



APSA  
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# Fetal Diagnosis and Therapy

## A Reference Handbook for Pediatric Surgeons

from the  
Fetal Diagnosis and Treatment Committee  
of the  
American Pediatric Surgical Association  
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## FOREWORD

This handbook is the culmination of the vision and efforts of those who have served on the Fetal Diagnosis and Treatment Committee of the American Pediatric Surgical Association over the past five years. Fetal diagnosis and counseling has gradually evolved from a niche practice to something that most pediatric surgeons should be involved in to some extent. While very few will be involved in prenatal treatment, most pediatric surgeons will care for anomalies and malformation detected prenatally. This handbook is a ready reference that provides concise information about some of the more common fetal anomalies relevant to the pediatric surgeon. As the field is rapidly evolving, the contents of this handbook reflect the current knowledge and practice. As newer diagnostic capabilities and treatment modalities are discovered, this handbook will be updated as needed. The vision of the prior chairs of the Fetal Diagnosis and Treatment Committee, Francois Luks and Hanmin Lee, have been brought to fruition by the efforts of the contributors and the editors Brad Feltis and Chris Muratore. This handbook will serve as a quick reference for the pediatric surgeon about to counsel a patient and a useful educational tool for the residents and fellows in training.

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# CHAPTER 1

## History and Overview of Maternal-Fetal Surgery

Eveline H. Shue and Shinjiro Hirose

Fetal intervention for congenital anomalies has evolved from a mere concept to a medical specialty over the past three decades. Advances in fetal imaging and diagnosis have allowed clinicians to accurately identify complex anomalies prenatally and stratify their severity. Data that has been accrued over the past three decades gives expectant families accurate outcomes so they can make informed decisions about the pregnancy and delivery plans. In some cases, fetal intervention can be considered to prevent the progressive physiologic organ damage that occurs from congenital anomalies.

Results from early experiences with fetal therapy generated a movement away from anatomic repair of congenital anomalies to physiologic manipulation of the developmental consequences (e.g., the shift from *in utero* repair of the CDH defect to balloon tracheal occlusion to promote lung growth). Techniques used in fetal intervention have also evolved from maximally invasive (e.g., open hysterotomy) to more minimally invasive techniques, such as fetal endoscopy, and image-guided percutaneous procedures. Advances in surgical techniques paralleled developments in fetal imaging, fetal diagnosis and the advent of maternal tocolysis to prevent preterm labor. Fetal intervention has become an important option for fetuses who would otherwise not survive gestation or who would endure significant morbidity and mortality after birth.

As the fetal surgery community amasses experience with fetal intervention, an emphasis has been placed on randomized controlled trials instead of retrospective clinical trials. In 1982, the International Fetal Medicine and Surgery Society (IFMSS) held its first annual meeting. This society continues to be an important international venue. In the 1990s, trials for fetal intervention were being performed in many different fetal treatment centers across the world. In 2005, a cooperative clinical research network, the North American Fetal Therapy Network (NAFTNet), was formed to promote multi-institutional trials in the United States and Canada to study fetal disease, develop prenatal interventions and improve outcomes. Similarly, the Eurofetus group was formed in Europe to promote multicenter clinical trials and foster innovation in fetal medicine. These international organizations of obstetricians, surgeons, perinatologists and sonologists were formed with an overarching goal to promote maternal safety while improving outcomes for patients with fetal anomalies.

Institutional centers dedicated to fetal treatment require a collaborative team of specialists who are dedicated to continuity of care for both the mother and the fetus. An obstetrician, who is an expert in prenatal diagnosis, amniocentesis, chorionic villus sampling, complications of pregnancy and family counseling, is important for management of the pregnancy. Pediatric surgeons and neonatologists, who understand the pathophysiology behind neonatal diseases and their treatment after birth, are important for developing a therapeutic plan. The skills of an obstetric sonographer and pediatric radiologist are also invaluable in delineating the fetal anomaly and in guiding diagnostic and therapeutic interventions. Depending on the fetal anomaly, a pediatric cardiologist, neurologist, nephrologist, neurosurgeon, anesthesiologist or endocrinologist can also be indispensable to the fetal treatment team.

With so many different specialties involved in fetal medicine and fetal surgery, personality conflicts are not uncommon and many questions surface. For instance, who should perform open fetal surgery? Should it be the pediatric surgeon, who has experience repairing complex congenital anomalies in neonates, or the obstetrician, who has experience operating on the gravid uterus? There is currently no specialty that completely encompasses all aspects of care involved in fetal surgery. Therefore, the key to a successful and productive fetal treatment program is a collaborative, multidisciplinary team, which includes an obstetrician, perinatologist, geneticist, sonologist, surgeon, neonatologist and anesthesiologist, in addition to experienced support personnel (Table 1). These interactions should be formalized with a weekly multidisciplinary meeting, where patients are discussed in depth and plans are formulated among all specialists and personnel involved. Through these weekly interactions, care plans and interventions are mapped with consensus across all disciplines.

A close working relationship between perinatal specialists is crucial to success in a fetal treatment program. However, the institution also needs to be adequately equipped to care for fetal patients. Together this requires a high-risk obstetric unit with obstetricians who are available around the clock and have experience delivering patients with a recent hysterotomy, a Level IIIC neonatal intensive care unit and an environment where research is combined with clinical care. Because fetal intervention is a new frontier, experience, success and failure must be critically analyzed, documented and shared to improve patient care and improve understanding.

Over the past 30 years, fetal surgery has evolved into a multidisciplinary, collaborative medical specialty that strives to improve outcomes in patients diagnosed with fetal anomalies. Physicians dedicated to fetal medicine and fetal surgery have formed a cooperative community dedicated to reporting both good and poor outcomes from fetal intervention. Through these collaborations, several multicenter, randomized, controlled clinical trials have been successfully completed. This frontier could not have been established without dedicated physicians, support staff and institutional support.

**Table 1: Basic Components of the Fetal Care Team**

- |   |
|---|
| <ul style="list-style-type: none"> <li>• Designated team leader</li> <li>• Care coordinator</li> <li>• Pediatric cardiologist to perform fetal echocardiogram</li> <li>• Fetal surgeon – usually a pediatric surgeon or a perinatologist</li> <li>• Genetic counselor</li> <li>• Pediatric radiologist to interpret fetal MRI</li> <li>• Maternal fetal medicine specialist</li> <li>• Neonatologist</li> <li>• Obstetric anesthetist</li> <li>• Pediatric anesthetist</li> <li>• Social worker</li> <li>• Ultrasonologist</li> </ul> |
|---|

## CHAPTER 2

### Congenital Lung Lesions

Timothy Lee

Congenital lung lesions (CLL) comprise a diverse spectrum of pathologic conditions. These conditions range from small cystic lung lesions that are asymptomatic to large lesions which may lead to a lethal outcome *in utero*. Many of these lesions arise along a spectrum of developmental pathways with the most common being the congenital pulmonary airway malformation (CPAM). CPAM was formerly termed cystic adenomatoid malformation (CCAM). Bronchopulmonary sequestration (BPS) and bronchial atresia should also be considered in the differential for any CLL. Other rare lesions such as congenital lobar emphysema, pleuropulmonary blastoma and fetal lung interstitial tumors are outside of the scope of this review. The diagnosis and management of these lesions may be challenging in the prenatal period, and some may require urgent fetal intervention. An understanding of the pathology and treatment strategies is critical in the prenatal management of these patients.

#### Pathophysiology of CLLs

##### *Congenital Pulmonary Airway (Cystic Adenomatoid) Malformation (CPAM)*

The natural history of congenital lung lesions can be quite variable. CPAMs usually arise from a single lobe, but rarely can affect both lungs. If a single lobe is involved, the most common location is in the lower lobes. These lesions may have an unpredictable growth pattern from 18 to 26 weeks gestation (Bianchi, Adzick). However, after this growth period, the growth curve will plateau and often regress. Although rare, it has been reported that these lesion may regress enough where they even disappear from the pulmonary parenchyma (Roggins, McGilvaray, Kunisaki). In regards to classification, the original Stocker classification system stratified these lesions from type 1 to type 3 based on cyst size. The new classification system includes the original types (1-3) and adds types 0 and 4 (Stocker). The relevance of this classification in clinical decision making is minimal. A more relevant classification system is to classify the cysts as macrocystic (>5mm in diameter for single or multiple cysts) or microcystic. The clinical relevance of this classification system lies in the differing treatment options and outcomes for these pulmonary lesions.

##### *Bronchopulmonary Sequestration*

Pulmonary sequestrations are areas of non-functioning lung which have no connection to the bronchial tree. These anomalies can be classified as intra-lobar or extra-lobar. An intralobar sequestration is located within the lung parenchyma, while the extralobar sequestration is separate from the lung, including a separate pleural covering. These lesions possess a systemic arterial blood supply which often arises from the aorta, and the venous drainage may drain into the pulmonary veins, the azygous system or the inferior vena cava. The existence of hybrid CLLs which share characteristics of both BPS and CCAM suggest that these two pathologic entities share an embryologic origin.

### *Bronchial Atresia*

Bronchial atresia is characterized by stenosis of the bronchus at any level within the bronchial tree. Due to the stenosis, the distal lung develops progressive mucostasis and hyperinflation. The pathology of bronchial atresia has been hypothesized to be due a vascular insult to the bronchus (Langston); however, no definitive pathologic pathway has been proven. The increasing frequency of this diagnosis has been felt to be due to the increased use of prenatal imaging, but these lesions are often associated with other pulmonary malformations such as CCAMs or BPS. In isolation, bronchial atresia will rarely need fetal intervention; however, mainstem bronchial atresia has been described as a fatal process. Keswani et al. reported two cases where both fetuses died, one while during an open fetal pneumonectomy. Our experience is similar; mainstem bronchial atresia has been a fatal *in utero* process even with fetal intervention.

