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Case Report

A Case of Idiopathic Premature Closure of the Ductus Arteriosus

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Abstract

Premature closure of the ductus arteriosus (DA) is a rare condition that can present as stillbirth, premature delivery, or persistent pulmonary hypertension (PPHN) in neonates. The incidence and prevalence of premature closure of the DA are not well documented in the literature, as it is a very rare condition. Maternal exposure to NSAIDs, polyphenol-containing foods, and other drugs such as betamethasone is associated with this rare condition. Treatment is mainly aimed at maintaining the patency of the ductus arteriosus and treating pulmonary hypertension. We report a case of this rare condition in a premature neonate who had no risk factors for the disease, was diagnosed postnatally, and responded well to pharmacological therapy.

Keywords: *Ductus Arteriosus (DA); Persistent Pulmonary Hypertension (PPHN); NSAIDs*

Introduction

This case report highlights a premature infant diagnosed postnatally with premature closure of the DA. This rare condition can lead to PPHN, right ventricular failure, and intrauterine mortality. The diagnosis is usually made antenatally by echocardiogram. Treatment is aimed at reducing pulmonary pressure and keeping the DA open. Our case highlights this rare condition and important diagnostic and treatment modalities.

Case Presentation

A female neonate (birth weight 2060 gm) was delivered via emergency LSCS due to non-reassuring CTG at 35+1 weeks gestation to a 37-year-old (gravida 2, para 1) mother. The antenatal course was uneventful until 34 weeks of gestation. There was no history of flu-like illness or medication intake during the pregnancy. The fetal anomaly scan was unremarkable. The pregnancy was complicated by oligo-hydramnios during the last trimester, and steroid cover was provided on week 34. The mother reported to the emergency department during the 35th week due to reduced fetal movements, and an emergency C-section was performed.

The neonate's Apgar scores at the 1st and 5th minutes of life were 7 and 8, respectively. The neonate was euthermic, and no gross congenital anomalies were seen on physical examination. The neonate was shifted to the NICU due to desaturation and mild respiratory

distress. The patient was connected to CPAP, requiring a FiO_2 of 100% to maintain a SpO_2 of 90 - 92%. The patient was intubated due to desaturation and high FiO_2 requirements. One dose of surfactant was administered, considering the possibility of respiratory distress syndrome.

Her blood parameters, including the sepsis screen, were normal. An X-ray of the chest and abdomen was done, and it showed no significant abnormality. A screening echo showed right ventricular hypertrophy, which was suggestive of persistent pulmonary hypertension due to premature ductus arteriosus closure. The DA was closed, and a small patent foramen ovale (PFO) resulted in a right-to-left shunt. There was a flat ventricular septum. No other structural abnormalities were detected. We ruled out that there was no right ventricular outflow tract obstruction.

The neonate was started on inhaled nitric oxide (INO) therapy along with oral sildenafil. There was a slow decrement in the FiO_2 requirements and improvements in PaO_2. The vitals were closely monitored, along with serial echocardiography. The INO was tapered off and stopped by day 6 of life. Neonate was weaned off the high-flow nasal cannula (HFNC) by day 6 of life and then gradually to room air by day 10 of life. The patient was able to maintain saturation on room air. The patient was discharged on the 14^{th} day of life. The patient was followed up periodically in the outpatient cardiology department. We noted a complete resolution of pulmonary hypertension in the next two months, and the patient was weaned off of oral sildenafil.

Case Discussion

The ductus arteriosus normally remains patent during fetal life, and its patency is usually maintained by the prostaglandin E2 and prostaglandin E1 produced by the ductus [1]. It closes 12 - 72 hours after birth, but spontaneous closure can occur in utero and is usually seen as a side effect of pharmacological agents. The function of the ductus arteriosus in utero is to bypass the pulmonary circulation because the lungs are non-functional during the intrauterine period [2]. Indomethacin, which is an NSAID, is the most common drug known to cause premature ductus arteriosus closure. It works by inhibiting cyclooxygenase, an enzyme responsible for the breakdown of arachidonic acid into dilatory prostaglandins, and disrupting the active process of maintaining the patency of the ductus arteriosus in utero. Prolonged use of indomethacin by the mother can result in complete and irreversible constriction of the DA. Indomethacin can cause immediate closure in some cases, while in others, the ductus remains patent despite repeated exposure. Several other pharmacological agents have been known to cause premature closure of the DA, such as betamethasone, which is used for fetal lung maturation but can cause transient reversible constriction of the DA in utero [3]. The etiology of idiopathic closure of DA remains unknown but has been linked to the maternal ingestion of foods and beverages rich in polyphenols and flavonoids, such as herbal tea, grape, and orange beverages. Polyphenol-rich foods work by interfering with prostaglandin metabolism through their anti-inflammatory and anti-oxidant side effects [2].

Antenatal closure of the ductus results in increased right ventricular afterload, leading to increased right ventricular pressure, tricuspid regurgitation, and eventually right heart failure. Pulmonary hypertension results from medial thickening of the pulmonary vessels due to increased blood flow to the premature lungs [4].

It was almost impossible to diagnose premature closure of DA before the use of echocardiography, and it was usually diagnosed after fetal demise. Echocardiograms can be used for definitive diagnoses of premature closure of the DA in the third trimester of pregnancy. Echo will show cardiomegaly, dilated pulmonary arteries with a lack of flow through the ductus arteriosus, and pulmonary valve regurgitation. When premature closure of the DA is confirmed by sonogram, premature delivery should be considered because it provides a favorable outcome [1].

Symptomatic Infants delivered after in-utero DA closure have been treated with inhaled nitric oxide. INO is approved in the US for the treatment of premature closure of the ductus arteriosus in infants delivered after > 34 weeks of gestation. A body of evidence suggests

the safety of INO in younger gestational-age infants, and some evidence from a few studies suggests its association with intraventricular hemorrhage. The pediatric pulmonary hypertension network, which has its headquarters in the US, advises INO for specific subgroups of preterm children who have pulmonary hypertension linked to oligohydramnios, pulmonary hypoplasia, or sepsis. The European pediatric pulmonary vascular disease network recommends milrinone, which is a PDE3 inhibitor, as an alternative to INO if there is evidence of impaired systolic ventricular function with pulmonary hypertension (PH) [4].

In utero, it may cause congestive heart failure, hydrops fetalis, and intrauterine death. However, the range of clinical manifestations may range from mild symptomatology to complete respiratory failure [5].

In this case, we chose to use INO and sildenafil (PDE5) inhibitors for the treatment of PPHN. The patient's condition improved with treatment. On discharge, sildenafil was continued for pulmonary hypertension. A good response was observed post-discharge, and sildenafil was discontinued 3 months post-discharge following a normal echo.

Conclusion

Premature closure of the ductus arteriosus is a rare condition that can have catastrophic results. Detection usually occurs during antenatal anomaly scans. Premature closure can lead to pulmonary hypertension and right heart failure. Postnatally, drugs that maintain patency of the ductus arteriosus and those that reduce pulmonary pressures are the mainstay of treatment for this condition. In this case, the patient demonstrated a good response to treatment and complete resolution of pulmonary hypertension.

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