Case Report

A Unique Case of Thiamine-Responsive Acute Pulmonary Hypertension of Early infancy (TRAPHEI): A Positive Outcome Against the Odds

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ABSTRACT

Thiamine deficiency in infants can lead to severe metabolic disturbances, including pulmonary arterial hypertension (PAH). Thiamine-Responsive pulmonary artery hypertension of early infancy (TRAPHEI) is a rare condition that warrants early recognition and intervention. We present a case of a 4-month-old exclusively breastfed infant referred for respiratory distress. The infant exhibited signs of tachypnoea, tachycardia, and prolonged capillary refill time. Initial investigations revealed metabolic acidosis, and echocardiographic findings of severe pulmonary hypertension (PASP 71 mmHg). Managed with intravenous normal saline, sodium bicarbonate, oxygen support, and IV thiamine (100 mg). Rapid clinical improvement was noted after thiamine supplementation. A repeat echocardiogram 24 hours post-treatment showed resolution of pulmonary arterial hypertension. This case underscores the critical importance of early diagnosis and treatment of thiamine deficiency in infants, particularly those with nutritional risks. Thiamine supplementation can significantly improve outcomes and reduce morbidity associated with TRAPHEI.

Key words: Thiamine, Metabolic acidosis, Pulmonary Artery Hypertension, TRAPHEI

Pulmonary artery hypertension is a life-threatening condition characterized by increased pulmonary vascular resistance, resulting in right heart failure. Pulmonary hypertension (PH) in infants is defined as the resting mean pulmonary artery pressure (mPAP) more than 25 mm Hg [1]. Pulmonary artery hypertension in infants may be often associated with congenital heart defects or may be idiopathic. There is a distinct subset of infantile PAH which is responsive to thiamine supplementation. It is commonly manifested in breastfeeding infants as acute cardiac failure and severe pulmonary hypertension (PH). Predisposing factors are respiratory tract infection or other infections [2]. Administration of thiamine results in rapid reduction in pulmonary arterial pressure and recovery in these infants.

Thiamine, also known as vitamin B1 plays an essential role in energy metabolism, particularly in the pyruvate dehydrogenase complex. It's deficiency or impaired metabolism is associated with various disease conditions, including neurological and cardiovascular disorders [3]. Thiamine deficiency in lactating mothers is accelerated mainly by the use of polished rice. Other causes include postpartum dietary restriction, and thiaminase-containing foods like tea, coffee, or betel nut [4]. Infants who are exclusively breastfed are at a high risk of developing Thiamine responsive acute pulmonary hypertension in early infancy (TRAPHI) due to the extremely low thiamine levels in the breast milk of this mothers [5].

In the appropriate geographic and cultural context, a child who was previously well and presents with quick breathing difficulty, feeding difficulties, tachycardia, and hepatomegaly should be suspected of having TRAPHI. The clinical presentation mimics sepsis or lower respiratory tract infection. It can also be presented as sudden onset life threatening lactic acidosis and cardiac failure [6]. In this case an echocardiography or chest X-ray do not reveal a pulmonary or cardiac reason for PAH. The diagnosis is made based on clinical clues and the presence of lactic acidosis. Thiamine deficiency is difficult to diagnose in laboratories for a number of reasons. High thiamine pyrophosphate (TPP) and low erythrocyte transketolase activity (ETKA) point to a functional thiamine deficiency [7]. They are expensive and not routinely done. Without particular therapy, there is a high mortality rate. Respiratory support, pulmonary vasodilator therapy, inotropes, diuretics, and thiamine administration have all improved the outcomes of these babies [8].