### **Fetal Imaging for CLLs**

The diagnosis and characterization of congenital lung lesion are made primarily by the use of ultrasound. The initial categorization of CLLs is as a solid or cystic mass. Cystic lesions are further classified as macrocystic, microcystic or hybrid lesions. Sequestrations appear as a solid, echogenic lesion. Using Doppler, the systemic feeding vessel can often be identified in these lesions.

All centers recommend that fetal patients with CLL receive an initial ultrasound. Decisions regarding the utility of fetal MRI and fetal echocardiogram are based on the interpretation of the ultrasound. The CVR (see below), presence of hydrops, mediastinal shift, reversal of flow within the umbilical vein and abnormal cardiac echo are all useful parameters to aid in the determination of whether fetal therapy may be beneficial.

Fetal hydrops is defined as the accumulation of fluid within two or more body cavities (ascites, pleural effusion, pericardial effusion or skin/scalp edema). Hydrops is often a harbinger of poor fetal or postnatal outcomes. Abnormal fetal echocardiogram findings can be defined as increased or decreased cardiac output, ventricular hypertrophy, atrial or ventricular chamber dilation, cardiomegaly, significant valvular regurgitation, diastolic dysfunction or findings of heart failure. Finally, the presence of placentomegaly (>5cm in thickness) can be a harbinger of imminent *in utero* demise.

### **CVR (CAM Volume Ratio)**

The CVR or CAM volume ratio has emerged as one of the most useful tools in predicting outcomes in prenatally diagnosed pulmonary lesions. The CVR is a measurement of tumor volume normalized by gestational age and is calculated by using ultrasound to measure the pulmonary lesion in 3 dimensions (length, width, height). This volume is multiplied by a constant (0.52) and divided by head circumference (which normalizes for gestational age). The CVR equation is  $(L \times H \times W) \times 0.52 / \text{head circumference}$ . The initial report documented that 80% of fetuses with a CVR >1.6 went on to develop hydrops (Crombleholme). A more recent study described a similar predictive value of CVR, but with a cutoff of 2.0 (Cass). In this series, 56% of fetuses with CVR >2.0 required prenatal intervention compared to 3% of the fetuses with



CVR <2.0. Clearly, the CVR is a useful prognostic tool for CLLs, but one which is continuing to be studied and refined

### **Fetal Therapy**

There are no absolute criteria for fetal intervention; however, fetal therapy is reserved for only the most severe congenital lung lesions (i.e., expect significant respiratory distress at birth or high risk of *in utero* demise). Smaller (CVR <2.0) lesions or asymptomatic (non-hydronic) larger lesions can be safely followed with weekly or bi-monthly ultrasound. Because certain CLLs can undergo rapid expansion up to 28 weeks, this is a crucial time period to monitor for any changes in the baby's physiologic status.

### **Maternal Mirror Syndrome**

A fetus with a large lung mass that has developed hydrops and placentomegaly may also place the mother at significant risk for maternal mirror syndrome (Adzick). Mirror syndrome is a maternal complication which results in the mother's health state mirroring that of the fetus. The mother can develop symptoms such as hypertension, vomiting, pulmonary edema and proteinuria. Untreated, these symptoms can progress in severity and can potentially threaten the life of the mother. The only treatment for the severe form of this syndrome is delivery of the baby (Braun).

### **Minimally Invasive Approaches to Symptomatic Lung Lesions**

#### *Maternal Steroids (Betamethasone)*

The initial intervention that should be considered in patients with large, symptomatic solid or microcystic CLLs is the administration of prenatal steroids. This therapy has been described in several case series, yielding a variable but definite response (Curran, Morris). Although there are currently no definitive recommendations and no conclusive data to support the use of prenatal steroids for symptomatic CLLs, several centers have independently noted lesion regression and hydrops reversal after administration. The administration of steroids is a two-dose maternal regimen of betamethasone given 24 hours apart. The exact mechanism as to how betamethasone induces lesion regression is not clearly defined.

#### *Cyst Drainage*

For large, symptomatic macrocystic disease, most centers would employ a minimally invasive approach to decompress the large lesions. This can be accomplished via ultrasound-guided cyst aspiration or deployment of a thoraco-amniotic shunt. Cyst aspiration quickly reduces the volume of the CCAM; however, it is frequently only a temporizing solution, as reaccumulation of the fluid within 48-72 hours is common. The use of a thoraco-amniotic shunt has been described with excellent survival rates in patients with macrocystic disease (Wilson, Schrey). Practically, shunt dislodgement after placement is common phenomenon (usually caused by the baby) that may necessitate a repeat procedure.

### *Open Fetal Surgery and EX Utero Intra Partum Treatment (EXIT)*

Open fetal surgery has been employed for resection of prenatally diagnosed high-risk lung lesions and can be offered when there is impending fetal demise. These procedures are considered on a case-by-case basis and are usually offered prior to 30 weeks gestation. In patients greater than 30 weeks gestation, the EXIT procedure is used to provide a transition from fetal to post-natal life. Patients who may need an EXIT-to-resection can be symptomatic or asymptomatic *in utero*. Following delivery and positive pressure ventilation, the lung mass may increase in size, leading to worsening of cardiac compression and cardiovascular collapse. The resection of the chest mass, while on placental support, prevents this sequelae.

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## CHAPTER 3

### Congenital Diaphragmatic Hernia

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#### Introduction

The incidence of congenital diaphragmatic hernia (CDH) is estimated to be between 1 in 2,200 to 5,000 live births<sup>1-2</sup>; however, the true incidence is likely closer to 1 in 2,200 as this defect can be associated with intra-uterine fetal demise and stillborns which are difficult to capture in epidemiologic studies<sup>2-3</sup>. Determining an accurate mortality rate for CDH is also a moving target given variable referral patterns that tend to triage sicker babies to tertiary referral centers; the best available estimates have reported mortality rates as high as 75% for prenatally diagnosed CDH<sup>4-5</sup>. Most other estimates put the mortality rate around 50%<sup>4-6</sup>. CDH is being more commonly diagnosed antenatally (usually by 25 weeks gestation) with early prenatal care, enhanced imaging modalities and a heightened awareness of findings associated with CDH. While advances in medical management of CDH have improved outcomes in the last century, our ability for prenatal diagnosis of CDH has not affected the grim prognosis associated with defects that result in fatal pulmonary hypertension.

The role of fetal interventions for CDH is still an area of intense investigation and currently is not widely available; however, the pediatric surgeon will be asked to counsel families caring for pregnancies complicated by CDH. The diagnosis of CDH has significant immediate implications for the family regarding delivery at a tertiary referral center, the need for neonatal intensive care, the decision for extra-corporeal membranous oxygenation (ECMO) and other aggressive resuscitative measures, and even termination of the pregnancy. Therefore, it is critical that pediatric surgeons are capable of interpreting antenatal studies and counseling families so they can make informed decisions regarding the pregnancy.

#### Diagnostic Modalities and Prognostic Indicators

##### *Fetal Ultrasonography*

Ultrasonography (US) is routinely performed during the prenatal period. Polyhydramnios has been implicated in CDH from kinking of the stomach, as well as mediastinal compression on the esophagus impairing the fetus' ability to swallow amniotic fluid<sup>7</sup>. Once the suspicion for CDH has been raised, a more thorough investigation of the thorax can be undertaken to identify herniated abdominal contents. It is widely accepted that the presence of abdominal structures seen at the same level as the four-chamber heart view on US confirms the presence of a diaphragmatic hernia<sup>1</sup>. Abdominal viscera, visualized above the tip of the scapula, can also be used as a reference point<sup>1</sup>. In some cases, US can visualize the defect in the diaphragm, making the diagnosis very clear.

The presence of liver herniation reproducibly predicts a worse outcome for CDH<sup>8-9</sup>; therefore, position of the fetal liver should be assessed during fetal US. Kinking of the sinus venosus and the presence of left lateral segment portal veins above the diaphragm are the most reliable

indicators of liver herniation into the left chest<sup>10</sup>. For right-sided defects, the presence of the gallbladder above the level of the diaphragm can confirm the location of the liver<sup>2</sup>.

The lung-to-head ratio (LHR) is another important prognostic indicator. It is obtained by measuring the right lung area at the level of the four-chamber view of the heart and dividing by the head circumference. In multiple studies, an LHR <0.6 was associated with 100% mortality, while an LHR >1.35 was associated with 100% survival<sup>11-14</sup>. When measured correctly, the LHR can be invaluable; however, reproducibility has limited its application. In fact, there are now three different standardized methods for obtaining the LHR which have different survival outcomes<sup>2</sup>. Regardless, the LHR (or variants of the LHR) has been widely accepted.

Another factor affecting LHR is the gestational age of the fetus. The fetal lung and head grow at different rates, especially up to 32 weeks gestation when lung growth begins to level off relative to the head circumference<sup>9</sup>. This prompted investigators to propose the observed-to-expected ratio for LHR (O/E LHR) based on what the mean expected LHR would be for a specific gestational age in fetuses not affected by CDH<sup>15-16</sup>. As lung growth plateaus, there is a decrease in the O/E LHR. For example, an LHR of 1.0 correlates with an O/E LHR of 32% at 23 weeks gestation, and an O/E LHR of 23% at 33 weeks gestation for a left-sided defect<sup>17</sup>. In the original description of the O/E LHR for left-sided defects, O/E LHR of <25% was associated with an 18% survival; O/E LHR of 26-45% was associated with a 66% survival; and O/E LHR of >45% was associated with an 89% survival<sup>15,18</sup>.

