Management of congenital diaphragmatic hernia

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Abstract

Congenital diaphragmatic hernia (CDH) is a challenging condition. It is commonly associated with high mortality due to associated lung hypoplasia, pulmonary hypertension and co-existent anomalies. This review highlights recent progress in the perinatal management of CDH and addresses long term outcome issues for survivors indicating the need for multidisciplinary follow up.

Keywords congenital diaphragmatic hernia; fetal therapies; minimally invasive surgery; outcomes

Definition and aetiology

Congenital diaphragmatic hernia (CDH) is a defect in the fetal diaphragm allowing the contents of the abdominal cavity to protrude into the thorax. CDH has an incidence of 1 in 2500 live births in the UK. The birth defect may be associated with other major anomalies and the lesion may become apparent in the fetus, newborn or older child. Some forms of CDH remain asymptomatic and may not present until adulthood.

Most defects are sporadic and isolated (70%) with a number of gene mutations identified, e.g. Deletions of 4p, 8q, 15q. Links have been made to environmental factors such as: thalidomide, nitrofen and vitamin A deficiency. CDH may be associated with other chromosomal abnormalities e.g. Fryn's and Pallister Killian syndromes.

Pathology

The precursors of the diaphragm begin development during the 4th week of gestation in the form of the septum transversum and lateral folds of mesenchymal tissue. These partition the abdominal and thoracic compartments with the formation of the pleuroperitoneal membrane occurring by the 8th week. As development continues muscle fibres migrate into this membrane. Failure of these stages of development will result in either a 'true' diaphragmatic defect (CDH) or a complete, yet hypoplastic, diaphragm resulting in a diaphragmatic eventration.

Normally closure of the right hemi diaphragm occurs before the left, which probably accounts for the higher incidence of left sided diaphragmatic defects (84%). Right diaphragmatic defects comprise 13% of lesions and 2% are bilateral defects, the remaining cases comprising the rarer variants such as complete diaphragmatic agenesis. The commonest lethal form of CDH is the lesion occurring in the posterolateral aspect of the developing diaphragm (Bochdalek hernia). Less commonly there are defects in the anterior-lateral diaphragm (Morgagni hernia).

Outcome in CDH remains highly variable. The reported mortality rates vary between 20 and 60% in centres worldwide. The morbidity and mortality of CDH is traditionally related to the mechanical compression of the herniated viscera on the developing lung leading to pulmonary hypoplasia and pulmonary hypertension. The histological changes seen at post mortem in the underdeveloped ipsilateral lung on the affected side of the defect are also mirrored in the contralateral lung suggesting that whatever insult is responsible for the failure of the diaphragm to develop may also have a global impact on the primordial development of the respiratory system.

Antenatal care (fetal CDH)

Antenatal diagnosis: antenatal diagnosis has been reported as early as 11th week of gestation, however, in the UK, it is more often diagnosed at the 20 week anomaly scan. A multidisciplinary team (paediatric surgeons, neonatologists and obstetricians) is usually involved in the diagnosis and counselling of the family. This multidisciplinary approach also allows treatment and delivery planning. Within the wider European region a multicentre study found that 60% of cases of CDH were identified antenatally with a mean gestational age of 24.2 weeks at diagnosis. Recent studies suggest that care in specialist, high volume centres (more than five cases per annum) achieves an improved survival rate compared to low volume centres.

Associated anomalies: antenatal investigations aim to identify associated anomalies. This facilitates more accurate counselling, as survival in babies with associated anomalies remains dismally poor (less than 10%). Amniocentesis is recommended to identify chromosomal anomalies, which are present in up to 10% of cases, e.g. Trisomies 13, 18 & 21, Donnai-Barrow and Fryns syndromes. A thorough sonographic evaluation of the urinary, gastrointestinal and central nervous system should be performed to detect further structural malformations (seen in 33%). Fetal echocardiography is utilised to detect cardiac anomalies, which co-exist in up to 18% of cases. It is also helpful to measure pulmonary artery diameters, which have been reported to be predictors of postnatal pulmonary hypertension and mortality.

Predicting outcome: defining antenatal predictors of outcome in CDH has been the subject of intense study over the last few years. Most current methods rely on indirect techniques, e.g. US/MRI to make an assessment of fetal lung volume. Measurement of the contralateral fetal lung area to head circumference ratio

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(LHR), using 2D ultrasound (US) imaging, as a predictor of outcome was first proposed by Harrison's group based at UCSF, San Francisco in the mid-1990s. LHR gained popularity as a good prognostic marker and led to a randomised clinical trial that guided decision making for fetal intervention in CDH. A systematic review and meta-analysis conducted in 2007 suggested that further refinement with regard to LHR criteria was needed to more accurately predict fetal outcome. More recently LHR measurements have been improved to account for the four fold relative increase of lung area to head circumference that occurs between 12 and 32 weeks in the fetal period. Jani and colleagues (antenatal-CDH registry group) utilising the observed to predicted (O/E) LHR indicated more accurate prognostic scoring in 354 cases of unilateral, isolated CDH.

