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Case Report

A Rare and Unusual Case of Severe Persistent Pulmonary Hypertension in a Newborn due to Accidental Drug Exposure in Mother

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Abstract

Persistent pulmonary hypertension is a life-threatening illness that can be fatal if not diagnosed early. Some medications, notably selective serotonin reuptake inhibitors (SSRIs), can cause severe persistent pulmonary hypertension in newborns if administered antenatally, especially after 20 weeks of gestation. We present a case in which the use of selective serotonin uptake inhibitors during pregnancy resulted in severe chronic pulmonary hypertension in a newborn. A 2.5-kilogram male newborn was delivered via caesarean section and was asymptomatic for one day. On day 2 of life, the baby suffered cyanosis and difficulties breathing, necessitating intubation. In retrospect, the mother was taking sertraline for the treatment of depression. Based on the clinical characteristics and presentation, an echocardiogram was performed, which revealed severe chronic pulmonary hypertension. The baby was successfully treated with pulmonary vasodilators and high flow oscillating ventilation.

Keywords: Maternal drug exposure, Maternal depression, Newborn, Persistent pulmonary hypertension, Serotonin reuptake inhibitors, Vascular remodeling.

سبب نادر وغير عادي لارتفاع ضغط الدم الرئوي المستمر الشديد عند المولود الجديد بسبب التعرض العرضي للأدوية لدى الأم

الخلاصة

ارتفاع ضغط الدم الرئوي المستمر هو مرض يهدد الحياة ويمكن أن يكون قاتلا إذا لم يتم تشخيصه مبكرا. يمكن أن تسبب بعض الأدوية، ولا سيما مثبطات امتصاص السيروتونين الانتقائية (SSRIs)، فرط ضغط الدم الرئوي المستمر الشديد لدى الأطفال حديثي الولادة إذا تم إعطاؤها قبل الولادة، خاصة بعد 20 أسبوعا من الحمل. نقدم حالة أدى فيها استخدام مثبطات امتصاص السيروتونين الانتقائية أثناء الحمل إلى ارتفاع ضغط الدم الرئوي المزمن الوخيم عند الأطفال حديثي الولادة. ولد طفل حديث ولادة يبلغ وزنه 2.5 كيلوغرام عن طريق الولادة القيصرية ولم تظهر عليه أعراض لمدة يوم واحد. في اليوم الثاني بعد الولادة، عانى الطفل من الزرقة وصعوبات في التنفس، مما استلزم التنبيب. في وقت لاحق، كانت الأم تتناول سيرترالين لعلاج الاكتئاب. بناء على الخصائص السريرية والعرض التقديمي، تم إجراء مخطط صدى القلب، والذي كشف عن ارتفاع ضغط الدم الرئوي المزمن الشديد. تم علاج الطفل بنجاح باستخدام موسعات الأوعية الدموية الرئوية والتهوية المتذبذبة عالية التدفق.

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INTRODUCTION

Pulmonary hypertension is a devastating condition of neonates that primarily affects the pulmonary vascular bed and musculature, resulting in high mortality. It is commonly accompanied with other parenchymal disorders. Overall, one out of every 500 neonates develop chronic pulmonary hypertension. 10–50% of them may die because of the disease's severity, and some may have late problems, such as neurodevelopmental delays [1]. During the shift from fetal to newborn circulation, pulmonary blood flow increases tenfold, while pulmonary pressure drops by nearly half. Persistent pulmonary hypertension (PPHN) in newborns can be caused by a number of factors that happened before birth, such as exposure to medications, especially nonsteroidal anti-inflammatory drugs and selective serotonin reuptake inhibitors (SSRIs), addiction, cesarean delivery, and diabetes [2]. Any substance administered during the prenatal period should be taken with caution because it may harm the developing fetus. Many studies have found that kids whose mothers were exposed to SSRIs and nonsteroidal anti-inflammatory medicines during pregnancy are more likely to develop PPHN [3,4]. The occurrences can range from 1.5 to 2.72 per 1000 moms exposed to SSRIs [4]. SSRIs have been linked to PPHN in neonates born to women who took them after 20 weeks of gestation [5]. Antenatal use of SSRIs can cause severe PPHN in newborns, which is a common cause of death and prolonged NICU admission [6]. The use of SSRIs should be emphasized over the harmful effects of severe depression in mothers, which have harmed their and their newborns' health, resulting in poor results and increased morbidity. Any medicines administered during the antenatal period must be used with caution, since they may result in poor outcomes and malformations in newborn babies.