#### *Fetal Magnetic Resonance Imaging*

Fetal magnetic resonance imaging (MRI) is an emerging imaging modality in the work-up of specific prenatally diagnosed congenital anomalies including CDH where it has primarily been studied in measuring lung volumes for antenatal prognostication. The most important measurement obtained, and studied, by MRI is the percent predicted lung volume (PPLV)—also known as the observed to expected fetal lung volume (O/E FLV)<sup>19-20</sup>. This calculation is made by subtracting the mediastinal volume from the thoracic volume to determine the expected lung volume. The actual lung volume is then measured and divided by the expected lung volume to create a percentage<sup>19</sup>.

Exactly how the PPLV should be interpreted is not agreed upon. In one study, 15% appeared to be the determinant of survival, where those with a PPLV >20% had 100% survival, whereas a PPLV of <15% was associated with only 40% survival<sup>21</sup>. In another study, the cutoff appeared to be 25% where PPLV <25% was associated with a 13% survival, and a PPLV >35% was associated with an 83% survival<sup>20</sup>; however, some have reported that PPLV is inferior to LHR in predicting outcomes<sup>2</sup>. Furthermore, LHR can be obtained by US and does not require a fetal MRI. In fact, MRI is not a routine part of the work-up for CDH at all fetal treatment centers<sup>12</sup>.

Other groups have looked at the raw fetal lung volume (FLV) as a prognostic indicator<sup>22-23</sup>. In a series of FLV obtained via MRI at 34-35 weeks gestation, the investigators reported that survivors had a mean FLV of 35ml, those requiring ECMO had a mean FLV of 18ml, and non-survivors had a mean FLV of 9ml<sup>23</sup>.

The group from CHOP has also reported that the presence of the liver-up on MRI, as well as the percentage of herniated liver, were also prognostic by multivariate analysis. Liver-up is widely accepted as a poor prognostic indicator. In their series, liver-up was associated with 45%

survival, whereas liver-down was associated with 94% survival<sup>28</sup>. Again, this can also be determined by US and does not necessitate a fetal MRI; however, they also looked at herniated liver volumes as determined by fetal MRI and found that survivors had a mean 17% of liver herniated compared to non-survivors who had a mean 28% liver herniated ( $p=0.004$ )<sup>28</sup>.

### *Imaging for Associated Anomalies*

It is important that an assessment be made to determine if there are any associated anomalies, as these have a significant, negative impact on survival. In fact, 95% of stillborns with CDH have an associated anomaly<sup>24</sup>. These anomalies can include congenital heart disease, genitourinary abnormalities, intestinal atresia, bronchopulmonary sequestrations and neurologic defects—most of which can be detected through prenatal US<sup>2</sup>. Further delineation of suspected anomalies may be better assessed by fetal MRI, especially if this information would impact the management of the pregnancy.

Amniocentesis should be offered for karyotyping, as well as comparative genomic hybridization microarray, to identify chromosomal abnormalities. This information may be helpful for families making decisions regarding the pregnancy and post-natal care. Up to 20% will have a chromosomal abnormality such as trisomy 21, trisomy 18 or trisomy 13<sup>2</sup>. CDH can also occur in association with multiple syndromes including Beckwith-Wiedemann, Fryns and Pierre-Robin. Lastly, since most fetal interventions are investigational, normal chromosomal studies are oftentimes used as inclusion criteria.

## **Fetal Interventions**

Fetal interventions are not to be taken lightly. Any fetal intervention carries a risk to both the fetus and a healthy mother. In fact, something as simple as an amniocentesis carries a 0.5-1.4% risk of fetal loss<sup>25</sup>. Fetal interventions are associated with fetal demise, pre-term labor, the risk of premature rupture of membranes, chorionic membrane separation, chorioamnionitis and bleeding. Open fetal procedures run the additional risk of uterine dehiscence and rupture with the current pregnancy and any future pregnancies. Vaginal delivery is not an option after open fetal surgery, and mothers require planned cesarean section for any future pregnancies. For these reasons, fetal intervention should be reserved for those situations where a clear benefit exists for the fetus. There is no benefit for the mother, only risk; therefore, families need to be counseled thoroughly on the risks, benefits and alternatives before proceeding with any fetal intervention.

### *Open Fetal Repair*

In 1990, Dr. Michael Harrison and his team at UCSF published the first successful open fetal CDH repair<sup>26</sup>. This was followed by a prospective trial comparing open fetal repair ( $n=4$ ) to postnatal repair ( $n=7$ ) in pregnancies referred to UCSF at  $<30$  weeks gestation complicated by an isolated left-sided CDH with significant volume displacement of the ipsilateral lung and an intrathoracic stomach. There was no difference in survival comparing postnatal repair to fetal repair (86 vs 75%) or need for ECMO; however, the fetal repair group had a much younger mean gestational age (32 vs 38 wks) and longer duration of hospitalization (38 vs 27 days)<sup>27</sup>.

### *Tracheal Occlusion*

Open fetal repair has since been abandoned in favor of tracheal occlusion. When the fetal trachea is occluded, fluid normally made by the fetal lung parenchyma builds up and leads to pulmonary hyperplasia<sup>28</sup>. This hyperplasia can be so dramatic that it causes eversion of the diaphragms. Since pulmonary hypoplasia is what contributes to morbidity and mortality associated with CDH, this physiologic process was applied to fetal lambs with CDH<sup>29-30</sup>. The results were favorable, so clinicians have targeted fetal tracheal occlusion (FeTO) as potential antenatal intervention for CDH patients with an unfavorable prognosis.

FeTO was originally performed via an open hysterotomy with tracheal clip application. In the first series of eight patients, there was only one survivor, although three of the demised patients demonstrated favorable pulmonary hyperplasia<sup>31</sup>. Interestingly, the clip application required a strict delivery plan to remove the clip prior to delivery to prevent asphyxiation. This gave rise to *ex utero* intrapartum treatment (EXIT) where the uterine-placental circulation was preserved to the fetus so the clip could be removed prior to dividing the cord and completing the delivery<sup>32</sup>.

One of the confounding factors in this initial series was the use of an open hysterotomy for FeTO which contributed to prematurity (range 27-32 weeks gestation)<sup>31</sup>; therefore, fetoscopy with tracheal clip application was used in the subsequent study which compared fetoscopic FeTO (n=8) to open FeTO (n=8) and postnatal CDH repair (n=13) in pregnancies referred to at <25 weeks gestation for isolated left-sided CDH with liver-up and LHR <1.4. Survival was greatest in the fetoscopic FeTO group (75%), followed by the postnatal repair group (38%) and the open FeTO group (15%)<sup>33</sup>.

Given these promising findings, a prospective randomized trial was initiated at UCSF for pregnancies complicated by isolated left-sided CDH with liver-up and LHR <1.4. Additionally, use of tracheal clips was abandoned in favor of tracheal balloon occlusion. Subjects were randomized to either fetoscopic bronchoscopy through a 5mm port with tracheal balloon occlusion or postnatal care. The primary outcome was 90-day survival, and the study was powered for a 77% survival rate in the FeTO group which required an enrollment of 40 patients. The study was terminated at 24 patients because no survival benefit was found. The non-treatment group had a survival rate much higher than historical controls and what had been expected in the study (77 vs 73%, p=1.0) which became a major criticism of the study. Yet this improved survival in the postnatal therapy group was likely a reflection of improved peri-natal care and “gentilation” techniques. An additional criticism was the inclusion of LHR 1.0-1.4, as these defects were likely not as severe as if the study had been limited to an LHR <1.0<sup>34</sup>.

While FeTO lost momentum in North America following the UCSF trial (and the lack of an FDA-approved device that could be applied more broadly), in Europe investigators continue to study the technique and report more favorable results. Jan Deprest has described fetoscopic tracheal occlusion using a balloon through a 3.3mm port between 26-28 weeks and through pooled data from the FETO consortium reported survival rates as high as 48% in 210 cases of CDH where the OE LHR was <30% for left-sided CDH and <45% for right-sided CDH<sup>17</sup>. These results have been criticized because survival rates for CDH with unfavorable prognostic signs have improved recently without the need for fetal interventions as demonstrated in the UCSF trial. Nonetheless, in Europe, the consensus has been to move forward with FeTO, and currently the Eurofetus group is sponsoring a multi-centre, prospective trial that is studying the optimal timing for FeTO. Investigators in North America have proposed a multi-centre, prospective trial

on FeTO for CDH but are still awaiting FDA-approval for the balloon device currently in use throughout Europe.

### *EXIT to ECMO*

In the absence of tracheal occlusion, some investigators have proposed that EXIT-to-ECMO may be a viable alternative to improve outcomes for unfavorable CDH. The exact criteria for EXIT-to-ECMO remain uncertain. One group published their results from 14 cases using an LHR <1.4 and PPLV <15%. Each patient underwent an EXIT procedure after 36 weeks. An airway was established and a ventilation trial was performed. Eleven patients failed the trial and were cannulated and then delivered. Three patients passed the trial of which two eventually required ECMO after delivery. Overall survival was 64%<sup>35</sup>; however, this same group followed up their experience and found no survival benefit for EXIT-to-ECMO (33% survival) compared to those CDH patients requiring ECMO but not undergoing an EXIT procedure (50% survival)<sup>36</sup>. Currently, there does not appear to be a convincing role for EXIT-to-ECMO.

### **Outcomes**

The vast majority of prenatal evaluations will not be candidates for a fetal intervention; therefore families will expect counseling on what to anticipate during the neonatal period and beyond. Clinicians should be prepared to have an in-depth discussion with families during prenatal consultation that encompasses worst- and best-case scenarios, operative timing and types of repair, ECMO and long-term outcomes. The immediate post-natal management for CDH is beyond the scope of this text; however, long-term outcomes are reviewed in this section.

