The Role of Fetal Surgery in Life Threatening Anomalies

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The development and evolution of fetal surgery and the recognition of the fetus as a patient came from two sources. First, were those obstetricians and perinatologists who detected life threatening anomalies before birth, and re-described a hidden mortality arising from death in utero. Ultrasonography, color Doppler ultrasound and ultrafast fetal magnetic resonance imaging have since enhanced the accuracy of prenatal evaluation. Second, were those pediatricians responsible for treating newborn infants with extremely serious problems, and that appeared untreatable, although, it was believed that they could have been treated at an earlier stage of development. After the natural history of several correctable lesions had been determined and the selection criteria for intervention developed, fetal surgery emerged as a means of improving the overall morbidity and mortality rates.

Until the early 1980s, the treatment of the intrauterine fetus was limited to chemotherapy, for a few infectious diseases, and hormonal supply in certain endocrine disorders of the mother. The first successful intrauterine transfusion of a fetus with hemolytic disease was performed by Liley in 1963.[1] The principal obstacle to the open technique was the fear that opening the amniotic cavity would lead to disturbances in the placental circulation and result in expulsion of the fetus.[2] However, meticulous study has been undertaken on the natural history and pathophysiology of fetal disease in animal models over the past two decades. As a result of this investment in basic

and clinical research, anesthetic, tocolytic, and surgical techniques for hysterotomy and fetal surgery have been refined. Fetal surgery now offers a high chance of survival in selected circumstances, when the prognosis is otherwise dismal.

PREOPERATIVE AND POSTOPERATIVE CARE

It is important to select fetuses that are likely to benefit from fetal intervention. The selection criteria, which invariably are predictors of fetal death should be refined. Overridingly, fetal surgery must be safe for the mother, and significant potential risk and discomfort resulting from the procedure should be minimized. There have been no maternal deaths, no compromised fertility, and few postoperative complications in the mother.

An active maternal transport system, a high risk obstetric unit, and a high standard intensive care unit are essential surgical facilities. Patients transferred to a fetal surgery center should be evaluated by a multidisciplinary team, which includes specialists from pediatric surgery, obstetric and reproductive genetics, maternal and fetal medicine, radiology, echocardiography, obstetric and fetal anesthesiology, neonatology, special nursing, genetic counseling, ethics, social work, and many others. The evaluation includes detailed ultrasonography, to confirm the diagnosis, ultrafast fetal magnetic resonance imaging, fetal echocardiography, and amniocentesis or umbilical blood sampling for fetal karyotyping.[3-6]

The correct anesthesia contributes greatly to fetal surgery. Halothane provides myometrical relaxation without any significant degree of fetal or maternal hypotension. Nitric oxide was found

to be an important intermediary in uterine relaxation, and to bean inhibitor of preterm labor. This finding has proven useful in the clinical situation.[7]

Adequate analgesia can be obtained via an epidural catheter postoperatively. The tocolytic regimen includes an indomethacin rectal suppository preoperatively and then postoperatively. MgSO4 infusion is maintained for 48 to 72 hours postoperatively with serum magnesium monitoring. On the second postoperative day, terbutaline in administered subcutaneously using pump based system. It should be noted that all patients that receive fetal surgery require cesarean delivery to avoid uterine rupture during labor.[3]

Complications specific to fetal surgery include maternal pulmonary edema, amniotic fluid leakage, and chorioamniotic separation. Maternal pulmonary edema results from a capillary leak. Restricted fluid administration decreases the risk of pulmonary edema, however, this can compromise the maternal-placental-fetal circulation and induce premature preterm labor. Postoperative intravenous fluid and furosemide diuresis dramatically reduces this incidence. Amniotic fluid leakage can develop either from the hysterotomy site or via the vagina, due to membrane rupture. A running absorbable monofilament suture to the myometrium and membranes, interrupted full thickness sutures, and an omental patch can prevent this complication. In addition, chorioamniotic separation can lead to amniotic band formation and membrane rupture. Serial ultrasound evaluation and fetal monitoring is recommended to detect this complication postoperatively.

CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

CDH occurs once in 2200 births, when stillbirths are included. Of the CDH cases identified in utero, 70% to 75% are associated with polyhydramnios. The presence of polyhydramnios is associated with a mortality of 72 to 89%.[8] In the absence of polyhydramnios, the mortality remains in excess of 50%. Poor prognostic factors are early gestational age at diagnosis, severe mediastinal shift, polyhydramnios, a small lung-thorax trans-

verse area ratio, left heart underdevelopment, and the presence of liver in the chest. The most important prognostic factor is liver herniation. The absence of liver herniation is indicative of a good prognosis with a survival of 93%, whereas associated liver herniation is associated with survivalof 43%.[9-11] The ratio of right lung area to head circumference (LHR) is a reliable predictor of postnatal outcome for left CDH. No patients with a LHR of less than 0.6 have survived, whereas all patients with a LHR greater than 1.35 have survived. LHR values between 0.6 and 1.35 are associated with a survival of 57%. The liver-down group has a uniquely good prognosis, and therefore, fetal surgery is unlikely to improve upon their already good probability of survival.[12,13]

Originally open fetal surgery proved technically impossible when liver herniation was present, because acute reduction of the liver into the peritoneal cavity compromised umbilical venous flow, and result in fetal bradycardia and arrest. In 1993, Wilson et al.[14] reported that experimental pulmonary hypoplasia can be prevented by tracheal ligation. Obstructing the flow of fetal lung fluid accelerates fetal lung growth, gradually reduces herniated viscera, and prevents pulmonary hypoplasia.[15]