Case Presentation

A 2.5-kilogram male baby born to a primigravida mother via cesarean section. The baby cried right after birth, and his APGAR score was 8, 9, and 10. The baby's color was normal, and all vital signs were stable on a standard neonatal assessment. The infant was moved to his mother's side for standard hospital care. Mother underwent regular prenatal exams and screenings. The mother has a history of depression and is now on SSRIs. Relatives admitted that the mother had schizophrenia and had been on antipsychotic medication for the past two years. Initially, doctors prescribed her fluoxetine, an SSRI, and clonazepam. However, her symptoms escalated over the previous year, prompting her to add sertraline, another SSRI, to manage the flare-ups. She has been taking this medication since last year. There has been no history of fever, rash, NSAID use, diabetes, hypertension, oligohydramnios, or decreased fetal movement. On day two of life, the newborn presented to the hospital with rapid breathing, grunting, respiratory distress, and cyanosis. The capillary refill time was less than 3 seconds, with 92% oxygen saturation in the right hand and 78% in the left hand. Dusky skin with minor cyanosis was evident, as was labile hypoxia, with a 14% difference in saturation between preductal and post-ductal. The assessment of the respiratory system revealed rapid breathing, a grunt with a Downs' score of 6, and equal air input on both sides. There was no murmur, but the tachycardia was evident, and the P2 was audible. The neurological evaluation was normal. The laboratory results were Hb 17.5 g/dL, total leukocyte count 17600/mm, platelet 2.24 x10^9/L, C-reactive protein 1.0 mg/dL, and the remaining of the tests, including a septic screen, renal function test, and electrolytes, were normal. There was mild oligemia on the chest x-ray, and metabolic acidosis was found in the blood, with a pH of 7.12, pO_2 of 65 mmHg, pCO_2 of 29 mmHg, HCO_3 of 12.8 mmol/L, and a base excess of 2 meq/L. The baby was originally put on CPAP and supportive care, but when his condition deteriorated, he was moved to invasive ventilation. Our differential diagnoses included early-onset septicemia, congenital cyanotic heart disease, lung parenchymal disease, and PPHN. Another alternative diagnosis was ruled out because there was no history of birth asphyxia, and it was an in-hospital delivery, which we attended. The septic screening was normal, and the chest x-ray revealed no signs of parenchymal pulmonary illness. We confirmed the diagnosis of PPHN after ruling out other options. The baby's echocardiography revealed no visible structural cardiac defects, indicating congenital cyanotic heart disease. The cardiac contractility was good, with an appropriate ejection fraction. The modified Bernoulli formula yielded a right ventricular systolic pressure of 65.55 mmHg. A color Doppler scan of the tricuspid valve, as shown in Figure 1, revealed tricuspid regurgitation with a pressure difference of 61 mmHg and a tricuspid jet velocity of 392 cm/sec.

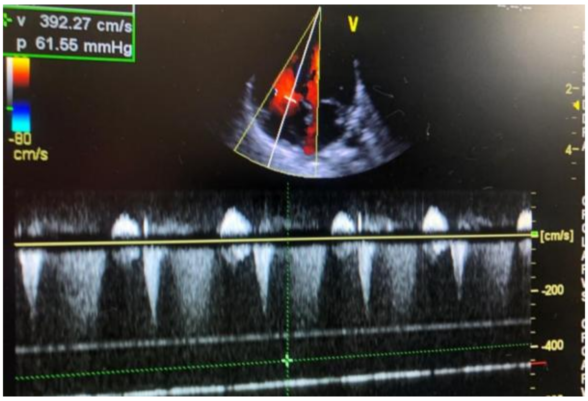

Figure 1: Color doppler at tricuspid valve shows tricuspid regurgitation with pressure gradient of 61.55 mmHg and tricuspid regurgitation jet velocity 392 cm/sec suggestive of severe pulmonary hypertension.