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CASE REPORT

4 months old female child presented with history of cough, cold and low-grade fever of 3 days duration and respiratory distress for one day. Child was treated as bronchiolitis from outside hospital. She was born to 40 years old P3L1A1 mother at term gestation, appropriate for gestational age via normal vaginal delivery with a birth weight of 2700 grams. Antenatal ultrasound revealed polyhydramnios and placenta previa. Mother was on polished and washed white rice-based diet. She had skin lesions similar to vitamin deficiency as seen in image 3. Baby was on exclusive breast feeds. On examination child had acidotic breathing, tachycardia, tachypnoea with weak peripheral pulses and prolonged capillary refilling time. Hepatomegaly was present on per abdominal examination. Possibility of septic shock and inborn errors of metabolism considered initially. Complete blood count was normal. Arterial blood gas showed severe metabolic acidosis (pH-6.86, HCO3-5.9, pCO2-33, Lactate-2). Chest x-ray showed oligemic lung fields.

Liver and Renal function test were normal and normoglycemia was maintained. Blood culture sent and antibiotics were started. Fluid bolus and sodium bicarbonate given for shock. HFNC support given for respiratory distress. Echocardiography done reported as no structural anomalies, grossly enlarged RA/RV, tricuspid regurgitation with pulmonary hypertension (PSAP: 71 mmHg) (image 1). In view of suspicion of TRAPHEI, Thiamine 100 mg given intravenously slowly over 30 minutes. Following which child symptomatically improved. After improving saturations, the baby was transitioned from HFNC to low flow O2 and finally to room air. ECHO repeated after 24 hours showed only mild PAH (PASP-23 mmhg) (image 2). Child found healthy on follow up. Counselling given to mother regarding her diet and thiamine supplements started for her. Metabolic screen for inborn errors of metabolism came negative later.

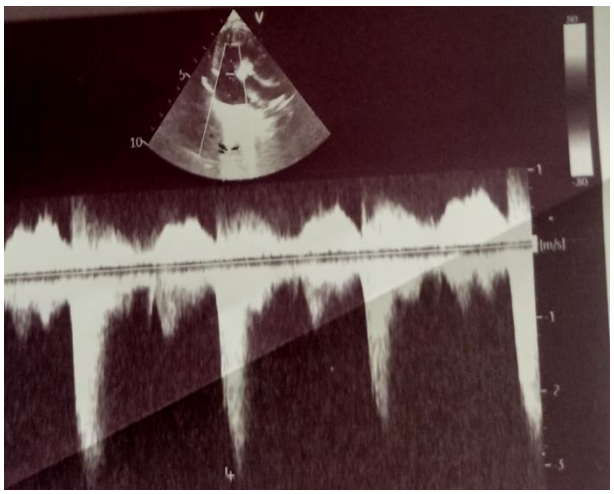

Image 1: ECHO done at admission showing increased pulmonary artery systolic pressure gradient (PASP=71 mmHg)

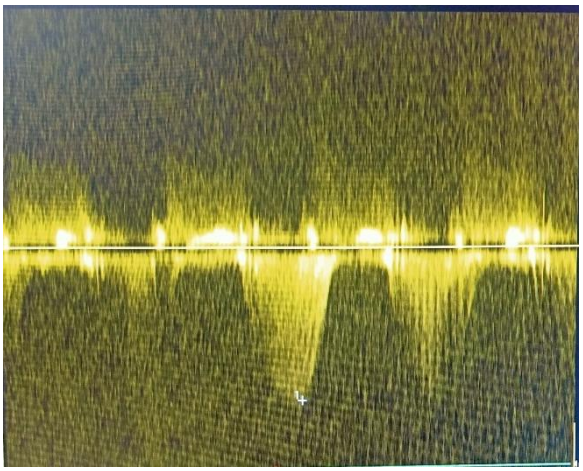

Image 2: Repeat ECHO 24 hours after thiamine injection showing reduced pulmonary artery systolic gradient (PASP=23 mmHg)

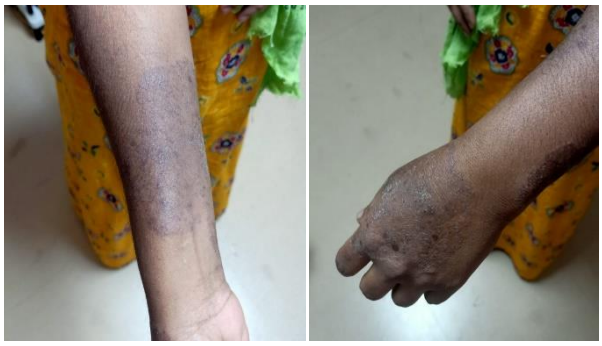

Image 3: Dermatological manifestation in mother due to Dietary vitamin deficiency.

