Prenatal Management of CDH

Definition

Congenital Diaphragmatic Herniation (CDH) is defined as a hole in the diaphragm resulting from a developmental problem with the progenitor structures during the 6th to 8th weeks of gestation. CDH is most typically (>80%) in the posterior lateral portion of the diaphragm (a Bochdalek hernia) but may also occur more anteromedial (a Morgagni hernia). CDH may occur on the left or right side of the diaphragm with resulting herniation of abdominal contents (liver, spleen, stomach, intestine, kidneys) into the chest cavity. Most babies born with CDH have significant problems with lung hypoplasia on the affected side as well as pulmonary hypertension of both lungs; which may be a considerable source of morbidity.

Etiology

The etiology of CDH remains unclear [5]. Development of the pleuroperitoneal membrane and mesenchymal progenitors ultimately forming the diaphragm is still poorly understood and multiple genetic factors are involved. It is likely that CDH is the end result of multiple different genetic anomalies which may explain its association with other congenital defects. Genes that are being evaluated include those controlling Retinoic Acid signalling, the Sonic Hedgehog pathway, Fibroblast Growth Factor and Receptor development, and many others. Given that lung and diaphragm development appear linked, it is not surprising that babies born with this condition suffer from both diaphragm and pulmonary disease.

Incidence

- Congenital diaphragmatic hernia incidence 1/3000 live births
- While CDH may occur as an isolated defect, 40% of cases are associated with an additional anomaly, frequently cardiac conditions.
- Cardiac anomalies are found in about 1/3 CDH patients.
- Post natal survival in cases of isolated CDH is 50-70%.
- Birth defects of all other systems may be associated with CDH.
- Genetic causes have been identified in both isolated and non-isolated cases.
- Left sided in 85%
- Major cause of morbidity/mortality is pulmonary hypoplasia and pulmonary hypertension

Guideline Eligibility Criteria

Patients identified prenatally or postnatally with CDH.

Guideline Exclusion Criteria

Patients without CDH

Prenatal Diagnostic Evaluation

History

- Several anatomic features and indices derived for prenatal sonographic measurements are useful in differentiating CDH from other chest lesions and in prediction of neonatal outcomes.
- Detailed fetal anatomic survey
- Laterality of CHD, stomach and liver position
- Screening for other malformations

Imaging

- Echocardiography to evaluate cardiac morphology and function.
- Consider referral for MRI if lung outline is not clear by US or if the patient is potentially a candidate for fetal treatment.
- Calculate o/e LHR using the tracing method.
- MRI protocols are in development at DCMC radiology.

Critical Points of Evidence

Evidence Supports

- Once diagnosis of CDH is made, fetal ultrasound and MRI allow for determination of severity of disease by measuring certain prognostic variables[4]. Fetal ultrasound is the standard modality for screening and diagnosis of CDH. Development of prognostic criteria with accurate ultrasound measurements has allowed for risk stratification and more informed counseling and interventions.
- Fetal MRI is nearing standard of care for evaluation of CDH. Given its availability and cost, it is not a reasonable screening tool, but rather an adjunct once the diagnosis is made. It is less subjective than ultrasound, less user dependent, and less affected by variables such as maternal body habitus or fetal movement [8]. Herniated liver, Lung-Head ratio (LHR), and observed to expected fetal lung volumes (O/E – TFLV) are all measurements on MRI which have been shown to estimate the amount of support the infant will require after birth [9,7]. These data are used for prenatal counseling of families and assessment of disease severity and mortality risks.
- The trial for moderate CDH has closed, and, according to the website, "Treatment of fetuses with moderate hypoplasia is experimental, and until the results of the study become available, this experimental therapy should not be offered to patients carrying a fetus with moderate hypoplasia anymore." This leaves only the severe trial accruing patients, and the criteria include severe hypoplasia defined as observed over expected lung area to head circumference <25%.
- The GA for entry into the trial for patients with severe disease is 29 weeks, 6 days, so early evaluation and counseling is important to determine if these patients are candidates for prenatal intervention, and should be done in a timely fashion with all members of the CDH team as soon as reasonable after the diagnosis and initial images are acquired.
- While CDH may occur as an isolated defect, 40% of cases are associated with an additional anomaly, of which[MTA2] half are cardiac conditions. Fetal echocardiogram should be performed soon after prenatal diagnosis, as structural heart disease portends poorer prognosis and may alter the indications for prenatal intervention or postnatal interventions (i.e. ECMO) [11]. In addition, birth defects of all other systems may be associated with CDH. Genetic causes have been identified in both isolated and non-isolated cases. In addition to imaging, identifying a genetic cause for CDH may give additional information about prognosis and management. Evaluation by a genetic counselor and a thorough genetic evaluation including a physical examination, family history, and chromosome microarray by amniocentesis may be warranted [12].
- The "hidden mortality" of CDH is that historically a large number of the most severe defects did not survive until birth, but with better monitoring strategies, these numbers are thought to be less than ten percent [3].
- Early term versus term delivery for these infants is controversial. Some studies indicate that early term delivery may improve survival hypothesizing that pulmonary hypoplasia and hypertension may worsen with later gestational age [10]. Other studies suggest that infants with CDH born before 39 weeks are more likely to have neurodevelopmental delay [2]. Therefore, the ideal timing of gestational age for delivery is unknown.