This means that the patient has severe pulmonary hypertension. The interventricular septum was pushed to the left, flattening from its normal deflection. As pressure in the right ventricle rises, the septum straightens, resulting in a D-shaped left ventricle, as seen in Figure 2A. Color Doppler flow across the ductus arteriosus and foramen ovale demonstrated bidirectional flow, as seen in Figure 2B.

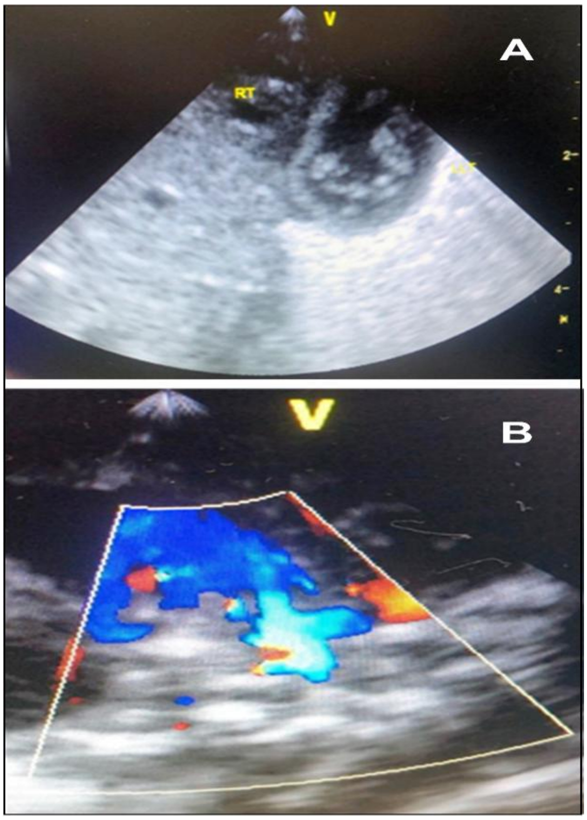

Figure 2: A) Shows right ventricular hypertrophy and increased pressure on RV leading to deviation of septum towards left ventricle making it flatten and D shape appearance to left ventricle; B) A Color doppler image shows the flow across ductus arteriosus showing bidirectional flow from pulmonary artery to aorta and vice versa due to increased pulmonary artery pressure

There was no other cause of PPHN identified in the baby. Therefore, we reexamined the baby's medical history and found that the mother had a history of using sertraline, a medication that occasionally causes PPHN in neonates and may have contributed to the child's deterioration, ultimately leading to the development of PPHN. Mother has used SSRIs throughout her pregnancy. Various studies have revealed that antidepressants are commonly suggested to moms with underlying psychiatric illnesses during pregnancy, with serotonin reuptake inhibitors being the most common. These are commonly prescribed kinds of medicines that are linked to the development of PPHN in neonates. The newborn was treated with pulmonary dilators such as sildenafil and milrinone, as well as inotropic and respiratory assistance. The baby required high-frequency ventilation due to its inadequate response. Following care, we were able to extubate the baby. We did not use inhaled nitrous oxide because it was unavailable at a rural hospital. The psychiatrist was consulted about the mother's continued medication use and breastfeeding of the infant. The mother's history of using SSRIs provided an indication, which allowed us to detect the PPHN early; otherwise, it could have been fatal. The clinical appearance, cyanosis, and respiratory distress are all essential aspects of the given case to investigate. The pulse oximetry is usually always easily available, indicating saturation fluctuation and differences in pre- and post-ductal saturation. On echocardiography, no structural cardiac abnormality was discovered. Because there was no history of passing meconium and the lung fields were clear on a normal chest x-ray, the likelihood of meconium aspiration was also ruled out. Additionally, the infant cried immediately after birth. Finally, we validated the diagnosis of PPHN after ruling out other alternatives, which were supported by characteristic echocardiographic features of PPHN. We were able to manage and extubate the youngster following intense management and high-quality care. After intense management and high-quality care, we were able to extubate the youngster and effectively discharge him following sufficient family counseling. Following consultation with a psychiatrist, the medication was continued in the mother, and the mother and caregiver were properly counseled on feeding and newborn safety. The mother and baby were successfully discharged, and the youngster is doing well after 15 days of follow-up.