Survival has been the primary outcome analyzed repeatedly to determine the best strategies for managing CDH; however, CDH covers a broad-spectrum of severity, and it can be difficult to predict which end of the spectrum each case will fall. Overall survival is still quoted at 50%, and if the defect is prenatally diagnosed mortality may be as high as 75%<sup>4-6</sup>. These values reflect a very heterogeneous patient population confounded by the fact that not all patients make it to tertiary referral centers or may have delayed presentation to a tertiary center, which would explain why there are published survival rates as high as 90%<sup>2</sup>.

Survivors are still at risk for other long-term problems. Prolonged ventilator dependence can lead to bronchopulmonary dysplasia in 33%, and there is a higher rate of reactive airway disease in children with a history of CDH<sup>37-38</sup>. Pulmonary function tests are normal in 50-70% of survivors; however, 25% will have evidence of obstructive airway disease after five years. Abnormal pulmonary function tests can show restrictive and mixed disorders of pulmonary function<sup>37</sup>.

Up to 50% have some degree of neurologic sequelae which is independent of the need for ECMO. Sensorineuronal hearing loss can manifest later in life and requires routine follow-up. Children with CDH can be affected by cerebral palsy, delay in speech and verbal skills, vision loss and seizure disorders<sup>39</sup>.

Gastroesophageal reflux can be a problem in up to 60% of which 10-15% will require an antireflux procedure<sup>40-41</sup>. Nutrition can be a problem for these children who can have respiratory symptoms during feeding contributing to poor growth and failure to thrive with 50% falling in the less than 25<sup>th</sup> percentile. Fortunately, this delay in growth appears to normalize by two years,



but one-third will require a gastrostomy tube<sup>37, 42</sup>. Growth can also be affected by chest wall deformities in 20% who will develop a pectus excavatum defect and 10% that will develop scoliosis<sup>42</sup>.

Recurrence rates are high after repair of the defect and overall are reported between 5-20%; however, if a prosthetic patch was required, then recurrence is as high as 50%<sup>37</sup>. The group in Salt Lake City has published favorable rates using an internal oblique muscle flap for large defects with a recurrence rate of 4% at a median follow-up of four years<sup>43</sup>. Recurrence with incarceration, as well as adhesions and volvulus, can contribute to intestinal obstruction which occurs in 20% of CDH patients<sup>37</sup>.

## **Conclusion**

CDH is a frequently encountered congenital anomaly that spans a wide spectrum of severity. Improved prenatal diagnosis has led to the detailing of several prognostic parameters that are critical (albeit imperfect) in counseling families and determining candidates for fetal intervention, but has had little impact on survival. Most pregnancies will not be a candidate for fetal intervention or, if so, will decline given the risks; however, the pediatric surgeon will still be able to provide valuable prognostic information that will guide families as they decide what level of care they want for their baby, who may ultimately benefit from a delivery plan that ensure the availability of appropriate resources.

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## CHAPTER 4

### Sacrococcygeal Tumors

Corey W. Iqbal

Sacrococcygeal tumor (SCT) is a rare neoplasm that is being diagnosed with increasing frequency *in utero*. Fetuses with SCT are susceptible to intra-uterine fetal demise (IUFD). SCTs can grow to a tremendous size in relation to the fetus and can cause high-output cardiac failure and non-immune hydrops through vascular shunting. Rarely, tumors can hemorrhage internally or externally, resulting in fetal anemia, hypovolemia and IUFD. Other potential problems for a fetus with a large SCT are dystocia and pre-term labor. Delivery can be particularly difficult when the diagnosis has not been made prenatally. A traumatic delivery may result in tumor rupture and/or hemorrhage. Most clinicians favor cesarean delivery for fetuses with large SCTs. Thus, prenatal diagnosis and careful obstetrical planning are critical in the appropriate management of such pregnancies.

#### Tumor Volume to Fetal Weight Ratio

Recent evidence has identified the tumor volume to fetal weight ratio (TFR) as an important prognostic indicator for SCT<sup>1</sup>. Tumor volume is calculated using the greatest length, width and height of the tumor as measured by US or MRI; fetal weight is calculated by US using the Hadlock formula. In the initial report from Texas Children's Hospital of 10 fetuses with SCT, a TFR >0.12 was associated with an 80% incidence of hydrops and a 60% mortality rate, whereas a TFR <0.12 was associated with 100% survival.<sup>1</sup> UCSF has recently presented their experience in 37 fetuses with SCT and confirmed that a TFR <0.12 was a favorable prognostic finding up to 24 weeks. Between 24-32 weeks, a TFR of <0.11 was associated with more favorable outcomes. In addition, they also found that cystic SCTs had a more favorable prognosis than solid ones<sup>2</sup>.

#### Referral for Prenatal Therapy

The fetus with large SCT has a high risk for mortality especially when associated with non-immune fetal hydrops. A fetus with SCT and a TFR >0.12 should be evaluated monitored closely in an experienced center to determine the need for fetal intervention. SCT interventions to date have included fetal surgery, radiofrequency ablation (RFA) and EXIT-to-resection. Outcomes of fetal intervention are mixed, with survival ranging from 38-75%<sup>3-4</sup>. Survival in hydropic SCT patients not undergoing fetal intervention is likely < 10%<sup>3</sup>.

The most common approach for fetal resection of an SCT is a maternal hysterotomy with resection or debulking of the tumor. Typically, only Type 1 or Type II SCTs are amenable to fetal surgery. A predominantly cystic lesion may be amenable to percutaneous drainage or shunt placement; however, that is usually unnecessary as cystic SCTs carry a more favorable prognosis. Decompression of a large, cystic SCT may be indicated just prior to delivery to prevent dystocia or to facilitate Cesarean delivery. Tumor debulking using percutaneous coagulation techniques such as radio-frequency ablation or laser coagulation to decrease the vascular shunt are minimally invasive alternatives to open resection that have been reported and

may warrant further investigation<sup>5</sup>; however, long-term complications noted in the survivors due to injury to adjacent structures demands a better understanding of the application of these techniques for SCTs<sup>6</sup>.

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## CHAPTER 5

### Fetal Neoplasms

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#### Introduction

Fetal neoplasms are rare and most are benign; however, if they become large enough they can impede venous return to the heart or cause high output cardiac failure via arterio-venous shunting causing non-immune fetal hydrops. Hydropic changes can include polyhydramnios, placentomegaly, fetal skin and scalp edema and accumulation of fluid in the pleural, pericardial or peritoneal spaces. By definition, fetal hydrops is present when two or more compartments are affected (i.e., scalp edema and abdominal ascites). Left untreated, fetal hydrops is frequently fatal<sup>1-2</sup>. Congenital Pulmonary Airways Malformations (CPAM – previously termed CCAM) are the most common prenatally diagnosed neoplasm and are discussed in a separate chapter as are sacrococcygeal tumors. Other prenatally diagnosed neoplasms include pericardial neoplasms, ovarian and intra-abdominal cysts, fetal neck masses, and retroperitoneal masses.

#### Intracardiac and Pericardial Neoplasms

Cardiac neoplasms are exceedingly rare occurring with an incidence of approximately 0.1%<sup>3</sup>. The most common histologic type is a rhabdomyoma which accounts for three-quarters of cardiac neoplasms and can be multi-focal.<sup>4</sup> When rhabdomyoma is suspected, tuberous sclerosis as an underlying disorder should be considered and warrants careful evaluation of the fetus for other anomalies associated with this disorder such as renal lesions and intracranial anomalies<sup>5</sup>. Other sub-types include teratoma, fibroma, vascular malformations and myxoma<sup>4</sup>.

Cardiac lesions usually are detectable after 22 weeks gestation on prenatal ultrasound and can involve the pericardium, myocardium, cardiac valves and/or the major pericardial blood vessels<sup>6,7</sup>. The outcome for cardiac neoplasms is grim with a risk for IUFD as high as 57%<sup>3</sup>. If the fetus survives to delivery, the mass appears to stabilize or even regress; however, the mortality rate in the first year of life is as high as 80%<sup>8</sup>.

Once diagnosed, the presence of non-immune fetal hydrops needs to be assessed by ultrasound and dedicated fetal echocardiography. Currently, there is no standard for fetal intervention in the setting of a cardiac mass; however, experts have considered the presence of non-immune hydrops an indication to offer open fetal surgical resection of the mass through a maternal hysterotomy and fetal median sternotomy. To date, there have been no reported survivors after open fetal resection of a cardiac neoplasm.

#### Ovarian and Abdominal Cysts

Abdominal cysts are a frequently diagnosed prenatal lesion and are discussed more extensively in a separate chapter. They encompass a broad-spectrum of potential pathologic conditions including choledochal cysts, meconium pseudocysts, infra-diaphragmatic pulmonary sequestration, ovarian cysts, duplication cysts, mesenteric cysts, or simple cysts of the liver,

spleen or pancreas<sup>9</sup>. Ultrasound is paramount in distinguishing the anatomic location of the cyst, as well as characterizing the lesion to facilitate accurate diagnosis.

Any cyst can become problematic if it grows to a size that results in local compression of intra-abdominal structures; specifically the gastrointestinal tract or the urinary tract. Compression that results in a bowel obstruction can lead to polyhydramnios which can result in preterm labor; compression of the urinary system can result in urinary obstruction and renal damage. Although these types of obstruction can be readily relieved through percutaneous cyst aspiration, the rate of recurrence is high<sup>9</sup>. Fortunately, most intra-abdominal cysts identified prenatally rarely necessitate a fetal intervention. In fact, the most common indication reported for fetal cyst aspiration has been for diagnostic purposes. This is generally unnecessary as these lesions are rarely life-threatening<sup>10</sup>.

### *Ovarian Cyst*

Ovarian cysts arise from ovarian follicles, and their growth is believed to be stimulated by fetal, maternal and placental hormones; although once diagnosed, they do not appear to change in size and many spontaneously resolve postnatally<sup>11,12</sup>. The majority of cysts are unilateral and can be described as either simple or complex. When a complex cyst is present, ovarian torsion is the most likely etiology. Ovarian torsion has been reported in 40% of prenatally diagnosed ovarian cysts<sup>13</sup>.

