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Case Report

Congenital Diaphragmatic Hernia: An Autopsy-Based Diagnosis in Sudden Neonatal Death

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Abstract

In the age of advanced medical facilities and diagnostic equipment, Congenital Diaphragmatic Hernia (CDH) poses a challenge to the medical fraternity, specifically its detection. The last decade's overall survival rates have improved significantly. The significant contribution to that higher percentage of survivors is from the symptomatic cases detected at birth. Asymptomatic patients remain unnoticed, and later perceived only in the stage of no pediatric surgeons 'return to treat the defect. This case of type 2 Bochdalek CDH highlights the importance of considering an asymptomatic scaphoid abdomen as a potential CDH that needs medical intervention. The hour's need is to start considering asymptomatic scaphoid abdomen in neonates as potential cases of CDH. These babies escape the so-called "requirement" for early diagnostic procedures, increasing the burden for the treating physicians and surgeons at the later stage, contributing to otherwise avoidable Neonatal Mortality. Herewith we present a case of sudden neonatal death and CDH diagnosed at Autopsy with its characteristic findings.

1. Introduction

Diaphragmatic hernia is defined as a communication between abdominal and thoracic cavities with or without herniation of abdominal contents into the thorax.[1] The diaphragm consists of two parts, the peripheral muscular, and central tendon. It acts as a barricade between the abdominal and chest cavity and does not allow the abdominal contents to enter the thoracic cavity.[2]

The presence of a diaphragmatic defect allows the abdominal contents to ascend into the thoracic cavity as a result of negative intra-thoracic pressure during inhalation.[2] Among 2000 to 5000 live born, one is affected by CDH, out of which 80% to 85% occur on the left side 13% on the right side, and 2% are bilateral.[1,2,3] The defect is mostly sporadic (50-60 %).[4,5] Males are more frequently affected than females by a ratio of 1.5:1, and subsequent pregnancies offer low risk.[3] 70% to 95% of CDH are of the Bochdalek type.[2,3]

Severe hypoplasia of the lung is seen on the same side of the defect as the abdominal contents herniate and occupy the thoracic cavity reserved for the lung.[6] The exact cause of CDH is still unknown. However, many studies correlate it with first degree relatives, condition of the reproducing women, environmental factors, genetic factors, and pharmacological agents.[7] Associated chromosomal abnormalities are Killian syndrome (isochromosome or tetrasomy 12p);

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Turner's syndrome (XO); Pallister- Wolf-Hirschhorn syndrome (4p16 deletion); trisomies 22,21,18,13 and derivative chromosome 22 t(11;22) (q23;q11).[8] Single-gene disorders include craniofrontonasal syndrome (EFNB1), Cornelia de Lange syndrome (NIPBL, SMC3, SMC1A), Denys-Drash syndrome (WT1), Fryns syndrome, Donnai-Barrow syndrome (LRP2), Matthew-Wood syndrome (STRA6), Spondylocostal dysostosis (DLL3, MESP2, LFNG, HES7), and Simpson-Golabi-Behmel syndrome (GPC3). [8]

Vitamin A deficiency in these cases also points towards anomaly in retinoid-regulated target genes, leading to the development of CDH.[7] Association of GATA6 gene7 mutations and EDNRA m-RNA8 over-expression (triplication) has been proven.[6] The mortality related to pulmonary complications has been decreased to 10-20% in some tertiary care hospitals. However, for babies who develop bronchopulmonary dysplasia after high-frequency oscillation ventilation (HFOV) and extracorporeal membrane oxygenation (ECMO), mortalities are still on the higher side.[2] The crucial factor for successful treatment is early diagnosis. However, the asymptomatic babies with scaphoid abdomen fail to get it through due to the absence of any symptoms at birth. This case report signifies the importance of diagnostic procedures on "symptomless babies with the scaphoid abdomen," which itself should be considered as an important parameter for a potential CDH case.