Evidence Against

- The downside to fetal ultrasound is that it can be operator dependent and despite standardization of ultrasound across different institutions, there may be poor interrater reliability between individuals and institutions.

Evidence Lacking/Inconclusive

- There are no formal studies that review antepartum obstetric management.
- There is no evidence that routine cesarean delivery is beneficial.
- The reason for increased fetal demise is not fully understood.

Practice Recommendations

Initial Consultations

- Refer to Fetal Care Center Nurse Navigator at time of diagnosis.
  - Coordinates all further referrals, results & communication within the multidisciplinary Fetal Care Center team.
- Nurse manager of the comprehensive CDH team who will assist in coordinating care throughout the mother and her infant's time in the health care environment.
- Add patient to the perinatal care conference spreadsheet.
- Refer for genetic counseling within 3 days of diagnosis
- Differential diagnosis & prognosis based on presence of other anomalies
- Amniocentesis for microarray
- Referral for pediatric surgery consultation at time of diagnosis. Clarify that Pedi surgery wants to see pt before MRI, genetic tests are complete
- Consider referrals for NICU and palliative care consultation
- Coordinates communication with the CDH team re care plan as it evolves.
- Candidacy for fetal endoscopic tracheal occlusion
- Maternal-fetal medicine specialists monitor both mom and baby.
- Neonatologists who provide care at the time of delivery and during the first months of life
- Pediatric surgeons who perform the surgical repair of the diaphragmatic defect, as well as any other related procedures
- Fetal radiologist to assist in interpretation and evaluation of imaging findings
- Medical support team that includes social workers, genetic counselors, palliative care specialists, and more.

MultiDisciplinary Conference

- Given the severity of the diagnosis and the likely significant monitoring and intervention that these infants will require before and after birth, it is imperative that a multidisciplinary team be involved from early after the diagnosis through birth and well into childhood.
- Currently there is a multidisciplinary conference held the 2nd Wednesday of each month in the Seton Medical Tower. All pending cases of interest are discussed. It is attended by crucial members of the perinatal team, including neonatology, pediatric surgery, OB/MFM, palliative care, though not radiology/ultrasound, and can be used as a center/database for patients with CDH.
  - Because of the monthly occurrence of this meeting and the timely necessity of fetal intervention, additional team meetings may need to occur to discuss patients that may qualify for fetal intervention.
- The CDH team should discuss the case in a timely fashion and can make recommendations for prenatal monitoring and intervention. The only currently acceptable intervention is Fetoscopic Endoluminal Tracheal Occlusion (FETO). This procedure remains experimental, as there are ongoing multicenter trials investigating

its effectiveness[6]. The largest trial is still gathering patients (www.totaltrial.eu) There are two groups of patients undergoing study, a group with "moderate" lung hypoplasia, and a group with "severe" lung disease.

- Meeting with the patient and family members and establishing an ongoing relationship to build trust and confidence with the CDH team is important as well.
  - Though not as time-sensitive as assessing the need for potential fetal intervention, this meeting should involve as many members of the team as possible, and be used to structure the time line of events during the patient's pre and post-natal care.

Monitoring

Fetal monitoring will be determined by the patient's obstetrician and MFM.

MRI

Standardization of local MRI protocols will allow maternal-fetal medicine specialists and pediatric surgeons to appropriately counsel and monitor these patients.

- Certain measurements on MRI which have been shown to estimate the amount of support the infant will require after birth [2,4].
  - Herniated liver
  - Lung-Head ratio (LHR)
  - Observed to expected fetal lung volumes (O/E – TFLV).
  - These data are used for prenatal counseling of families and assessment of disease severity and mortality risks.

Ultrasound

- General recommendations:
- Monitor fetuses with serial ultrasound examinations no less than every four weeks to measure fetal growth and the amniotic fluid index
  - With evidence of growth restriction or fluid abnormalities, increase the frequency to biweekly.

Fetal echocardiogram

Should be performed soon after prenatal diagnosis.

Other Monitoring Considerations

- Many MFMs choose to obtain weekly biophysical profiles beginning at 32 to 34 weeks[9].
  - This may need to increase to more frequently for signs of fetal growth restriction, oligohydramnios, or severe polyhydramnios.
  - Antenatal testing recommendations will be driven primarily by co-morbidities, amniotic fluid volume, risk of cardiovascular compromise.
  - Antenatal steroids
- The fetus is monitored closely throughout gestation because growth restriction, oligohydramnios, meconium in amniotic fluid, or hydrops fetalis, may require early, emergent delivery.
- In addition to imaging, identifying a genetic cause for CDH may give additional information about prognosis and management.
  - Evaluation by a genetic counselor and a thorough genetic evaluation including a physical examination, family history, and chromosome microarray by amniocentesis may be warranted[5].