Like all other abdominal cysts, ovarian cysts can become problematic if they are large in size. When an ovarian cyst grows larger than 6cm, partial small bowel obstruction can lead to polyhydramnios and preterm labor.<sup>14</sup> Multiple reports have investigated percutaneous aspiration of the fetal ovarian cyst citing two benefits: prevention of polyhydramnios and prevention of ovarian torsion<sup>15,16</sup>. In the most cited series, Crombleholme recommends that a cyst size of >4cm, the presence of a “wandering” mass or rapid growth of the cyst should be indications for aspiration primarily to prevent torsion and loss of the ovary<sup>16</sup>. In the absence of these findings, ovarian cysts can be observed and studied postnatally with ultrasonography, as 50% will resolve spontaneously once the neonate is out of the hormonal milieu.

### **Fetal Neck Mass**

The cervical mass poses a significant risk to the fetus with a nearly 20% risk of IUFD and a 35% risk of death prior to airway stabilization immediately after delivery<sup>17,18</sup>. Obstruction of the trachea and esophagus can result in polyhydramnios and preterm labor, and local compression can lead to craniofacial defects and cranial nerve injury. Highly vascular lesions can lead to cardiac failure with non-immune fetal hydrops and subsequent IUFD<sup>19</sup>. The majority of these lesions will be comprised of either cervical teratoma, cystic hygroma or other vascular malformations<sup>20</sup>. Rarely neck masses can include thymic cysts or congenital neuroblastoma<sup>21,22</sup>.

These lesions are readily identified on prenatal ultrasound. Once the presence of a cervical mass has been recognized, fetal MRI should be obtained to better characterize the mass, specifically to distinguish between cystic hygroma and teratoma. This distinction is based on the presence or absence of fat within the lesion<sup>23</sup>. The tracheoesophageal displacement index (TEDI) can be a useful prognostic measurement. The TEDI is defined as the sum of the lateral and ventral



displacement of the trachea and esophagus from the ventral-most aspect of the cervical spine<sup>20</sup>. In a series of 24 prenatally diagnosed neck masses all patients with a TEDI of >12mm had a complicated airway whereas only 46% of those with a TEDI <12mm had a complicated airway. Furthermore, the authors found that the presence of a cervical teratoma or polyhydramnios also increased the risk for a complicated airway<sup>20</sup>.

Pregnancies complicated by a fetal cervical mass require close surveillance. Large masses that cause significant extension of the neck require delivery via cesarean section due to the risk of dystocia<sup>24</sup>. In the presence of fetal hydrops prior to 30 weeks gestation, open fetal resection may be considered although, to date, only one successful open fetal resection has been reported<sup>19</sup>. After delivery, immediately securing the airway is paramount. This cannot be accomplished quickly enough in up to 35% of cases. If the airway cannot be secured, the neonate dies immediately due to airway compromise<sup>17, 18</sup>. Left untreated, large neck masses can carry an 80-100% mortality rate<sup>24</sup>. For this reason, the *ex utero* intra-partum treatment (EXIT) procedure has been advocated to permit adequate time for airway stabilization prior to complete delivery.

It is critical to understand that an EXIT procedure is not a “glorified” cesarean section. Contrary to a cesarean section, deep maternal anesthesia is required during an EXIT procedure to maintain complete uterine relaxation and preserve utero-placental circulation so the fetus does not undergo premature transition from fetal to neonatal circulation. In a cesarean section, contraction of the uterus is ideal because it is hemostatic; in an EXIT procedure uterine contraction would be detrimental to the fetus but also puts the mother at greater risk for hemorrhage.

During an EXIT-to-airway procedure, the uterus is exposed and a hysterotomy is made to deliver the fetus’ head and neck. Direct laryngoscopy can be attempted for endotracheal intubation. Means to establish an airway can be escalated using bronchoscopy or tracheostomy if laryngoscopy is not successful. The trachea is oftentimes deviated, and this displacement must be recognized prior to tracheostomy. In cases of large cystic lesions, decompression of the cyst may facilitate establishing an airway by relieving any airway compression. When an airway still cannot be obtained, resection of the mass, while still on utero-placental circulation, may be necessary. This procedure is termed “EXIT-to-resection.” Once an airway has been established, the umbilical cord can be divided and the baby completely delivered.

Post-delivery and post-resection hypothyroidism and hypoparathyroidism are the most common complications, particularly with cervical teratomas<sup>24</sup>. Therefore, an endocrinology work-up should be initiated with consultation as indicated. Given the small malignant potential for cervical teratomas, screening for recurrence should also be implemented by following alpha-fetoprotein levels and obtaining surveillance imaging.

### **Retroperitoneal Mass**

Retroperitoneal masses are uncommonly found *in utero* and rarely, if ever, need direct fetal intervention; however, when a retroperitoneal mass is diagnosed, it is important to think of an appropriate differential diagnosis so that appropriate work-up, counseling and management occur depending on the diagnosis. First, where is the mass coming from? Appropriate adrenal pathology to consider includes adrenal hematoma, neuroblastoma and sometimes a second hydronephrotic collecting system or liver mass may be confused with adrenal masses. Renal

pathology includes mesoblastic nephroma, Wilms' tumor (rare), multicystic dysplastic kidney and of course other urinary collecting system pathologies such as hydronephrosis, infantile polycystic kidney disease (autosomal recessive), Meckel-Gruber syndrome, benign glomerulosclerosis, adult dominant polycystic kidney disease, trisomy 13, Beckwith-Weidemann syndrome and Perlman syndrome. Other diagnoses to be considered when seeing a retroperitoneal mass include extra-lobar pulmonary sequestration, ovarian masses and choledochal cysts. These should be considered in the differential during counseling and subsequent fetal ultrasounds.

We will briefly cover adrenal hematoma, neuroblastoma, mesoblastic nephroma and Wilms' tumor. There is very little data regarding direct fetal intervention for these pathologies. If the adrenal hemorrhage was moderate to severe, then this should prompt the mother to deliver at a facility that can manage neonatal shock. Congenital mesoblastic nephroma is a massive, usually benign hamartomatous, solitary renal tumor that rarely has malignant degeneration. Risks to the fetus include prematurity and polyhydramnios, and this influences post-natal outcome. Historically, mesoblastic nephroma was called Wilms' tumor, we now recognize that Wilms' tumor is extremely rare in fetuses. In all renal tumors, liver metastasis and locoregional lymph nodes should be evaluated also. Although hydrops fetalis, dystocia and tumor rupture have all been reported, fetal intervention is not considered standard therapy, although every case should be evaluated independently. We would advocate for delivery at a tertiary center capable of caring for neonatal cardiopulmonary compromise. After appropriate neonatal resuscitation, gentle ventilation techniques, and radiological imaging, standard of care is complete surgical resection. Chemotherapy and radiation is rarely needed for mesoblastic nephroma. Wilms' tumor has an excellent prognosis when diagnosed prenatally or within the first month of life, and standard work-up and resection should occur.

Neuroblastoma can cause elevated maternal catecholamine metabolites and maternal antenatal symptoms; however, no direct fetal intervention is needed other than early delivery for fetal compromise or maternal distress. As with other retroperitoneal solid tumors, polyhydramnios and fetal hydrops have been reported as well as hemorrhage during vaginal delivery, therefore cesarean section should be considered. Standard post-natal work-up should occur followed by appropriate risk-stratified therapy. Neuroblastomas diagnosed *in utero* or within the first weeks of life have a significantly better prognosis than neuroblastoma diagnosed after 18 months and many (including 4S metastatic neuroblastoma) regress spontaneously. COG trials may be open for non-surgical therapy—therefore consult COG before offering final therapeutic decision to family.

### **Ovarian Mass**

As previously discussed in this chapter, ovarian masses in fetuses are almost always benign corpus luteal cysts responding to maternal hormones. Unlike older children, complex cysts in the fetus and newborn are almost never associated with neoplasms and therefore intervention in the fetus or neonate based on malignancy is not warranted even with “complex” cysts. Although usually echo-free, echoes and septations can appear in the setting of torsion. Cystic masses can be found outside the pelvis in the abdomen. An appropriate differential includes duplication cysts, mesenteric cysts, omental cysts, lymphangioma, choledochal cysts, meconium peritonitis, ureteral cysts, liver cysts, urachal cyst, hydrometrocolpos and SCT.

Polyhydramnios has been reported in association with ovarian masses, and those fetuses should be monitored for pre-term labor, hydrops-fetalis and cardiopulmonary distress immediately after birth. Aspiration of ovarian cysts for polyhydramnios is controversial, but has been performed safely. Although it makes sense to aspirate larger cysts to avoid torsion, aspiration carries with it certain risks as well such as bleeding, intestinal injury, pre-term labor and fetal demise. Some authors have advocated aspiration of “larger” (>4cm) cysts, however, this recommendation has not won widespread support. Moreover, cyst recurrence after prenatal aspiration is frequent. Others have advocated cesarean section for massive (>9cm) cysts, but this is also controversial. Aspiration of the cyst when hydrops-fetalis occurs seems pragmatic. Overall, no fetal intervention is required for ovarian masses unless hydrops fetalis occurs.

