Chapter

Prenatal Diagnosis of Diaphragmatic Hernia

Marina Sica, Carlotta Plessi and Francesco Molinaro

Abstract

Congenital diaphragmatic hernia (CDH) is a condition characterized by a defect in the diaphragm leading to protrusion of abdominal contents into the thoracic cavity interfering with normal development of the lungs. The pathophysiology of CDH is a combination of lung hypoplasia and immaturity associated with persistent pulmonary hypertension of newborn (PPHN) and cardiac dysfunction. Prenatal assessment of lung to head ratio (LHR) and position of the liver by ultrasound are used to diagnose and predict outcomes. However, fetal therapy is indicated in cases where negative prognostic factors are detected in screening investigations (liver herniation, LHR <1.0). Immediate management at birth includes bowel decompression, avoidance of mask ventilation and endotracheal tube placement if required. The main focus of management includes gentle ventilation, hemodynamic monitoring and treatment of pulmonary hypertension followed by surgery. Although inhaled nitric oxide is not approved by FDA for the treatment of PPHN induced by CDH. Surgical treatment of CDH should be planned in election, after the achievement of hemodynamic stability. The only case in which it is acceptable to perform an emergency operation is when there are signs of ischemia of the herniated intestinal loops. Extracorporeal membrane oxygenation (ECMO) is typically considered after failure of conventional medical management for infants ≥ 34 weeks' gestation or with weight > 2 kg with CDH and no associated major lethal anomalies. Prematurity, associated abnormalities, severity of PPHN, type of repair and need for ECMO can affect the survival of an infant with CDH. With advances in the management of CDH, the overall survival has improved.

Keywords: lung hypoplasia, pulmonary hypertension, extracorporeal membrane oxygenation, prenatal diagnosis

1. Introduction

Congenital diaphragmatic hernia (CDH) is a congenital malformation of diaphragm, which leads to a defect in separation between the thoracic and abdominal cavities [1, 2]. It appears to be due to an error in the development of the pleuro-peritoneal canals and therefore develops around 6 weeks of gestation [1]. Its incidence is 1:3000 live births. Progress in the management of these patients has significantly increased survival rates (up to 90% [3]), but disease-related morbidity remains very

high: the main problem is the compression exerted by the herniated viscera on the developing lungs, development, which causes pulmonary hypoplasia and hypertension [4].

2. Classification

CDH can be classified, depending on the location of the defect, into postero-lateral, or Bochdalek's hernia (70–75%), anterior or Morgagni's hernia (23–28%) and central or hiatal hernia (2–7%) [4]. Morgagni's hernia is often discovered incidentally in older children, as it rarely causes such a mass effect on the thoracic level as to compromise the development of the lungs. Bochdalek's hernia is the form that is classically referred to when talking about this pathology and to which we will refer accordingly in the next paragraphs (26). Most often it is located on the left side (85%), but it can also be right (13%) or bilateral (2%) [4].

3. Pathogenesis

The pathogenesis of CDH is complex and currently still little known. Some studies have shown that pulmonary hypoplasia in these patients arises before the development of the diaphragm itself. This discovery opened the door to the so-called "double hit theory" which sees pulmonary hypoplasia as the result of two insults: the first, affecting both lungs, would be due to genetic and environmental factors (for example alcohol, smoking, obesity, low intake of retinoids during pregnancy); the second, which would affect only the lung ipsilateral to the defect, would consist of the compressive effect of the herniated viscera and their interference with normal fetal respiratory movements. Multiple studies have demonstrated the importance of the genetic component in the pathogenesis of ECD: they often fall within syndromic pictures, and about 40% of cases are associated with other congenital anomalies, especially cardiovascular (11–15% of ECD) [4].

4. Antenatal management

Given the potential severity of the disease, prenatal counseling represents a fundamental phase of the diagnostic-therapeutic process of CDH: parents must be adequately informed about all the steps to be taken and the risks in terms of mortality and morbidity.

4.1 Antenatal diagnosis

Ultrasound currently represents the gold standard in CDH diagnosis, although it has been calculated that less than two-thirds of CDHs are detected on prenatal screening ultrasound scans. The mean gestational age at diagnosis is 24–25 weeks, more advanced in cases of isolated defects than in CDHs associated with other anomalies. The typical ultrasound sign is the presence of abdominal organs (intestinal loops, stomach, liver) in the chest. Indirect signs of CDH can be changes in the heart axis, polyhydramnios, mediastinal shift. The differential diagnosis includes all congenital pulmonary malformations, bronchial atresia, intestinal duplications and mediastinal

masses [5, 6]. The execution of genetic tests and second-level imaging tests is essential for defining the prenatal management strategy, whether it is inclined towards termination of pregnancy, or whether it is oriented towards fetal therapies. One of the main prognostic factors is represented by the lung to head ratio (LHR), which by measuring the length of the lung contralateral to the hernia normalized for the head circumference, provides an indirect estimate of pulmonary hypoplasia. More specifically, since the LHR changes with advancing gestational age, we prefer to use the ratio between observed LHR and expected LHR (observed/expected LHR or o/and LHR).

One or/and LHR <25% is indicative of severe hypoplasia, while one/and LHR of 25–35% or an LHR of 35–45% with herniated liver are indicative of moderate hypoplasia. In fact, another prognostic factor is represented by the position of the liver: since the liver and the fetal lung are poorly distinguishable ultrasonographically, there may be an indication to perform a fetal magnetic resonance [3–6]. It allows to evaluate not only the presence or absence of liver in the thoracic cavity, but also to quantify the observed/expected total fetal lung volume (or/and TFLV), which was a better predictor in terms of postnatal survival. As an alternative to magnetic resonance evaluation of the or/and TFLV, some authors have demonstrated a close relationship between the liver herniation, the position of the stomach (which being anechoic is much more easily identifiable) and the postnatal outcome. Finally, given the high frequency with which EDC is associated with cardiovascular anomalies, there is an indication to perform fetal echocardiography [7, 8].