Two approaches can be taken to occlude the fetal trachea: open fetal surgery and a video-fetoscopic technique (Fetendo Clip). Open tracheal clipping is carried out by hysterotomy by exposing the upper extremities. The occlusion of the trachea is accomplished by applying two large hemoclips. Great care must be taken not to injure the recurrent laryngeal nerves. Complications associated with the hysterotomy and open surgery severely compromised survival. Currently, there is a movement away from surgically invasive procedures to less invasive fetoscopic techniques. The technique of placing a plug inside the trachea can cause considerable damage. However, when the metal clip is placed outside the trachea, the clip does not harm the trachea. There, the specialized endoscopic method was developed, involving dissecting out the trachea, and placing fetendo clips endoscopically.[16-19]

The next problem is that the fetus trachea is completely occluded at birth, and therefore, the ex

utero intrapartum treatment or EXIT strategy was developed. The infant is half delivered with the placental circulation left intact. There is no rush to secure an airway, so the infant is bronchoscoped and the clip pulled off before wound is repaired.[20,21] The fetoscopic technique is better for the mother, as the mothers have fewer respiratory complications and preterm labor compared with open fetal surgery. Pulmonary edema developed in three of eight Fetendo clip patients and 11 of 13 open clip patients.[16]

CONGENITAL CYSTIC ADENOMATOID MALFORMATION(CCAM)

CCAM is defined as a multicystic mass of pulmonary tissue in which there is a proliferation of bronchial structures at the expense of alveoli. This disease is considered a focal pulmonary dysplasia, rather than a hamartoma, since in many cases the cyst walls contain skeletal muscle.[22] A large lesion is usually noncystic and produces mediastinal shift, and this lesion usually has a poor prognosis. Approximately 20% of fetal CCAM lesions decrease in size or even disappear ultrasonographically. However, all patients with a large CCAM and hydrops died before or shortly after birth.[23] Defining prognostic criteria allows the appropriate selection of patients for standard postnatal care, termination, or fetal intervention. The CCAM volume ratio (CVR) is obtained by dividing the CCAM volume by the head circumference, to correct for differences in fetal size. None of the fetuses with a CVR of less than 1.2 developed hydrops. Polyhydramnios is the result of esophageal obstruction by the thoracic mass and decreased fetal swallowing of the amniotic fluid.[24-26]

Maternal mirror syndrome can follow fetal hydrops, placentomegaly, and a large fetal lung mass. This syndrome has progressive symptoms of preeclampsia including, vomiting, hypertension, peripheral edema, proteinuria, and pulmonary edema. The condition may result from the release of vasoactive amines from the edematous placenta. Its reversal cannot be achieved by treating the fetal anomaly alone, and is considered a contraindication to fetal surgery.

Isolated CCAM with fetal hydrops before lung maturity is the only indication of fetal surgery. Thoracoamniotic shunting is effective in a large predominant cyst, but this approach is not a reasonable therapeutic choice for multicystic or predominantly solid CCAM lesions. Fetal lobectomy is the treatment of choice for these lesions23. Fetuses without hydrops usually survive until birth, and therefore, they can be managed postnatally. Sixty eight percent of hydropic fetuses survived after fetal CCAM resection. In highly selected cases, fetal CCAM treatment is safe, technically feasible, it reverses hydrops, and allows sufficient lung growth to permit survival.

SACROCOCCYGEAL TERATOMA (SCT)

The sacrococcygeal site is the most common site of newborn teratomas and the most common extragonadal locus of teratomas and malignant germ cell tumors. The majority of SCT are Altman's type I of II,[27] and therefore, have a characteristic protuberance. Because of acoustic shadowing of the fetal pelvic bone, ultrasound cannot always delineate the extent of SCT. Ultrafast fetal MRI is better for defining the intrapelvic location.

Newborn babies with SCT do well after early surgical resection, even in the minority of the tumors showing malignant change. However, the prognosis of SCT diagnosed before birth has a mortality of 30% to 50%. The hemodynamic effect of SCT involves a large blood flow to the tumor, and it creates a vascular steal from the placenta and the fetus. Moreover,the vascular steal increased placental thickness and abnormal umbilical venous flow.[28] Placentomegaly and fetal hydrops can lead to maternal mirror syndrome as in cases with CCAM. Fetal intervention before the related maternal preeclampsia is recommended.[29]

Resection of a large SCT can reverse high output cardiac failure and early intervention offers the best hope of fetal survival. Fetal surgery is considered in fetuses of less than 32 week of gestation, and fetal hydrops and placentomegaly are normally reversed 10 days after surgery.[30] Radiofrequency thermal ablation and laser therapy, to occlude the arteries feeding an SCT are

alternatives of open fetal surgery.[31-34] These techniques can be performed percutaneously with ultrasonographic guidance, significantly decreasing the incidence of preterm labor and maternal morbidity as compared with open fetal surgery.

FUTURE PERSPECTIVES

The advantage of fetal surgery is evident in certain life threatening diseases, but the further development of the technique is not. Currently, there is a developing trend away from surgically invasive technique to less invasive fetoscopic procedures. The key to endoscopic procedure within the uterus is not the visualization, but the ability to link videoendoscopy with sonography.[35] Several life threatening anomalies have been considered to be indications of fetal surgery to date, but endoscopic intervention may allow the prenatal treatment of non-life threatening diseases like craniofacial defects and myelomeningocele. The fundamental limiting factor remains the problem of preterm labor. The pharmacological control of uterine contraction would represent a breakthrough for fetal surgery.

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