Postnatally, any neonate with a symptomatic ovarian cyst warrants surgical exploration. Postnatal serial ultrasounds should be performed to document resolution of asymptomatic cysts. Other investigations may be required if the diagnosis is not clear. A controversy with ovarian cysts is when and how to intervene after delivery. Some have advocated surgical intervention for masses or cysts greater than 6cm, signs of torsion or hemorrhage, or lack of resolution. First, if the diagnosis is unclear, then more diagnostic procedures are warranted including exploration if needed. Second, most would agree that failure of resolution of cysts after 6-12 weeks, no matter how benign appearing, warrants exploration. Third, although no good evidence for intervening for masses greater than 5-6cm in neonates exists; it can be considered based purely on size to prevent torsion. Fourth, cysts being followed by serial ultrasound that demonstrates any enlargement or evidence of gastrointestinal or genitourinary abnormalities should be explored surgically. Fifth, best practices for intervention of persistent ovarian cysts have not been determined and aspiration, unroofing, laparoscopy and open exploration have all been used safely. Lastly, observation alone can be chosen if the family is willing and capable of bringing the patient back for appropriate follow up.

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## CHAPTER 6

### Prenatal Diagnosis and Therapy for Myelomeningocele

Nathan Heinzerling and Amy J. Wagner

#### Background

Myelomeningocele is a congenital defect that results from incomplete closure of the neural tube during development. This results in an open spinal canal with exposed neural tissue and leakage of cerebrospinal fluid. With an incidence of 1 in 2900 live births in the United States, myelomeningocele is the most common congenital birth defect of the nervous system<sup>1</sup>. The incidence of neural tube defects has decreased since the United States has mandated fortification of grain products with folic acid. However, folic acid supplementation has not eradicated the anomaly pointing to a multifactorial cause including exposure to drugs, toxins and genetic abnormalities<sup>2</sup>.

#### Associated Complications

Patients with myelomeningocele display a wide array of abnormalities related to the severity of their neurologic defect. Virtually all newborns with a myelomeningocele defect develop an Arnold-Chiari II malformation. This is caused by a pressure gradient from the continued leakage of cerebrospinal fluid resulting in hindbrain herniation. Of the patients with Arnold-Chiari II malformation, more than 90% will develop hydrocephalus<sup>3,4</sup>. Before the advent of ventriculoperitoneal shunting, hydrocephalus was the main cause of mortality among these patients. Even with the relief of pressure by shunting, children are still at risk for cerebellar and upper cervical nerve dysfunction. This can result in dysfunction of swallowing, vocal cord motion and upper extremity innervation and in severe cases central hypoventilation or apnea.

Additionally, patients with myelomeningocele have difficulty with bowel and bladder control due to nerve dysfunction of the distal bowel, anal sphincter, bladder and internal and external bladder sphincters. Poor outcomes are seen in patients who suffer from bladder sphincter dysynergy. These patients suffer from vesicoureteral reflux, which damages the upper urinary tract and may lead to renal failure. This can be abrogated by clean intermittent catheterization to prevent reflux<sup>5</sup>. Patients with a myelomeningocele are at risk for numerous complications throughout their life. This has inspired research into treating the myelomeningocele defect early to decrease the morbidity associated with the exposed neural placode.

#### Mechanism of Injury

The wide spectrum of neurologic deficits and associated morbidity from myelomeningocele can be explained by a “two-hit hypothesis” of injury. The first hit is the abnormality of the neural placode itself resulting in the defect. The second hit of myelomeningocele injury is the continued exposure of the neural tissue to amniotic fluid and intrauterine trauma throughout fetal development<sup>6,7</sup>. The two-hit model is supported by observations in human and animal development. First, patients with milder forms of neural tube defects in which the neural elements remain covered by skin or a membrane show improved neurologic development<sup>8</sup>. Also,

studies in both humans and mice with a myelomeningocele show near normal hind limb movement in early development with progressive loss of function *in utero* as pregnancy progresses<sup>9-11</sup>.

Animal models of surgically created myelomeningoceles in rodents, sheep, rabbits and nonhuman primates show a similar phenotype to that seen in humans. When the defects are surgically closed prenatally, there is marked improvement in motor and urinary function and reversal of the Arnold-Chiari malformation with near normal hindbrain development in the animal model<sup>12</sup>. This observation was important in the development of techniques to repair myelomeningoceles *in utero* and mitigate the effects of the second hit.

### **Fetoscopic Repair**

Early attempts at prenatal repair of a myelomeningocele with fetoscopy were by Vanderbilt Medical Center and the University of California, San Francisco<sup>13-15</sup>. Vanderbilt reported four cases of application of a maternal skin graft over the defect using a maternal laparotomy and three-port access to the uterus. Two of the fetuses survived to birth, both requiring reoperation as no evidence of the skin graft was present at birth. The University of California group reported three attempts at fetoscopic repair, two of which were converted to open repair due to intraoperative difficulties. The final patient had their defect covered with a decellularized dermal matrix. At birth there was incomplete coverage of the myelomeningocele defect requiring reoperation.

### **Open Repair and the MOMS Trial**

One of the first reports of open fetal myelomeningocele repair was published by Vanderbilt University in 1999. This study compared open repairs with historical controls and found improved hindbrain herniation with fetal repair and a decreased need for ventriculoperitoneal shunting<sup>16</sup>. UCSF and Children's Hospital of Philadelphia also found fetal surgery reverses hindbrain herniation, improved Chiari malformations and had a decreased need for ventriculoperitoneal shunting<sup>13, 17</sup>. Despite these initial promising results, further studies showed mixed results regarding neurologic outcomes in these patients<sup>18-19</sup>.

With unclear benefit to the child and risks of placental abruption, uterine dehiscence and preterm labor, further studies were needed to prove the benefit of fetal surgery over postnatal myelomeningocele repair. In 2003, the University of California, San Francisco, Children's Hospital of Philadelphia, Vanderbilt University and George Washington University collaborated with the National Institute of Health to conduct a randomized controlled study comparing fetal versus postnatal myelomeningocele repair (the MOMS trial). Their goal was to enroll 200 patients at gestational age 19 to 25 weeks with myelomeningocele defects between T1 and S1. The patients were randomized to open fetal repair of the myelomeningocele or repair after delivery. All patients undergoing fetal surgery underwent cesarean section at 37 weeks gestation to prevent the risk of uterine dehiscence. Enrollment for the study was stopped in December 2010 by the safety monitoring committee due to the efficacy of prenatal surgery shown in the first 183 patients<sup>20</sup>.

The primary outcomes investigated were fetal or neonatal death or the need for a ventriculoperitoneal shunt by 12 months of age. Additionally, a composite score of mental development using the Bayley Mental Development Index and the difference between anatomical and functional level of the lesion was calculated. There were no maternal deaths and two perinatal deaths in each group. The need for ventriculoperitoneal shunting in the prenatal and postnatal surgery groups at 12 months of age were 68% and 98%, respectively ( $p < 0.001$ ). Actual shunt placement was 40% in the prenatal group and 82% in the post-natal group ( $p < 0.001$ ). The second primary outcome showed significant functional and neurologic improvement at 30 months of age in the prenatal surgery group ( $p = 0.007$ ). The prenatal surgery group had numerous other benefits in *post hoc* analyses. The most notable include an improved ability to walk without devices or orthotics in the prenatal surgery group (42% versus 21%,  $p = 0.01$ ) and decreased hindbrain herniation at 12 months in the prenatal surgery group (64% versus 96%,  $p < 0.001$ ). Additionally, even though the prenatal surgery group had more severe anatomical lesion levels, the prenatal surgery group had better motor function than the postnatal surgery group when measured with either the Bayley or Peabody motor scales.

Significant maternal morbidity related to prenatal surgery included uterine dehiscence, oligohydramnios, placental abruption, spontaneous rupture of membranes and chorioamniotic separation. The study continues to follow the long-term outcomes of these children by assessing the lasting effects prenatal surgery has on motor and neurologic development, bowel and bladder continence.

## **Summary**

The *in utero* treatment of myelomeningocele contributes to improved outcomes in children with reduction of hindbrain herniation, less need for VP shunt and enhanced motor outcomes. Further research and improved techniques are still needed to minimize the risks to both the fetus and mother. Future directions include the use of stem cells or biomaterials such as cellulose scaffolds to improve the neurologic outcomes and provide coverage during fetal myelomeningocele repair<sup>22, 23</sup>. As this is the first non-lethal indication for fetal surgery, we must strive for improved outcomes and minimize the morbidity to both the fetus and mother.

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## CHAPTER 7

### Abdominal Wall Defects

Shaheen Timmapuri

#### GASTROSCHISIS

##### **Prenatal Diagnosis:**

- Elevated AFP – suggestive of diagnosis
- Ultrasound
  - o May identify GS as early as first trimester
  - o Exteriorized bowel in relation to the anterior abdominal wall, no covering layer
  - o Follow-up ultrasounds weekly after 28-32 weeks gestation
- Finding of intra-abdominal bowel dilatation may be suggestive of intestinal complications (bowel obstruction, atresia)
  - o No standard definition of dilatation - ? >20mm in diameter
- Other prenatal parameters suggested to correlate with poor postnatal outcomes
  - o IUGR, thickened bowel, stomach herniation, stomach dilatation
  - o No evidence to support
- No fetal interventions

##### **Perinatal Management:**

- Prenatal diagnosis and counseling
- Mode of delivery
  - o No evidence of difference in outcome between C-section and vaginal delivery
- Timing of delivery remains controversial with some advocating spontaneous delivery and others advocating early (i.e., 36-38 week) delivery.
  - o Rationale for early delivery
    - Decreased exposure time of intestine to amniotic fluid
    - Ability to ensure delivery at center with appropriate resources
  - o Early delivery – May be correlated with worse outcomes
    - Complications of prematurity
    - Increased ventilation requirements
    - Prolonged time to full enteral feeding
    - Prolonged hospital stay
- Delivery at/near tertiary center is associated with decreased morbidity compared to delivery at community hospital
  - o Availability of pediatric surgeon and level III NICU
- Neonatal resuscitation
  - o IV access
  - o NG decompression
  - o Bowel protection

- Prevent heat and fluid losses

### **Timing of Surgery:**

- Intervention immediately after birth

### **Surgical Options:**

- Primary closure
- Silo placement/delayed closure
- “Plastic closure” – nonoperative

