway management. Because it was impossible to predict which airways intervention would be effective, all the team was prepared to follow the planned algorithm (5). The neonatologist team was the first to attempt the intubation by direct laryngoscopy, followed by the team of otolaryngologists for the video laryngoscopy and rigid bronchoscopy, and the team of pediatric surgeons for the retrograde intubation and tracheostomy. However, the direct laryngoscopy was successful, and no additional procedures and fetal anesthetics were needed. During the procedure, maternal normotension was critical to maintaining the uteroplacental circulation: phenylephrine 0,5 mcg/Kg/min was administered as the patient need to keep maternal systolic pressure within 10% of baseline values.

The entire procedure required 6 minutes to be completed from the head extraction. After confirmation of the correct endotracheal placement of the cannula, the umbilical cord was clamped, and the anesthesiologic goal changed from uterine relaxation to uterine tone. Nitroglycerin, Phenylephrine, and Sevoflurane were discontinued, and total intravenous anesthesia (TIVA), oxytocin, and postoperative nausea and vomiting prophylaxis (PONV) were initiated. The placenta was removed, and the cesarean section was complete as the usual technique without surgical complications. The total blood loss was estimated at 400 ml. The puerperium was uneventful.

The fetus, female sex, 3360 g weight, reported an Apgar of 1, 5, and 8, respectively, at the 1<sup>st</sup>, 5<sup>th</sup>, and 10<sup>th</sup> minutes of life. The arterial Ph was 7.20, with a -4.9 base excess. After stabilization, she was transferred

to the neonatal intensive care unit, and further imaging investigations were performed. Neonatal thorax-abdomen X-ray and echocardiography did not show any pathologic findings. On the 3<sup>rd</sup> day of life, a neck MR confirmed a non-homogeneous complex solid mass in the soft tissue of the right lateral neck, with a large feeding vessel originating from the right internal carotid. Moreover, the tumor compressed the homolateral internal jugular vein without an apparent cleavage plane. Multiple minor nodulations were identified cranial to the major mass and resulted in having the same vascular supply. After the confirmed stretch-elastic consistency of the mass and the more accurate exclusion of significant airway obstruction, the neonate was successfully extubated. To assess the histopathology of the mass, on the 17<sup>th</sup> day of life, multiple biopsies were performed, with the demonstration of vascular origin. Moreover, a progressive reduction of the mass size was observed in the first two weeks of life; therefore, based on the benign nature of the mass and the progressive decrease in the size, a close long-term follow-up was planned.

## Discussion

There are no published guidelines discussing the indications for the EXIT-to-airway procedure. However, it should always be considered whenever there are concerns that airway access and patency will not be established at delivery in a short time in the presence of suspected or confirmed extrinsic and intrinsic airway obstruction (2,8). Teratomas are the most common extrinsic obstructive lesions, followed by branchial anomalies and cervical lymphatic malformations. Intrinsic airway obstruction can be caused by subglottic stenosis or atresia, tracheal or laryngeal agenesis, webbing, or atresia. All these intrinsic obstructive lesions result in congenital high airway obstruction syndrome (CHAOS) (1–3). Conversely, in severe CDH or cardiothoracic anomaly, the EXIT-to-airway procedure has been substituted by the EXIT-to-ECMO procedure, which is used to maintain oxygenation by the placenta circulation during the set-up of extracorporeal membrane oxygenation (9).

The EXIT-to-airway procedure is aimed to provide the time required to secure airways. Nevertheless,

prenatal imaging cannot predict the airway intervention that will be effective, except the CHAOS, which requires tracheostomy (4). Indeed, despite advances in radiologic technologies, the size and location of the extrinsic obstructive mass are non-specific. Therefore, the strategy can easily change during the EXIT-to-airway procedure, and escalating management from the direct intubation by direct laryngoscopy followed by a more invasive procedure until tracheostomy is recommended (5). A helpful indirect sign of complex airway instrumentation is the proposed tracheal-esophageal index (TEDI) score, which measures the degree of displacement between the esophagus and trachea. It can be used to measure the anatomic compression and predict the difficulty of intubation (10). Moreover, further signs of airway impairment, with or without aerodigestive obstruction, are polyhydramnios, absent fetal gastric bubble, hyperexpanded lungs, or flattened diaphragm (4,11). Therefore, current recommendations suggest that the EXIT-to-airway procedure performed in these cases should be considered with a higher risk of difficult airways control (12–14). In our case, none of these elements were identified, and, consistently, the control of the airways was achieved at the first attempt by direct laryngoscopy. Noteworthy, although all these markers of airways impairment are indications for the EXIT procedure, they are not required. Indeed, delivery by EXIT procedure is considered safer than normal delivery even when the airways impairment cannot be confirmed (14–16). In this regard, the maximum diameter of the cervical mass is considered and proposed as the main indication for the EXIT procedure regardless of the nature and the presence of airway obstruction, with both a diameter  $\geq 3.5$  cm or  $\geq 5$  cm proposed as cut-off (4,17).

