THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 12 Issue 11

CASE REPORT

A toddler presenting with persistent pulmonary hypertension of the newborn: And treatment at a Primary Health Centre

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OPEN ACCESS

PUBLISHED
30 November 2024

CITATION
Daga, S., 2024. A toddler presenting with persistent pulmonary hypertension of the newborn: And treatment at a Primary Health Centre. Medical Research Archives, [online] 12(11). https://doi.org/10.18103/mra.v12i11.5952

DOI
https://doi.org/10.18103/mra.v12i11.5952

ISSN
2375-1924

ABSTRACT

A growth-restricted baby boy was born at term with a birthweight of 1.9 kg. He was given NICU care for nine days. The echocardiographic studies done for respiratory distress and murmurs revealed left-to-right shunts at atrial, ventricular, and ductal levels and severe pulmonary hypertension. However, the pulmonary artery pressure values were not available. Financial constraints did not permit surgery. He presented at the Primary Health Centre for shortness of breath and growth failure at four-and-a-half years of age. The child received sildenafil for pulmonary hypertension with a "treat and repair" approach. The child is steadily improving in breathing, outdoor games, and schooling. The pulmonary pressures were still high (60 mm) on repeat echocardiographic studies performed after 18 months of sildenafil treatment. Six-monthly echo studies are planned to guide the future course of action.

Keywords: Persistent Pulmonary Hypertension of Newborns; Pulmonary artery hypertension; Respiratory distress in a child; Sildenafil for pulmonary hypertension of newborns.

Introduction

Persistent Pulmonary Hypertension in Newborns (PPHN) is commonly caused by the adverse perinatal course, most often secondary to pulmonary parenchymal diseases[1]. PPHN results in the faltered fetal-to-neonatal vascular transition wherein a physiological fall in pulmonary vascular resistance (PVR) and rise in systemic vascular resistance fail to appear. The accompanying left-to-right shunts may accelerate the progression of pulmonary hypertension (PH). The type and size of the shunt determine the rise in PH. The PH rises rapidly in cases of ventricular septal defect (VSD), patent ductus arteriosus (PDA), and large-size defects. The left-to-right shunts add to the PH by constant exposure to increased blood flow. The resulting tissue hypoxia and following organ dysfunction demand early repair of the defect/s. The shunt closure on patients with PH above a certain threshold runs the risk of postoperative persistence of PH and a worse long-term outcome[2].

There may be situations in low-resource settings where timely surgical intervention may not be possible or may be delayed even in the presence of significant PH. In such a situation, preventing/ delaying inoperability status by not letting PH rise substantially is essential. Resorting to therapies such as phosphodiesterase-5 inhibitors, endothelin-receptor antagonists, and prostacyclin analogs may slow the progression of PH. We report a case of PPHN, although diagnosed in the newborn period, presented as a toddler with shortness of breath and growth failure, "converted to an operable status" by using oral sildenafil, an affordable option.

Case report

A 54-month-old boy, a resident of a village 5-6 km away from the Primary Health Centre (PHC) headquarters, presented with rapid breathing since the age of 2-3 months. He was born at term with a birth weight of 1.9 kg and nine days of NICU stay. He became breathless during breastfeeding and was taking pauses while feeding. His indoor mobility meant only creeping up to two years, then crawling and walking at three. There was a history of frequent colds and coughs.

On examination, the child looked stunted. His height was 96 cm, and his weight was 12.2 kg. There was no cyanosis or clubbing of fingers, but his skin had a purplish hue.

He had two systolic murmurs, one on the lower sternal edge and the other in the second left intercostal space. Echocardiographic studies were conducted at three, twelve, and thirteen months. All the reports mentioned severe pulmonary hypertension, without a mention of further details, and a patent ductus arteriosus, a ventricular septal defect, and an atrial septal defect. Persistent pulmonary hypertension of newborns (PPHN) with left-to-right shunts was diagnosed. The surgeon advised closure of the defects. The family could not afford the surgery. The child received treatment for the frequently occurring respiratory illnesses at the PHC.