Other markers of poorer prognosis in CDH include: liver herniation, lung-to-head ratio (LHR) less than 1 on prenatal ultrasound and/or observed-to-expected LHR less than 25%, and/or observed-to-expected total lung volume (o/eTLV) less than 25%. Studies have shown that fetuses with an increased volume of liver within the thoracic cavity, designated "liver up" cases, are associated with a larger hernia defect, a greater need for prosthetic patch repair and decreased survival. Regarding left vs right CDH, a recent study showed an increased requirement for pulmonary vasodilatory therapy and requirement for tracheostomy in patient with right CDH compared to left sided ones. The high incidence of pulmonary complications indicates increased severity of pulmonary hypoplasia in right CDH.

Fetal intervention

Initial interest in fetal intervention concentrated on open repair of the diaphragmatic defect following maternal hysterotomy. Trials were discontinued due to preterm labour with poor outcome. The dramatic changes seen in lung growth achieved by occluding/'plugging' the fetal trachea, led to refinements in fetal surgical techniques for CDH. In 2003 Harrison et al., reported a randomised controlled trial of fetal endoscopic tracheal occlusion (FETO) showing equivalent survival to a group of 'high risk' fetuses managed by conventional postnatal care in specialist CDH centres. This study led to further efforts to improve better case selection for fetal intervention using LHR (O/E) and 'liver up' entry criteria to identify those with the very worse prognosis that may justly benefit from FETO procedures.

European fetal medicine programmes using selective entry criteria (O/E LHR less than 27–28% and liver herniation) have found a statistically significant improved survival rate in a FETO treated CDH group in comparison to same severity controls. A recent systematic review and meta-analysis showed that the FETO procedure increased neonatal survival at 30 days and 6 months; however, it presented a higher rate of premature rupture of membrane, preterm birth less than 37 weeks, and decreased the gestational age at delivery by 2 weeks. Results from an ongoing European prospective randomised clinical trial are eagerly awaited.

Newborn management – postnatal care

Delivery: with an increasing antenatal detection rate of CDH, expert opinion regarding the mode of delivery remains a subject of debate. In 2007, the CDH study group interestingly reported a marginal (non-significant) survival benefit for elective delivery by Caesarean section. Further randomised studies are needed to draw definitive conclusions. In order to maximise pulmonary development delivery should be planned as near to term (more than 37 weeks) as possible. Delivery should be co-ordinated in specialist centres equipped with full neonatal intensive care facilities with ready access to paediatric surgeons. Elective intubation following birth and 'gentle' ventilation (avoiding barotrauma) is recommended. All babies should have a nasogastric tube promptly inserted to avoid gastric distension and vascular access secured to aid delivery of fluids and pharmacological agents. Following stabilisation, a full clinical examination is required to exclude associated anomalies. Chest X-ray confirming the diagnosis and echocardiogram is performed to screen for cardiac anomalies.

Postnatal diagnosis – 'late presenting CDH'

Despite antenatal imaging, 30% of patients with CDH may remain undetected until after delivery. These cases may present in the immediate newborn period or first few days after birth; whilst others may remain asymptomatic until later life. Symptoms may include mild respiratory distress or feeding problems. Delayed presentation may occur with small diaphragmatic defects in which there is little or no herniated bowel at birth. Herniation of intestinal viscera as a later dynamic event may follow an episode of increased intraabdominal pressure seen with a respiratory tract infection.

Clinical examination may reveal signs of decreased air entry on the affected side and rarely mediastinal shift. Very occasionally, bowel sounds may be heard in the chest, although this is usually only obvious to clinicians once the diagnosis of CDH has been made. Diagnosis is most often made on chest X-ray but may require an upper gastrointestinal contrast study for further confirmation.

Stabilisation

'Gentle' ventilation: a major advance in the management of CDH in the last 20 years has been the introduction of 'gentle ventilation' strategies (permissive hypercapnia) to reduce iatrogenic lung injury from barotrauma. This is characterised by preservation of spontaneous ventilation, permissive levels of hypercapnia (paCO2 60–65 mmHg or 9 kPa) and avoidance of high inspiratory airway pressures (ideally not exceeding 25 cm H_2O). A number of specialist centres steadily report improving outcomes (more than 80% survival) with this approach together with a reduced need for ECMO.

HFOV: high frequency oscillatory ventilation (HFOV) has also been utilised in the perinatal management of CDH both as a 'rescue therapy' prior to extracorporeal membrane oxygenation (ECMO) and as a primary ventilatory modality in an attempt to reduce pulmonary barotrauma. There have been several reports of increased CDH survival with HFOV strategies. However in a recent randomised trial (VICI 2016), there was no statistically significant difference in the combined outcomes of mortality between the conventional gentle ventilation and HFOV groups in prenatally diagnosed CDH. Importantly though, shorter ventilation times and lesser need of extracorporeal membrane oxygenation, favoured conventional ventilation.

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