2. Case History

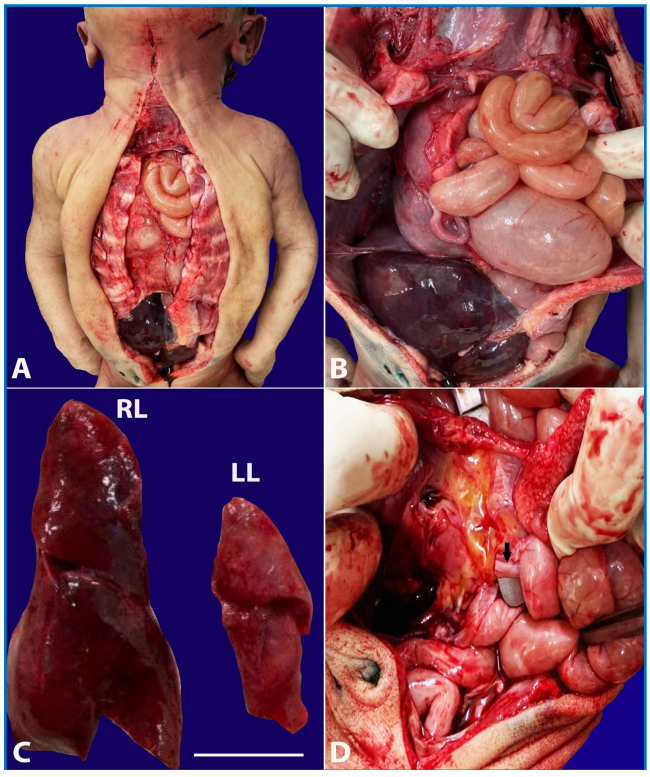
A twelve-day-old male neonate was brought dead to our tertiary care center. He had a history of mild breathlessness for three days. As per the mother's statement, the baby started coughing, followed by vomiting when she breastfed him on the day of his death. On the fateful day, the baby had an episode of coughing later continued with labored breathing. He then reached our tertiary care institute in the next 30 minutes. On arrival, he was declared dead, and as per prevalent rules, a medicolegal autopsy was advised, as a case of sudden death without a diagnosis for the immediate condition.

The mother was primiparous and had no history of past abortions or any significant medical illnesses. Her course of pregnancy was uneventful; the neonate weighed 2.874 Kilogram(kg) at birth. The mother had visited the primary health center of their village for antenatal check-ups and routine ultrasound examinations. However, a fetal anomaly scan was not conducted as the parents were from impoverished backgrounds.

3. Autopsy Findings

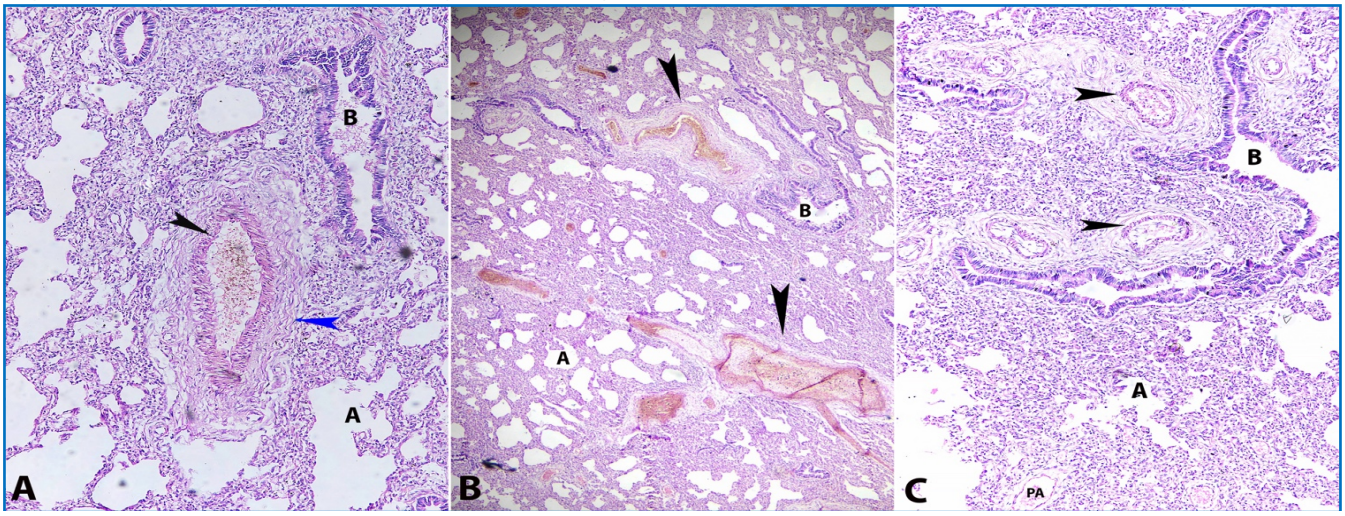
The external examination showed a male child weighing 2.654 kg with a length of 44 Centimeters (cm). His head and chest circumferences were 35cm and 30cm, respectively (reference range [RR] 32 – 35 cm and 34–37 cm, respectively). His abdomen was scaphoid-shaped, and abdominal circumference at the umbilicus level was 26 cm (RR; 31 – 33 cm). We noticed progressive weight loss from an actual birth weight of 2.874 kg to 2.654 kg (0.22 kg, over 12 days). The ossification centers for the lower end of the femur have appeared suggestive of full-term delivery. Upon opening the thoracic cavity, the stomach and intestine have occupied the whole of the left hemithorax (**Figure 1A**). These were markedly distended by air without any obstruction throughout its length. The abdominal cavity contents, i.e., stomach, small intestine, and spleen, were found herniating into the left chest cavity through a left posterior hemi-diaphragmatic defect (**Figure 1B**).