DISCUSSION

Persistent pulmonary hypertension is a significant cause of mortality and morbidity in neonates, particularly in resource-limited settings with inadequate facilities. It is also known as chronic fetal hypertension, and it is caused mostly by fetal circulation maladapting to external circulation [1]. Arshad *et al*. [6] found in their study that different etiologies, including idiopathic and secondary to birth asphyxia, meconium aspiration, congenital diaphragmatic hernia, and medications, are related to the development of PPHN in neonates. The key signs include tachypnea, retractions, grunting, and cyanosis, all of which indicate PPHN. There may also be an increase in oxygen demand, hypoxia, grunting, cyanosis, SpO_2 fluctuations, and differential cyanosis. The primary underlying pathophysiology is impaired vascular remodeling, muscularization, and elevated pulmonary vasculature pressure [1,6]. This illness is distinguished by a prolonged increase in pulmonary vascular resistance, which causes extrapulmonary shunting of blood from left to right via the ductus arteriosus and foramen ovale, resulting in cyanosis and severe hypoxia. It may lead to respiratory failure and circulatory collapse [7]. The other possible diagnoses include meconium aspiration syndrome, severe pneumonia, congenital cyanotic heart disease, septic shock, and structural heart defects [8]. Various studies have indicated that antidepressants are consistently suggested to moms who have an underlying psychiatric condition during pregnancy, with SSRIs being the most prescribed. In this regard, Berard et al. [9] and other writers have observed that these medicines increase the chance of developing PPHN in neonates [2-5,9]. The risk is not directly tied to SSRI exposure and varies according to the kind, amount, and timing of the mother's drug use. In our case, the mother has been taking sertraline for the previous two years. Munk-Olsen *et al*. [10] and Chambers et al. [11] suggest that most of the harmful consequences occur after 20 weeks of gestation. The risk of developing persistent pulmonary hypertension increases with the use of SSRIs, reaching its peak after 20 weeks [10,11]. The actual pathophysiology and process of producing PPHN in infants is unknown. Studies on fetuses and animals have demonstrated that exposure to high amounts of it raises serotonin and norepinephrine levels in cells. It stimulates and elevates the blood level of S100B, a protein produced in astrocytes that mediates calcium transport inside the cells. The stimulation of 5-HT1A receptors on astrocytes results in the production of S100B, which causes neuronal damage. The level of S100B in the blood was higher in moms who were given SSRIs than in those who had not been exposed [12]. It also influences muscular hyperplasia in the right ventricle, as well as vascular and muscular remodeling in the pulmonary bed [2,7,12]. Clinical presentation, fluctuation in oxygen saturation, cyanosis, and respiratory distress are the most common indicators of the diagnosis. Echocardiography is a diagnostic tool that primarily detects an increase in pulmonary vascular bed pressure, which may be greater than systemic pressure; patent foramen ovale and ductus arteriosus; right ventricular hypertrophy; interventricular septum deviation toward the left ventricle; and a regurgitant jet across the tricuspid valve [13]. The treatment consists primarily of nursing in a calm environment with minimal stimulation to prevent oxygen fluctuations; providing controlled oxygenation and good ventilatory support; using inotropes, vasoactive agents, and pulmonary dilators such as sildenafil, milrinone, prostacyclin, and inhaled nitrous oxide; and ECMO therapy [7,8]. The decision to continue or discontinue this medicine during pregnancy is not easy. The benefits-risk ratio should be evaluated. Given the patient's condition, severe depression, and its repercussions, it can be continued. The benefit of maintaining SSRIs should outweigh the danger, as severe depression in mothers has a negative influence on maternal and newborn health, resulting in poor outcomes and increased morbidity [4]. All aspects should be considered, and the case should be examined by a neurologist before discontinuing or starting the medicine antenatally. We sought the psychiatrist's advice, and given the severity of the sickness, the medications were continued in the mother. Our patient was treated satisfactorily and discharged.