### **Associated Anomalies:**

- Atresias
- Undescended testes
- Malrotation

### **Complications:**

- Perforation
- Midgut volvulus
- Necrotizing enterocolitis
- Line sepsis

### **Neonatal Morbidity:**

- Overall survival greater than 90%
- Morbidity related to:
  - Bowel complications – atresias, perforation
  - Short bowel syndrome
  - Prolonged TPN
  - Prematurity (BPD)

### **Long-term Outcome Measures:**

- Correlation of prenatal ultrasound findings to outcomes
- Time to feeding
- Ventilation requirements
- Complications

## **OMPHALOCELE**

### **Prenatal Diagnosis:**

- Elevated AFP
- Ultrasound
  - May identify omphalocele in late 1<sup>st</sup> or early 2<sup>nd</sup> trimester

- Central lesion (covered with a sac) anterior to abdominal wall fascia, umbilical cord attached to sac
- Ruptured omphalocele may be confused with gastroschisis
  - Omphalocele suggested by umbilical cord location, presence of extra-abdominal liver
- Sonographic findings thought to be predictive of postnatal morbidity/mortality (none completely reliable)
  - “Giant” omphalocele (>5cm) – difficult to define in fetus
  - Extracorporeal liver
  - O/HC (omphalocele/head circumference) ratio – if  $\geq 0.21$ , may predict need for staged versus primary closure
- Follow-up ultrasounds weekly after 32 weeks gestation
- Associated anomalies (cardiac, CNS, chromosomal, Beckwith-Wiedemann) common so need to evaluate
- Fetal MRI – allows better assessment of defect as well as associated anomalies
- Fetal echocardiography
- Amniocentesis (karyotype)
- Smaller defects associated with higher incidence of associated anomalies
- No fetal interventions

### **Perinatal Management:**

- Prenatal diagnosis and counseling
  - Attempt to identify associated anomalies to effectively counsel families
  - Termination rate may be 50-80%
  - Fetal demise, spontaneous abortion ~ 5-10%
  - ~1/3 of patients thought to have isolated omphalocele on prenatal screen will have multiple anomalies detected after birth
- Mode of delivery – No studies comparing outcomes for vaginal versus cesarean deliveries (both successfully done with small lesions)
  - Cesarean section recommended for giant omphaloceles or presence of extra-abdominal liver
    - Risk of omphalocele rupture, dystocia or liver injury
- Timing of delivery – No indication for early delivery unless obstetric indication
- Delivery at/near tertiary center
  - Availability of pediatric surgeon
- Neonatal resuscitation
  - IV access
  - NG decompression
  - Glucose monitoring (Beckwith-Wiedemann syndrome)
  - Cover sac with nonadherent dressing to protect and keep moist

### **Timing of Surgery:**

- Depends on size of defect and stability of patient/presence of comorbid conditions (i.e., cardiac or respiratory insufficiency)

### **Surgical Options:**

- Primary closure – for small- to moderate-sized defects
- Delayed (nonoperative) closure – when defect is too large or patient not clinically stable for closure
  - o Treatment of covering membrane with eschar-forming agent to promote epithelialization of sac → ventral hernia to be closed at later time
  - o Historically used agents (mercurochrome, alcohol, silver nitrate) found to be too toxic
  - o Currently used agents (silver sulfadiazine, povidone-iodine solution, antibiotic ointments) may be combined with compression dressing
- Staged closure – for giant omphaloceles
  - o Options:
    - Amnion inversion – use of covering membrane to reduce contents gradually and then close defect
    - Use of prosthetic or biologic mesh to cover defect after removing amnion membrane
- Ruptured omphalocele
  - o Urgent closure/coverage
  - o Large defects – challenging problem

### **Associated Anomalies:**

- Chromosomal anomalies (Trisomy 13, 18, 21) – up to 50% of patients
- Cardiac defects
- CNS abnormalities
- Pentalogy of Cantrell (abdominal wall defect, anterior diaphragmatic hernia, cardiac anomaly, pericardial defect, sternal cleft)
- Bladder extrophy
- Beckwith-Wiedemann syndrome
- Malrotation

### **Complications:**

- Abdominal compartment syndrome
- Respiratory insufficiency
- Necrotizing enterocolitis
- Midgut volvulus
- Hernias
- Line sepsis

### **Neonatal Morbidity:**

- Overall survival 23-52%
- Morbidity related to:
  - o Associated anomalies
  - o Chromosomal defects
  - o Pulmonary hypoplasia

- Gastroesophageal reflux
- Prolonged TPN

### **Long-term Outcome Measures:**

- Correlation of prenatal findings with morbidity and mortality
- Outcome of staged closure techniques
- Ventilation requirements
- Complications

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## CHAPTER 8

### Intestinal Obstructions, Atresias and Abdominal Cysts

Tracy Grikscheit

(adapted from FI Luks, SR Carr and LP Rubin - Brown University BIOMED-572)

#### Intestinal Obstruction

Differential diagnosis

1. High obstruction (esophageal atresia, duodenal atresia)
  - a. Fetus cannot swallow amniotic fluid which leads to **polyhydramnios**
  - b. Polyhydramnios on prenatal ultrasound is a trigger to look for a high obstruction
  - c. The higher the obstruction, the more severe the polyhydramnios
2. Low obstruction (mid-, distal small bowel, colon)
  - a. Normal amniotic fluid volume
  - b. Distended intestinal loops on ultrasound

Potential etiologies of intestinal obstruction

1. Isolated atresia anywhere in the GI tract
2. Meconium ileus:
  - a. 20% of patients with cystic fibrosis will have meconium ileus as a newborn
  - b. 90-95% of newborns with meconium ileus will have cystic fibrosis
    - i. Therefore, all newborns with meconium ileus need to be tested for CF
3. Malrotation with midgut volvulus
4. Hirschsprung's disease
5. Compressive obstruction from abdominal cyst or mass
  - a. i.e., intestinal duplications, mesenteric, choledochal, ovarian, or renal cysts, tumors, etc
6. Combinations: i.e., meconium ileus → obstruction → volvulus → local bowel ischemia → segmental necrosis → atresia

Prenatal management

No indications for prenatal intervention

1. Delivery in tertiary center recommended
2. If underlying condition suspected, prenatal diagnosis may be possible
  - a. Meconium ileus and testing for cystic fibrosis
  - b. Duodenal atresia and karyotyping for Trisomy 21

#### Echogenic Bowel

Bright appearance of bowel or bowel wall on ultrasound

Etiology unclear – may be a secondary effect of several possible causes

1. Meconium ileus (cystic fibrosis)
2. Intestinal obstruction of varied causes
3. Swallowed blood (e.g., after amniocentesis)

Most often, echogenic bowel is idiopathic

Significance of echogenic bowel is unclear, but it is an indication for further testing

1. Infectious screen
2. Amniocentesis, consider cystic fibrosis; chromosomal anomaly (trisomy)
3. If associated with maternal bleeding: poor pregnancy outcome
4. If due to underlying condition: prognosis depends on that condition
5. If due to intestinal obstruction: good prognosis, but postnatal surgical intervention likely

### **Abdominal Masses and Cysts**

Ultrasound characteristics

1. Heterogeneous appearance
  - a. May have debris
  - b. Can be cystic or solid or mixed
  - c. Calcifications suspicious for teratomas or meconium peritonitis
  - d. Consider torsion (intestinal, ovarian)

Differential diagnosis

1. Intestinal obstruction (see above)
2. Meconium peritonitis:
  - a. Intestinal rupture/perforation → sterile peritonitis → inflammation causes pseudocyst/walled off meconium-stained pocket
  - b. Impressive abdominal distension, but rarely an emergency; prognosis depends on underlying condition (often cystic fibrosis)
  - c. Can frequently see calcifications
3. True cyst: etiology difficult to establish; process of elimination
  - a. Ovarian cyst (check gender)
  - b. Choledochal/liver cyst
  - c. Mesenteric cyst/lymphangioma
  - d. Cystic kidney disease
  - e. Adrenal cyst: adrenal hemorrhage
  - f. Cystic neuroblastoma
  - g. Intraabdominal pulmonary sequestration
  - h. Cystic teratomas (ovary, retroperitoneum)
  - i. Anterior neural tube defect/neurenteric cyst

Prenatal Management

1. Can almost always wait until after delivery
2. If very large: risk of dystocia/C-section may be indicated
3. Ovarian cyst:
  - a. Etiology: maternal hormonal stimulation
  - b. Regression postnatally is the rule (decreased hormone stimulation)



- c. If large (>4-5cm) risk of torsion and loss of entire ovary
- d. No consensus on if Antenatal intervention (needle aspiration) justified. Must always balance against risk to the fetus
- e. Usually best managed postnatally

## CHAPTER 9

# Operative Fetoscopy, Twin Gestations and Twin-to-Twin Transfusion Syndrome

Brad Feltis and William Block

### Introduction

In the USA, there has been a steady increase in the number of twin pregnancies over the past three decades. In 2009, 1 in every 30 babies born in the United States was a twin, compared with 1 in every 53 babies in 1980<sup>1</sup>. Twin-to-twin transfusion syndrome (TTTS, described below) occurs in approximately 1 in 50 twin pregnancies or about 4,000 babies per year<sup>2</sup>. Advanced (stage 2 or higher) TTTS is by far the leading indication for operative fetoscopy (Fig. 1). Although no data exists on the actual number of fetoscopic interventions annually in the USA, it is estimated to be around 500<sup>3</sup>. Most likely, not all indicated fetoscopic cases are being performed. Mainly, this is due to a lack of expertise and training in the procedure. For a variety of reasons, pediatric surgeons should familiarize themselves with the diagnosis of TTTS and with the technical details of operative fetoscopy.