The adoption of the EXIT-to-airway procedure lowered perinatal mortality, with an overall survival rate of 83% (18,19). Nevertheless, maternal and fetal complications are still present. The fetus is exposed to the risk of barotrauma and improper ventilation during airway securing, which requires that the adequate tube placement be verified before cord clamping (5). Moreover, the fetus is at risk of hypotension and hypothermia (4). In this regard, the amniocentesis of pre-heated saline solution 0,9% and the partial extraction of the fetus allowed us to preserve the fetal

normothermia and avoid the umbilical cord vasoconstriction caused by the loss of temperature.

Regarding the mother, complications are primarily related to general anesthesia and the risk of severe hemorrhages. Maternal normotension and uterine relaxation are required to maintain the uteroplacental circulation and provide the time to complete the procedure, preventing placental separation and cord compression. The anesthesiologist must balance tocolysis, hypotension, and fetal oxygenation; nevertheless, the uterine atony can cause severe maternal hemorrhage (12). Moreover, the traditional technique to maintain the anesthesia and adequate uterine relaxation requires administration of 2-3 MAC of volatile halogen (20). However, this high concentration of inhaled agents may cause maternal hypotension and placental hypoperfusion, as well as direct fetal cardiovascular depression (7). Besides, preclinical studies have shown evidence of neurotoxicity from volatile anesthetics in the developing brain, although it has not been demonstrated in humans (21). Therefore, although hypotension can be avoided by maintaining the blood pressure within +/- 10% of preoperative values with pressors, such as phenylephrine or ephedrine boluses (22), it is prudent to reduce the exposure to an excess dosage of volatile anesthetics. To decrease the fetal exposure to volatile agents and to facilitate maternal blood pressure control, supplemental intravenous anesthesia with remifentanyl or propofol infusions can be used, allowing to lower the volatile MAC to 1, maintaining the depth of anesthesia (6). In our case, we adopted the remifentanyl at maternal dose 0,1-0,2 mcg/Kg/min, which allowed us to maintain the sevoflurane at 1 MAC. Noteworthy, remifentanyl crosses the placenta more than other opioids, providing the fetal immobilization required for fetal airway manipulation. Moreover, it attenuates the stress responses to the surgery of both the mother and the fetus (23). However, although an appropriate level of anesthesia was maintained, the lower doses of volatile agents compared to traditional techniques may require other medications to obtain the proper uterine relaxation. In this regard, nitroglycerin can be the appropriate option making the uterine tone easily manageable, having a very rapid initiation (30-120 s) and termination (3 min half-life) (24). Based on this evidence and the successful application,

we support supplemental intravenous anesthesia with low doses of volatile agents as a good option for EXIT procedure thanks to the lower risks and the equal achieved results.

Another maternal risk factor related to adopting any EXIT procedure is the required cesarean section (4), which provides immediate risks associated with the procedure and indirect risks during subsequent pregnancies (25–28). However, it should be considered that the pathological conditions that require the adoption of an EXIT procedure may represent in any case an obstetrics indication to cesarean section (29). Therefore, the maternal risks provided by the EXIT procedure do not always include the cesarean section. In our case, the cervical mass of 7 cm would have represented in any case an indication for cesarean section, considering the high risk of dystocia, primarily related to the interference with the appropriate flexion of the fetal head and the acquisition of the vertex presentation (30).

## Conclusions

Cervical masses are a common indication for the EXIT-to-airways procedure, particularly if having a maximum diameter of at least 3.5 cm. In these cases, mainly if a cesarean section is anyway the delivery mode of choice, the EXIT procedure can be added, representing a safer option when airway impairment is possible regardless of confirmation by imaging. However, the procedure is a challenging treatment that involves multiple specialists and the adoption of specific procedures and precautions that are not used in the usual clinical practice. In this regard, the prevention of fetal and maternal complications is of paramount importance. The partial fetal extraction and the amnioinfusion of pre-heated saline had a key role in preventing fetal complications in our case. Moreover, the use of supplemental intravenous anesthesia with remifentanyl and better control of uterine tone with nitroglycerin allowed reducing the exposure to volatile halogen for both the mother and the fetus. Finally, the multidisciplinary team approach always requires accurate preoperative planning and practice simulation, which allowed us to perform the treatment safely in urgency. The strong cooperation among specialists, the

proper prenatal planning, and the adoption of all the required procedures and precautions are of paramount importance to successfully perform the EXIT-to-airway procedure.

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