Conclusion

Persistent pulmonary hypertension is a life-threatening illness that frequently affects newborns in intensive care units. After ruling out the most common causes of PPHN, causes should be investigated. Early diagnosis and aggressive management are critical to success. Some medications, particularly SSRIs, can induce severe pulmonary hypertension in newborns when taken by the mother, especially after 20 weeks of pregnancy. Gynecologists, psychiatrists, pediatricians, and other health care practitioners should understand SSRIs thoroughly before prescribing them. It is important to educate society and all pregnant women about this entity.

Conflict of interests

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

REFERENCES

1. Teng RJ, Wu TJ. Persistent pulmonary hypertension of the newborn. *J Formos Med Assoc*. 2013;112(4):177-184. doi: 10.1016/j.jfma.2012.11.007.
2. Delaney C, Cornfield DN. Risk factors for persistent pulmonary hypertension of the newborn. *Pulm Circ*. 2012;2(1):15-20. doi: 10.4103/2045-8932.94818.
3. Andrade SE, McPhillips H, Loren D, Raebel MA, Lane K, Livingston J, Boudreau DM, Smith DH, Davis RL, Willy ME, Platt R. Antidepressant medication use and risk of persistent pulmonary hypertension of the newborn. Pharmacoepidemiol Drug Saf. 2009 Mar;18(3):246-52.
4. Ng QX, Venkatanarayanan N, Ho CYX, Sim WS, Lim DY, Yeo WS. Selective serotonin reuptake inhibitors and persistent pulmonary hypertension of the newborn: An update meta-analysis. *J Womens Health (Larchmt)*. 2019;28(3):331-338. doi: 10.1089/jwh.2018.7319.
5. Huybrechts KF, Bateman BT, Palmsten K, Desai RJ, Patorno E, Gopalakrishnan C, et al. Antidepressant use late in pregnancy and risk of persistent pulmonary hypertension of the newborn. *JAMA*. 2015;313(21):2142-2151. doi: 10.1001/jama.2015.5605.
6. Arshad MS, Adnan M, Anwar-Ul-Haq HM, Zulqarnain A. Postnatal causes and severity of persistent pulmonary hypertension of newborn. *Pak J Med Sci*. 2021;37(5):1387-1391. doi: 10.12669/pjms.37.5.2218.
7. Singh Y, Lakshminrusimha S. Pathophysiology and management of persistent pulmonary hypertension of the newborn. *Clin Perinatol*. 2021;48(3):595-618. doi: 10.1016/j.clp.2021.05.009.
8. Sharma V, Berkelhamer S, Lakshminrusimha S. Persistent pulmonary hypertension of the newborn. *Matern Health Neonatol Perinatol*. 2015;1:14. doi: 10.1186/s40748-015-0015-4.
9. Bérard A, Sheehy O, Zhao JP, Vinet É, Bernatsky S, Abrahamowicz M. SSRI and SNRI use during pregnancy and the risk of persistent pulmonary hypertension of the newborn. *Br J Clin Pharmacol*. 2017;83(5):1126-1133. doi: 10.1111/bcp.13194.
10. Munk-Olsen T, Bergink V, Rommel A, Momen N, Liu X. Association of persistent pulmonary hypertension in infants with the timing and type of antidepressants in utero. *JAMA Netw Open*. 2021;4(12):e2136639. doi: 10.1001/jamanetworkopen.2021.36639.
11. Chambers CD, Hernandez-Diaz S, Van Marter LJ, Werler MM, Louik C, Jones KL, et al. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. *N Engl J Med*. 2006;354(6):579-587. doi: 10.1056/NEJMoa052744.
12. Pawluski JL, Galea LA, Brain U, Papsdorf M, Oberlander TF. Neonatal S100B protein levels after prenatal exposure to selective serotonin reuptake inhibitors. *Pediatrics*. 2009;124(4):e662-670. doi: 10.1542/peds.2009-0442.
13. de Boode WP, Singh Y, Molnar Z, Schubert U, Savoia M, Sehgal A, et al. Application of neonatologist performed echocardiography in the assessment and management of persistent pulmonary hypertension of the newborn. *Pediatr Res*. 2018;84(Suppl 1):68-77. doi: 10.1038/s41390-018-0082-0.