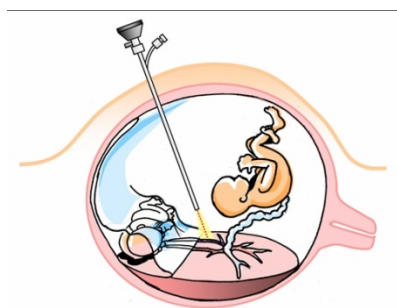


Fig. 1. Operative Fetoscopy for TTTS. Under US guidance a long needle is advanced into the gestational sac of the recipient twin. A wire is threaded and a Cordis (9-11 fr) is introduced via Seldinger technique. A 1-2mm telescope along with a laser fiber can then be placed through the Cordis to laser coagulate communicating vessels. (with permission, F. Luks, Brown Univ.)

### Chorionicity Definitions and Incidence

Dizygous twin gestations (2/3 of all twin pregnancies)

1. Dizygous twins are non-identical (fraternal) twins arising from two separate eggs fertilized by two separate sperm.
2. All are dichorionic (separate placenta) and diamniotic (separate gestational sac)
3. Because each twin has a separate placenta and gestational sac, these twins are not at risk for TTTS

Monozygous (MZ) twin gestations (1/3 of all twin pregnancies). “Identical” twins arising from single fertilized ovum dividing to form 2 embryos.

1. 1% of these twins share a gestational sac and a placenta (*Monochorionic, monamniotic gestation “MonoMono”*)
  - a. Two fetuses in single amniotic sac (rare)
  - b. High risk of fatal complications, such as cord entanglement means that many of these pregnancies result *in utero* demise.

2. 1/3 of all MZ twins will have their own placenta and their own gestational sac (Dichorionic diamniotic)
  - a. NOT at risk for TTTS
  - b. Remember, ALL Dizygous gestations are also dichorionic diamniotic
3. 2/3 of all MZ twins will each have their own gestational sac (diamniotic) and share a placenta (Monochorionic)
  - a. Single placenta, but each twin is in its own amniotic sac, so they do not get tangled.
  - b. Although all of these twins are at risk for TTTS, only 10-15% will develop

### **Twin-to-Twin Transfusion Syndrome (TTTS)**

Develops in 10-15% of all monochorionic (single placenta) pregnancies

Pathophysiology

- a) Most monochorionic twins share blood flow via AV, and sometimes AA and VV anastomoses
- b) Usually, this transfusion is balanced (net balance of twin A to twin B and twin B to twin A)
- c) In 10%-15% of monochorionic pregnancies the transfusion can become unbalanced
- d) This is called twin-to-twin transfusion syndrome (Fig. 1, TTTS)

Natural evolution

“Donor Twin” also called “stuck” twin

- a) Has a net blood volume flow towards the other twin
- b) Results in chronic hypovolemia and leads to chronic oliguria, which ultimately results in oligohydramnios
- c) Ultimately, this can lead to failure to grow, high output cardiac failure, hydrops and death
  - a. Fetal Hydrops or “Hydrops Fetalis” is the accumulation of fluid, or edema, in at least two fetal compartments (most commonly abdominal ascites, thoracic effusion or body wall edema)

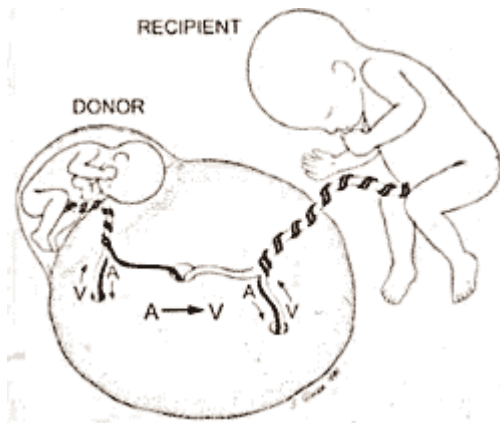


Fig. 1.

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### “Recipient Twin”

- a) Net blood flow is towards this twin
- b) Results in chronic hypervolemia resulting in chronic polyuria and Polyhydramnios
- c) Ultimately, this can lead to cardiomegaly, tricuspid regurgitation, hydrops and death

### Diagnosis

Prenatally by ultrasound findings:

- a) Single placenta (monochorionic), same gender
- b) One chorionic membrane, but two amniotic membranes (diamniotic)
- c) Polyhydramnios (>8cm fluid) in one twin *and* oligohydramnios (<2cm fluid) in the other
- d) Other signs (advanced TTTS):
  - a. Discordant size
  - b. Bladder not visible in the small twin
  - c. Hemodynamic anomalies (flow or velocity changes in umbilical or middle cerebral artery)
  - d. Cardiac changes (valvular regurgitation)
  - e. Hydrops in either twin

### Staging system “Quintero Stage”

Stage I: Oligo/polyhydramnios, but no fetal distress, bladders seen in both babies

Stage II: Donor bladder no longer visible (donor also has severe oligo/anhydramnios)

Stage III: Abnormal Doppler signal in either baby, namely, absent or reversed end-diastolic velocity in the Umbilical Artery (indicating significant hemodynamic stress)

Stage IV: Fetal hydrops

Stage V: Single or dual fetal demise

### Limitations of staging

- a) Disease evolution is unpredictable
- b) Not all cases worsen, some spontaneously improve
- c) Disease may skip stages or may remain same stage for several weeks

### **Complications and Treatment of TTTS**

Precise figures for morbidity and mortality of untreated TTTS are unknown. Previous studies have documented overall survival of only 30% in untreated pregnancies with Stage II or above TTTS<sup>4</sup>.

In untreated cases, if one twin dies, sudden hypotension in the survivor can result in intracranial hemorrhage or ischemia with neurologic impairment in up to 30% of cases.

## TTTS Treatment Options

1. Observation
  - a) Many cases remain at Stage I (or improve).
  - b) As of 2012, no prospective data exist defining the rates of progression or outcome for Stage I TTTS. Current retrospective estimates put progression rates at about 25%.
  - c) Unresolved controversy over recommendations for intervention with Stage I. Most practitioners do not think benefits outweigh risks. However, at least two busy Fetoscopic centers have reported improved outcomes after offering intervention for Stage I TTTS.
2. Amnioreduction (AR):
  - a) Volume reducing the polyhydramnios from the recipient twin.
  - b) Rationale: drainage of polyhydramnios reduces uterine overdistention and may prevent contractions, prolong gestation and improve blood flow in both twins.
  - c) Clinical threshold to initiate AR therapy is subjective
  - d) Arguably, most useful for relieving symptoms and possibly prolonging gestation in mild TTTS >26 weeks gestation
  - e) Technique is simple and widely available.
  - f) AR results in improved survival over observation alone. However, morbidity (30% neurologic impairment in surviving twin) continues to be high if there is *in utero* loss of a twin.
  - g) Risk of single AR is minimal, but does include:
    - a. Perforation of intervening twin membrane (septostomy)
    - b. PPROM (Preivable Preterm Rupture Of Membranes)
    - c. Bleeding
    - d. Chorio-amnionitis
    - e. Separation of the amnionic.chorionic membranes
  - h) Cumulative risk increases with serial drainage
  - i) A key limitation is that AR does not address underlying TTTS pathophysiology
3. Fetoscopic laser ablation (FLA) of communicating placental vessels
  - a) Rationale: eliminate all offending surface placental vascular anastomoses
  - b) Accomplished via fetoscopy with laser-occlusion of intertwin vessels
  - c) Currently accepted as the definitive treatment for severe TTTS (Stage II and above)
  - d) In 2012, FLA can be performed from 16-26 weeks gestation
    - a. FDA classifies fetoscope as “investigational” and limits its use to 26 weeks GA
    - b. Additional technical limitations with advanced pregnancy:
      - i. larger placental vessels (more challenging to coagulate)
      - ii. increased fetal vermix in amniotic fluid makes visualizing placenta challenging
  - e) Randomized controlled trials of FLA vs AR for severe TTTS mid gestation<sup>5-6</sup>
    - a. FLA significantly higher likelihood of survival of at least one twin (76% vs 56%) to 28 days of age
    - b. Babies with FLA had an 80% reduction in neurologic complications
    - c. Up to 25% of pregnancies result in double loss, even with FLA

- f) Complications of Fetoscopic Laser are common and, except for PROM, the rates are comparable to those seen with amnio reduction (reviewed in 2)
  - a. Premature Rupture Of Membranes (PROM)
    - i. The most common serious complication of fetoscopy
    - ii. 7 and 17% 1 and 3 weeks post procedure<sup>7</sup>
    - iii. May result in preivable delivery
  - b. Amniotic fluid leak into maternal peritoneal cavity (7%)
  - c. Vaginal bleeding (4%)
  - d. Placental abruption (2%)
  - e. Chorioamnionitis (2%)

#### Twin Reversed Arterial Perfusion (TRAP) Sequence (AKA Acardiac Twinning)

- a) Rare, occurs in approximately 1% of monochorionic twins
- b) One twin structurally normal
- c) Other “acardiac” twin is an abnormal mass of tissue consisting of legs and a lower body
- d) The “acardiac twin” does not have a heart, is most often anencephalic and has no chance of survival.
- e) The normal twin is referred to as the “pump twin” because its heart is used to pump blood to the abnormal mass.
- f) TRAP sequence: perfusion of acardiac by healthy twin via reversed flow in acardiac’s umbilical artery
- g) Danger for healthy twin: high output heart failure, hydrops, death

#### Management options

- a) If the acardiac twin remains small:
  - a. observe
- b) If impending hydrops of normal twin
  - a. Digoxin administration (to mother) → transplacental to fetus: to counteract cardiac failure
  - b. Definitive therapy is separating the vascular connections via US directed umbilical cord occlusion of acardiac mass with bipolar or radiofrequency ablation (RFA)

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