Discussion

At the PHC, oral sildenafil was started with the "treat with intent to repair." approach[3] at 1 mg/kg/6h. A 50 mg tablet was to be dissolved in 5 ml of water, of which 1 ml (10 mg) was to be administered four times daily. A practical demonstration of the preparation and administration of the medicine was given to the parents. On the next visit, the skin color had improved after a month and was no longer purplish. Three months later, his indoor mobility had considerably enhanced. After six months of treatment, he started to walk. The shortness of breath after playing outdoors disappeared, and his schooling began. Soon, he started participating actively in outdoor games. His cheeks were filling up, suggesting improving nutrition. During the last 18 months, he presented only once for respiratory complaints. His echocardiography, after 18 months of sildenafil, showed a moderate-sized atrial septal defect measuring 7 mm with a left-to-right shunt, a large inlet ventricular septal defect with predominantly left-to-right shunt, and a large patent ductus arteriosus measuring 9 mm with a low velocity left- to- right

shunt. The study also showed dilatation of all four cardiac chambers and good left ventricular function with an ejection fraction of 60%. The study also revealed pulmonary artery dilatation and high-velocity pulmonary regurgitation with pulmonary artery mean pressure of 60 mm.

The baby was born with a risk of PPHN in the form of intrauterine growth restriction, weighing 1.9 at term[4]. Besides, she had systemic-to-pulmonary shunts that have increased pulmonary blood flow, leading to pulmonary arterial hypertension (PAH), increased pulmonary vascular resistance (PVR), and shunt reversal over time. At this stage, the surgery is contraindicated since the shunt closure, in the presence of high PAH, often leads to progressive dilation and dysfunction of the right ventricle, having "lost their relief valve"[5]. Therefore, early closure of the cardiac shunt remains the best way to prevent pulmonary vascular changes. The consensus is to close a left-to-right shunt early in life, less than twelve months, for the post-tricuspid shunts, such as ventricular septal defect and patent ductus arteriosus. The closure of the pre-tricuspid, atrial septal defect can wait longer since it causes PAH late[6].

Our case has one pre-tricuspid and two post-tricuspid shunts requiring early surgical closure of the defects. It was not performed due to financial constraints. However, oral sildenafil treatment could have been started during infancy to delay the process of developing PAH and give surgery a chance. Our patient, even while the mean pulmonary artery pressure has reached 60 mm, has gained the physical milestones after sildenafil treatment, which suggests that a "point of no return"[7] has not been reached, and the "treat (PAH) and repair" strategy may well have a chance.

Targeting the endothelin, nitric oxide, and prostacyclin (PGI2) pathways reduces the load on the right heart[8]. Combination therapy in PAH, either upfront or sequentially, has become a widely adopted treatment strategy in severe cases[9]. The double oral combination of a phosphodiesterase type-5 (PDE-5) inhibitor and an endothelin receptor antagonist (ERA) is considered standard of care for most other patients with mild to moderate PAH. In our case, the probability of developing Eisenmenger syndrome appears to have receded, and a single oral drug, sildenafil, seems to have helped. Sildenafil, a phosphodiesterase inhibitor, selectively reduces pulmonary vascular resistance[10]. It can reduce mortality and improve oxygenation in neonates, especially in resource-limited settings where iNO is unavailable[11]. Pre- and post-sildenafil echocardiography comparison demonstrated decreased pulmonary arterial pressures when administered orally. Sildenafil is readily available and inexpensive, particularly advantageous for low-resource settings[12,13,14].

In summary, a child who was diagnosed with PPHN presented to a PHC at fifty-four months with rapid breathing and growth retardation. After sildenafil treatment, the growth picked up, and his schooling started. Echo studies continue to show pulmonary hypertension; comparison was not possible since earlier reports did not mention pulmonary artery pressure values. Six-monthly echo studies, hopefully, guide the future course of action.

Competing interest:

None

Funding:

None

Acknowledgment:

The author thanks Dr. Mohan Swaminathan for his help.

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