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Editorial

Prenatal diagnosis of congenital anomalies in the era of fetal surgery in Mexico

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The clinical utility of fetal ultrasound in the prenatal diagnosis of different congenital anomalies has been advancing towards better accuracy in recent years, mainly due to technological improvements in current ultrasound devices, and incorporation of formal programs for fetal ultrasound training by different international and national societies worldwide. A proportion of congenital malformations suitable for prenatal diagnosis, at risk of either intrauterine fetal demise or neonatal death if left untreated, have now the possibility to benefit from fetal surgery in order to improve prognosis, leading to mandatory accurate prenatal diagnosis and timely referral to a fetal surgery center. However, despite fetal intervention, a higher neonatal mortality might be expected in fetuses with congenital anomalies managed in countries like ours where termination of pregnancy is not allowed, suboptimal neonatal management due to limited neonatal intensive care unit capabilities, and the influence by social and economic factors.[1, 2] The following congenital malformations are good examples of fetal anomalies that should be detected by fetal ultrasound and must be referred to fetal surgery centers, allowing the possibility of fetal intervention: 20% of monochorionic twin pregnancies may be complicated with twin-to-twin transfusion syndrome (TTTS), secondary to the presence of placental vascular anastomoses between both twins. This complication is associated with a high risk of either intrauterine fetal demise of both twins or neurological damage in the survivor twin.[3, 4] Fetuses with congenital diaphragmatic hernia (CDH), associated with a high neonatal mortality rate due to the development of severe lung hypoplasia and/or pulmonary hypertension, secondary to lung compression by the thoracic herniation of abdominal organs.[1, 5]. Similarly, fetuses with severe congenital hydrothorax, the presence of fetal airways malformations such as bronchial atresia, laryngeal atresia, tracheal obstruction by external large cervical masses, or large intrathoracic lung masses with the potential of causing fetal hydrops such as bronchopulmonary sequestration or adenomatoid cystic malformation, who place the fetus at risk of death by compression of the heart or neonatal death due to abnormal lung development.[6-8] Low urinary tract obstruction either by posterior urethral valves or urethral meatus agenesis leads to entrapment of urine within the fetal bladder, with subsequent hydronephrosis and dilatation of both ureters, that induce either intrauterine fetal demise caused by heart failure ensued from mediastinal compression by megacystis or neonatal death related to bilateral renal failure.[9] Severe fetal aortic valve stenosis may progress to hypoplastic left heart syndrome, which is associated with 99% risk of neonatal death in Mexico.[10] Finally, fetuses complicated with open spina bifida face lifetime and sometimes severe disabilities such as motor dysfunction or paralysis, mental retardation, hydrocephalus requiring ventriculoperitoneal shunting, bowel and bladder dysfunction and neurological handicaps.[11]

Nowadays, these congenital anomalies are managed with fetal interventional techniques, who attempt to improve postnatal prognosis, avoid perinatal death, and decrease the risk of abnormal infant neurodevelopmental outcome. Notably, all existing fetal interventions are already introduced in our country and even some novel procedures or techniques have been first developed in Mexico. Fetoscopic laser coagulation of placental vascular anastomoses is considered the gold standard for the management of TTTS. The first fetoscopic procedures in Mexico were reported in 2011 by Hernández-Andrade E. et al.[12] in a cohort of 35 TTTS cases treated with placental laser

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between 16 and 26 weeks of gestational age (GA). In 77% of the cases at least one twin survived and in 48.5% of cases both twins survived. Recently, a higher number of cases with similar survival rates were reported by our group. We reported a prospective cohort of 248 TTTS cases treated with fetoscopic placental laser therapy at GA between 15 and 31 weeks showing survival of at least one twin in 87% of the cases and 53% of both twins.[13] In an attempt to foster lung growth and improve neonatal survival in CDH fetuses with severe pulmonary hypoplasia, Fetal Endoscopic Tracheal Occlusion (FETO) was performed in 25 isolated CDH fetuses at a mean GA of 29.3 (25.6 to 31.8) weeks. Our results showed a significantly higher neonatal survival in comparison with another 25 fetuses managed expectantly during pregnancy (32% vs. 0%, $p<0.01$ respectively).[14] A cohort of 15 fetuses with bronchopulmonary sequestration associated with lung compression, hydrothorax or hydrops were treated in our center with percutaneous fetal laser ablation of the feeding artery (FLAFA) at a median GA of 26.9 weeks, showing progressive decrease in lung mass size and normalization of both lung dimensions, and survival rate of 100%[15] This minimally invasive fetal intervention has demonstrated to prevent fetal death and even avoid the need of postnatal surgery.[16] Similarly, in a small cohort of 5 fetuses with cystic lung masses and systemic blood supply, we showed that FLAFA was also of benefit in improving survival and decreasing the need of neonatal intervention. Fetal bronchoscopy and intrauterine fetal endoscopic tracheal intubation are novel procedures that have shown a potential utility in fetuses with internal or external fetal airway obstruction, aiding in securing fetal airways and decreasing the risk of neonatal death or perinatal asphyxia.[17, 18] In a multicenter study including 3 different centers (Sao Paulo, Brazil; Strasbourg, France; and Querétaro, Mexico), a consecutive series of 50 fetuses with megacystis were selected for fetal cystoscopy with laser ablation of posterior urethral valves between 14 to 29 weeks of GA. Such intervention was associated with 54% long term survival and 73% of adequate and preserved renal function at 2 years.[19] In 9 consecutive singleton fetuses complicated with critical aortic stenosis at risk of progression to hypoplastic left heart syndrome, percutaneous fetal aortic valvuloplasty was successfully performed in our center at a mean GA of 26 weeks, showing long term survival of 44%.[10] In fetuses with open spina bifida and Chiari II malformation, intrauterine myelomeningocele repair by means of open fetal surgery is feasible and may decrease the need of ventriculoperitoneal shunting and improve neurological cognitive and motor outcomes.[20] Recently, our group developed an alternative technique minimizing the uterine incision to 15mm, reducing fetal manipulation, and maintaining a normal amniotic fluid volume.[21] In our initial series, 47 fetuses were operated between 22 and 27 weeks of gestation showing good perinatal outcomes and decreasing the need of ventriculoperitoneal shunting to less than 10%. In conclusion, even in settings with suboptimal neonatal management, fetal surgery may decrease perinatal mortality and infant morbidity from several congenital malformations. Pregnancies with congenital anomalies that could be candidates for fetal surgery should be referred to centers with training and expertise in these minimally invasive interventions, in order to decrease the rate of perinatal mortality. Although we recognize that some of these fetal procedures can be incorporated in new fetal surgery centers, fetal surgeons should complete a formal training program and achieve competence in the selection criteria and fetal surgery skills, in order to avoid technical problems, shorten surgical times and decrease both maternal and fetal complications, expected from new centers at the beginning of their learning curve. The impact of such surgical training should not be underestimated, considering the numerous maternal and fetal complications and technical difficulties that have been previously reported.[22-24] Our efforts should be made to encourage high quality training in prenatal detection of these congenital anomalies, in order to achieve timely referral to fetal surgery centers in countries like ours, where termination of pregnancy in this setting is not always allowed and perinatal mortality is high; this is also essential for counseling parents looking for a hope to avoid perinatal loss.

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