Figure 1: A – The sternum is cut out to expose the contents of the abdomen in the left hemidiaphragm; B - the contents of the abdomen expect the liver can be found in the left thoracic cavity; C - the left lung is hypoplastic. (scale bar = 20 mm); D -The defect is pointed by the black arrow shown with a metallic forceps.



There was a right mediastinal shift of heart and left lung. The left lung was hypoplastic and markedly compressed, whereas the right lung was hyperplastic with a weight of 0.006 kg and 0.024 kg respectively (RR; 0,029 kg and 0,026 kg respectively) (**Figure 1C**). The right hemidiaphragm was intact and unremarkable. The left-sided defect margin was smooth without any laceration or hemorrhage of the diaphragm or the surrounding soft tissue (**Figure 1D**). The size of the diaphragmatic defect was 5cm x 4cm. Histopathology examination findings were suggestive of pulmonary hypertension (**Figure 2A, Figure 2B, Figure 2C**). The gross examination of the heart was unremarkable, with no congenital anomaly on further dissection.

Figure 2: A - Microphotograph of right lung showing increased thickness of its media with smooth muscle hyperplasia (black arrowhead) and thickened adventitia (blue arrowhead) consistent with pulmonary hypertension (A: alveolus B: bronchiole, PA: pulmonary artery) (H&E, 10x); B - showing increased thickness of media and adventitia with narrowing of lumen consistent with pulmonary hypertension (H&E ,40x); C - Microphotograph of hypoplastic left lung showing thickened medial and adventitial layer (arrowheads)of pulmonary arteries diagnostic of Pulmonary hypertension (A: angulated airspaces suggestive of incomplete fetal lung maturation, B: bronchiole and PA: Pulmonary artery) (H & E, 10X).



The examination of the larynx and trachea showed no findings of aspiration. The herniated portion of the stomach, small intestine, and remaining loops of bowel were unremarkable. The liver was markedly congested, weighing 0.105 kg (RR; 0.123 kg). The pancreas and spleen were normal on gross examination, and both kidneys were lobular in shape, weighing 0.012 kg each (RR; 0,015 kg, each). The contents of the skull and spinal cord were unremarkable. The urinary bladder was empty, with no abnormality of its walls. Both testes were present in the scrotal sac, and the penis was unremarkable with no evidence of any stricture. After the postmortem examination, we opined the cause of death as pulmonary hypertension as a complication of CDH. The final opinion to cause of death was given as pulmonary hypertension as a complication of CDH.

4. Discussion:

The embryological formation of the diaphragm starts during the 4th week and concludes by the 8th to 12th weeks of gestation.[2,4,6] Muscularisation of the diaphragm develops from the innermost muscle layer of the thoracic cavity.[7] The muscular part is made up of radial muscles originating from the ribs, sternum, and spine.[7] During the embryological period, the junction of lumbar and costal muscle groups fuse at the final stage of diaphragm development to gain its strength.[7] A fusion of lumbosacral muscle groups in the diaphragm, is either delayed or discontinued at the later stages of development.[7] It gives rise to a weak spot situated in the posterolateral part between the junction of the lumbar and costal muscle layers, leaving the area vulnerable for herniation.[7] Victor Bochdalek first described this area in 1848.[7]

CDH is associated with anomalies and malformations of various organs of the body. 40-50% of those anomalies are reported from the central nervous system (CNS) and cardiovascular system (CVS). However, the malformations of CVS is one of the crucial prognostic parameters and includes minor (atrial and small ventricular septal defects) to very severe ventricular outflow tract obstruction (coarctation of the aorta, tetralogy of Fallot, and hypoplastic left heart syndrome) or high pulmonary blood flow