DISCUSSION

Thiamine-responsive PAH refers to cases of pulmonary artery hypertension in infants that improve with thiamine (vitamin B1) supplementation. Thiamine is crucial for carbohydrate metabolism and energy production. It also plays an important function in the production of neurotransmitters, myelin, and nucleic acids [9]. The recommended daily intake (RDI) of thiamine for infants are 0.2 mg/day and slightly higher amount required in older children [10]. Deficiency can lead to impaired endothelial function and increased vascular resistance, contributing to PAH. Infants with this condition may present with symptoms like tachypnoea, cyanosis, and signs of heart failure. Differential diagnoses for PAH in early infancy include congenital heart disease, infection (sepsis, pneumonia) and metabolic encephalopathy.

Diagnosis often involves echocardiography to assess right heart pressures. Most cases are seen in infants, particularly those who are malnourished or have inadequate dietary intake of thiamine. A key diagnostic criterion is the improvement of PAH symptoms with thiamine supplementation, often seen within days to weeks of starting treatment. In addition to thiamine, supportive care for respiratory and cardiac function

may be necessary, including oxygen therapy and diuretics. Infantile thiamine deficiency most commonly present between 1 – 7 months of age. Acute cardiac manifestation presents in less than 3 months. Cardiac dysfunction caused by thiamine deficiency results in decreased cardiac output, leads to backflow of accumulated blood, and that cause elevation in pulmonary pressure. This results in bi-ventricular dysfunction and right heart failure [11].

In this part of the world infants presenting with TRAPHEI is rare. So far two cases presented to our hospital. We suspected TRAPHEI in this infant as we observed skin lesions similar to vitamin deficiency in child's mother. On probing she gave a history of consuming polished rice-based diet. Notably, she had conceived for the second time after a 14-year interval and had self-imposed dietary restrictions while planning pregnancy, believing it would aid weight loss. Echocardiography report of severe pulmonary hypertension combined with her dietary history, led us to suspect thiamine responsive pulmonary artery hypertension in this infant and a trial of thiamine supplementation was given. Early recognition and diagnosis of thiamine deficiency is imperative as specific therapy decreases morbidity and mortality.

Several case reports and studies have documented the efficacy of thiamine supplementation in infantile pulmonary artery hypertension. The dose of thiamine required is not exactly described. Rao SN and Chandak [12] used 150 mg IV thiamine to treat breastfed children under 6 months old with heart failure, but Bhatt et al [13] treated effectively using 100 mg of thiamine daily. In our case we gave 100mg thiamine loading over 30 minutes followed by noted a clinical improvement in respiratory distress and falling of pulmonary pressure after 3 hours. Our infant had respiratory distress at admission and was provided respiratory support by high flow nasal canula, similar to case series by Venkat C.G et al [14] required HHFNC support for all three cases. Child got discharged on oral thiamine and pulmonary hypertension completely resolved at 4 weeks of follow-up. No recurrence was observed at 6 months of follow-up. Nazir et al [15] reported a case series of five infants with thiamine-responsive PAH, demonstrating significant improvement in pulmonary artery pressure and clinical symptoms.

The genetic basis of thiamine- responsive PAH is not known and thiamine's role in pulmonary vascular health is currently being studied. Future research on this subject should focus on screening methods for the early identification of thiamine deficiency in mothers who consume polished rice and in regions where reports of TRAPHEI cases are more common. This case demonstrates the vital relevance of including thiamine deficiency in the differential diagnosis of infantile pulmonary artery hypertension. The patient's significant response to thiamine supplementation emphasises the importance of early detection and treatment of this reversible cause of PAH.

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