Delivery Planning

- A planned induction of labor around 39 weeks of gestation allows the fetus to be monitored from the earliest stage of labor.
  - This also allows for pediatric surgery and neonatology services to be immediately available.

- There is no evidence that routine cesarean delivery is beneficial.
- Care conference at about 32-34 weeks to plan for contingencies, including presentation in spontaneous labor.
- Coordinate with neo & palliative care regarding immediate perinatal care plan
- Plan for delivery at 39 weeks (induction vs CS)

References

1. A, Hedrick HL et. "Congenital Diaphragmatic Hernia: Prenatal Issues." UpToDate, n.d.
2. Danzer, Enrico, Marsha Gerdes, Jo Ann D'Agostino, Judy Bernbaum, Casey Hoffman, Lisa M Herkert, Natalie E Rintoul, et al. "Younger Gestational Age Is Associated with Increased Risk of Adverse Neurodevelopmental Outcome during Infancy in Congenital Diaphragmatic Hernia." Journal of Pediatric Surgery 51, no. 7 (July 2016): 1084–90. https://doi.org/10.1016/j.jpedsurg.2015.12.010.
3. Deprest, Jan, Paul Brady, Kypros Nicolaides, Alexandra Benachi, Christoph Berg, Joris Vermeesch, Glenn Gardener, and Eduard Gratacos. "Prenatal Management of the Fetus with Isolated Congenital Diaphragmatic Hernia in the Era of the TOTAL Trial." Seminars in Fetal & Neonatal Medicine 19, no. 6 (December 2014): 338–48. https://doi.org/10.1016/j.siny.2014.09.006.
4. Gentili, A, L Pasini, E Iannella, V Landuzzi, M Lima, M L Bacchi Reggiani, and S Baroncini. "Predictive Outcome Indexes in Neonatal Congenital Diaphragmatic Hernia." The Journal of Maternal-Fetal & Neonatal Medicine : The Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians 28, no. 13 (September 2015): 1602–7. https://doi.org/10.3109/14767058.2014.963043.
5. Klaassens, M, A de Klein, and D Tibboel. "The Etiology of Congenital Diaphragmatic Hernia: Still Largely Unknown?" European Journal of Medical Genetics 52, no. 5 (2009): 281–86. https://doi.org/10.1016/j.ejmg.2009.05.005.
6. Kovler, Mark L, and Eric B Jelin. "Fetal Intervention for Congenital Diaphragmatic Hernia." Seminars in Pediatric Surgery 28, no. 4 (August 2019): 150818. https://doi.org/10.1053/j.sempedsurg.2019.07.001.
7. Oluyomi-Obi, Titilayo, Verena Kuret, Pramod Puligandla, Abhay Lodha, Helen Lee-Robertson, Kovid Lee, David Somerset, Joann Johnson, and Greg Ryan. "Antenatal Predictors of Outcome in Prenatally Diagnosed Congenital Diaphragmatic Hernia (CDH)." Journal of Pediatric Surgery 52, no. 5 (May 2017): 881–88. https://doi.org/10.1016/j.jpedsurg.2016.12.008.
8. Oluyomi-Obi, Titilayo, Tim Van Mieghem, and Greg Ryan. "Fetal Imaging and Therapy for CDH-Current Status." Seminars in Pediatric Surgery 26, no. 3 (June 2017): 140–46. https://doi.org/10.1053/j.sempedsurg.2017.04.002.
9. Ruano, R, D A Lazar, D L Cass, I J Zamora, T C Lee, C I Cassady, A Mehollin-Ray, et al. "Fetal Lung Volume and Quantification of Liver Herniation by Magnetic Resonance Imaging in Isolated Congenital Diaphragmatic Hernia." Ultrasound in Obstetrics & Gynecology : The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology 43, no. 6 (June 2014): 662–69. https://doi.org/10.1002/uog.13223.
10. Stevens, Timothy P, Edwin van Wijngaarden, Kate G Ackerman, Pamela A Lally, and Kevin P Lally. "Timing of Delivery and Survival Rates for Infants with Prenatal Diagnoses of Congenital Diaphragmatic Hernia." Pediatrics 123, no. 2 (February 2009): 494–502. https://doi.org/10.1542/peds.2008-0528.
11. Style, Candace C, Oluyinka O Olutoye, Mariatu A Verla, Keila N Lopez, Adam M Vogel, Patricio E Lau, Stephanie M Cruz, et al. "Fetal Echocardiography (ECHO) in Assessment of Structural Heart Defects in Congenital Diaphragmatic Hernia Patients: Is Early Postnatal ECHO Necessary for ECMO Candidacy?" Journal of Pediatric Surgery 54, no. 5 (May 2019): 920–24. https://doi.org/10.1016/j.jpedsurg.2019.01.022.
12. Wynn, Julia, Lan Yu, and Wendy K Chung. "Genetic Causes of Congenital Diaphragmatic Hernia." Seminars in Fetal & Neonatal Medicine 19, no. 6 (December 2014): 324–30. https://doi.org/10.1016/j.siny.2014.09.003.