(atrioventricular septal defects and large peri membranous ventral septal defects).[8] In babies of CDH associated with CNS anomalies, recent evidences suggest that the patients who received extracorporeal membrane oxygenation (ECMO) treatment have full-scale intelligence quotient (FSIQ) scores within the low-average and average range. However, hypotonia and other motor drawbacks are usually reported.[8]

Difficulty in breathing is one of the vital diagnostic signs in newborn babies with CDH. [1] It is generally observed at birth but can also present late after a delay period of about 48 hours. [1] Clinically, there is an increase in respiratory rate, unusual production of sound during breathing, and bluish discoloration of the body. [1] The diameter of the chest cavity is usually increased, and the abdomen is scaphoid shaped. [1] In cases of mediastinal shift, the apex beat area is shifted away from the hernia. [1] Coughing and vomiting raise the pressure on the defect. Thus, making the abdominal contents to herniate easily.[9,10,11] A study conducted by Rygl et al.[12] on the defect- diaphragmatic ratio (DDR) as a new parameter for assessing defect size concludes the DDR value as an objective criterion to evaluate the diaphragmatic defect's extent. More studies conclude that there is a strong correlation between the degree of developmental defects and survival.[13,14] In this case, a significant weight loss of 0.22 kg was seen over twelve days, whereas newborns usually regain their birth weight within seven days after an initial loss of a few grams in the first week .[15]

According to the classification of CDH, type 2 is often associated with unilateral lung hypoplasia.[16] Similar findings were noticed in this case. In cases below the age of one year, the commonest cause of death is respiratory insufficiency with pulmonary hypertension, whereas gastrointestinal related morbidities account for mortality among the higher age groups.[17] Initially, it was theorized that the abdomen's contents in the chest cavity led to lung hypoplasia. However, upcoming evidence-based studies confirmed that in few cases, hypoplasia precedes herniation as demonstrated in a nitrofen induced CDH mouse model.[1,18]

Past evidence on pathogenesis were based on a primary developmental defect in the diaphragm, herniation of abdominal contents, and lung hypoplasia resulting in severe postnatal respiratory distress and death.[19] But recent evidence-based studies propose a "dual hit hypothesis," which states that there is a participation of a common genetic pathway that regulates the development of the lungs and the diaphragm.[19] The disarrangement of the Shhptc-Gli pathway and the Retinoid signaling pathway is believed to be involved in the pathogenesis of CDH associated with pulmonary hypoplasia.[19] Downregulation of the Sonic hedgehog (Shh) expression in pulmonary hypoplasia is associated with CDH.[19] Shh prevents lung fibroblast growth, and normal Shh expression may contribute to interstitial thinning occurring at the late glandular (6-16weeks) and early canalicular phase (16-26 weeks) of lung development.[19] A disturbance in this channel would lead to arrested lung development and CDH.[19]

The defect can be diagnosed in utero by ultrasonography, which shows a ''stomach bubble." [6] Sometimes, prenatal diagnosis is not possible because the herniation occurs at the time of birth or after birth.[6] After diagnosing the defect, the diaphragm defect may be repaired, typically thoracoscopically by ''Plication, '' which uses the technique of the folding the eventrated diaphragm, which is then sutured in order to ''take up the slack ''of the excess diaphragm tissue.[6] Nonspecific parameters like APGAR scoring, associated abnormalities, diagnosis in utero, and birth weight can also be used as predictors to some extent.[20-22]

5. Conclusion

CDH diagnosis and management are already in an advanced form. However, the present percentage of mortality is due to delayed diagnosis in a symptomless baby with a scaphoid abdomen, addressed by our case. The proclamation of diagnostic follow up should not be limited to the ones with symptoms, but also the asymptomatic babies with the scaphoid abdomen.

Better diagnostic facilities and awareness about such non-specific symptoms in both the medical fraternity and the general public, will decrease the mortality of an otherwise preventable and operable case of CDH.

Ethical statement: Written informed permission for publishing scientific autopsy findings in academic journals, without disclosing identity has already been taken from the father of the deceased. Medicolegal autopsy was performed and all procedures were in accordance with the ethical standards of the Institute and existing laws of the country related to post-mortem examination.

Conflict of interest: None.

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