4.2 Antenatal therapies

The prenatal management of fetuses affected by CDH essentially provides for an ultrasound monitoring of the ultrasound parameters described above, associated in doubtful cases with second level examinations such as resonance. In recent years, however, fetal therapy has become increasingly popular on the international scene, indicated in cases where negative prognostic factors are detected in screening investigations (liver herniation, LHR <1.0). The purpose of these interventions is essentially to stop the mechanisms that induce the onset of complications such as pulmonary hypoplasia and pulmonary hypertension as early as possible. The technique currently most used is fetal tracheal occlusion (FETO): it is based on the principle that the occlusion of the trachea prevents the leakage of fluids, increasing the pressure in the airways and promoting lung growth. However, animal models have shown that tracheal occlusion reduces the maturation of type II pneumocytes, inducing a surfactant deficiency: for this reason the so-called "plug-unplug" sequence was devised, in which the patency of the trachea is first interrupted by the introduction of a balloon (or plug) and then re-established before delivery to allow lung maturation. This procedure can be performed percutaneously under ultrasound guidance or fetoscopy, typically between 27 and 32 weeks of gestational age, with the plug removed at 34 weeks. This procedure appears to be associated with increased survival in children with moderate and severe CDH, although further risk-benefit studies are certainly needed.

In children with CDH, the only medical treatment for which there is evidence of efficacy is corticosteroid therapy: maternal administration of one or two doses of corticosteroids at 34–36 weeks of gestation appears to be correlated with a reduction in respiratory morbidity at birth. Promising studies are also underway on the prenatal use of retinoids and phosphodiesterase inhibitors (Sildenafil) and on the use of stem cells from amniotic fluid in combination with FETO [4].

5. Postnatal management

The optimal timing and modality of delivery for children with CDH are still under discussion today. There seem to be no indications for induced delivery before 38 weeks of gestation, as well as there do not seem to be any advantages in performing a cesarean section. On the other hand, a unanimous consensus was found on the importance of planning the birth in a third-level center, where a multidisciplinary group (gynecologists, neonatologists, surgeons and pediatric anesthetists) is available, capable of managing the disease [4].

At birth, the main objective must be to ensure adequate ventilatory support (without triggering a vasospasm or further lung damage) and induce not too deep sedation (which would further compromise respiratory function). In case of respiratory distress, endotracheal intubation is carried out directly: in fact, ventilation with a facial mask must be avoided, as it would lead to distension of the stomach and intestinal loops, worsening the respiratory dynamics.

For the same principle, the positioning of a nasogastric tube is indicated at the same time, in order to decompress the stomach as much as possible. It is considered acceptable to maintain reduced saturation levels and a certain degree of hypercapnia, as long as the pH is kept above 7.2: in the presence of acidosis, in fact, vascular resistance would increase and consequently the risk of pulmonary hypertension. Another major problem in these patients is hemodynamic instability: to assess the need for inotropic support, these patients must be continuously monitored from a pressure point of view and postnatal echocardiography (within 48 h of life) must be performed if necessary repeated at 2–3 weeks. The indication for the ECMO, as a bridge to surgery in the most compromised patients, is still much debated. One of the biggest challenges remains the management of pulmonary hypertension: currently the most widely used treatment is inhaled nitric oxide, although encouraging new studies are underway on the use of Sildenafil [2, 4, 5].

Surgical treatment of CDH should be planned in election, after the achievement of hemodynamic stability. The only case in which it is acceptable to perform an emergency operation is when there are signs of ischemia of the herniated intestinal loops. As for the surgical technique, this can be performed openly (in thoracotomy or laparotomy) or by minimally invasive techniques. The intervention consists in the repositioning of the herniated organs within the abdomen and consequently in the closure of the defect, which can be primary or with a patch depending on the size of the defect. Minimally invasive techniques and the use of a patch were associated with a higher relapse rate [3, 4].

6. Long-term outcomes

In light of the increased survival of newborns with CDH, long-term outcomes, especially in terms of quality of life, have assumed increasing importance over time. The most compromised organs are certainly the lungs: in addition to the well-known pulmonary hypertension, these children experience alterations both in a restrictive sense (due to pulmonary hypoplasia) and in an obstructive sense (similar to bronchodysplasia of the premature infant) [8]. Pulmonary function seems to gradually restore during childhood, but recent studies have shown a slight deterioration of the same from childhood to adulthood. The respiratory system is not the only one affected by

this disease. Gastroesophageal reflux is present in 45–89% of children with CDH and appears to be correlated with the size of the defect. Stunted growth is also a frequent finding, affecting 69% of these children at 1 year of age. Neurological alterations (in terms of delay in neurodevelopment but also sensorineural deafness) represent one of the most feared and also most frequent complications of CDH, with incidence rates ranging from 12 to 77%, especially in children undergoing ECMO. Finally, musculoskeletal deformities (chest anomalies, hemithorax asymmetries, scoliosis) were reported in 21–48% of patients treated for CDH [3].

All this, together with the fact that a good percentage of CDHs fall into syndromic pictures or are associated with other congenital anomalies, justifies the importance of a long-term follow-up program.

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