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Thiamine-responsive acute pulmonary hypertension of early infancy (TRAPHEI): A case report

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Abstract
Background: Thiamine-responsive acute pulmonary hypertension of early infancy (TRAPHEI) is a rare but reversible cause of pulmonary hypertension in exclusively breastfed infants of thiamine-deficient mothers.
Case Description: A 2-month-old male infant presented with hurried breathing and excessive crying. Examination revealed tachycardia and hepatomegaly. Echocardiography showed dilated right atrium and ventricle with mild pulmonary arterial hypertension. Routine investigations were normal, and sepsis was ruled out. The infant showed rapid clinical improvement following thiamine supplementation.
Conclusion: TRAPHEI should be considered in infants presenting with unexplained pulmonary hypertension, especially in the context of maternal nutritional deficiency. Early recognition and treatment are lifesaving.

Keywords: Thiamine deficiency, TRAPHEI, pulmonary hypertension, infancy, cardiac beriberi

Introduction

Persistent pulmonary hypertension in early infancy represents a life-threatening condition characterized by sustained elevation of pulmonary vascular resistance, resulting in right-to-left shunting and impaired oxygenation. The etiology is often multifactorial, including structural cardiac anomalies, pulmonary parenchymal diseases, sepsis, and metabolic disorders. However, one important yet frequently under-recognized and reversible cause is thiamine deficiency, particularly in exclusively breastfed infants.

Thiamine (vitamin B1) is an essential water-soluble vitamin that plays a pivotal role in cellular energy metabolism, acting as a cofactor in key enzymatic pathways such as pyruvate dehydrogenase and the Krebs cycle. Deficiency leads to impaired aerobic metabolism, accumulation of lactate, and subsequent metabolic acidosis. This metabolic disturbance contributes to myocardial dysfunction, peripheral vasodilatation, and pulmonary vascular constriction, ultimately resulting in pulmonary hypertension. Thiamine-responsive acute pulmonary hypertension of early infancy (TRAPHEI) has been increasingly recognized in regions where maternal diets are predominantly based on polished rice, which is deficient in thiamine. These infants typically present between 1–6 months of age with acute respiratory distress, irritability, and signs of cardiac dysfunction. A hallmark feature of TRAPHEI is the dramatic and rapid clinical response to thiamine administration, which is both diagnostic and therapeutic.

Early identification of this condition is crucial, as delayed diagnosis may lead to severe complications, including cardiac failure, neurological impairment, or death. Increased awareness among clinicians is essential to ensure timely intervention.

Case Report

A 2-month-old male infant, born of a non-consanguineous marriage and exclusively breastfed, presented with complaints of hurried breathing and excessive crying of acute onset. There was no history of fever, seizures, feeding intolerance, or cyanosis prior to presentation.

On admission, the infant was alert but irritable. Vital parameters revealed tachycardia with a heart rate of 174 beats per minute and tachypnea with a respiratory rate of 68 breaths per minute. Oxygen saturation was maintained at 98% with supplemental oxygen at 2 L/min via nasal prongs. The infant was afebrile, with a recorded temperature of 98.7°F, and capillary blood glucose was within normal limits (137 mg/dL).

On systemic examination, hepatomegaly was noted, with the liver palpable 4 cm below the right midclavicular line, suggestive of right-sided cardiac strain. Cardiovascular examination revealed normal first and second heart sounds, with no audible murmurs. Respiratory examination demonstrated bilateral adequate air entry without adventitious sounds. Neurological examination was unremarkable, with no focal deficits.

Initial laboratory investigations, including complete blood count, C-reactive protein, serum electrolytes, and liver function tests, were within normal limits. Blood culture was sterile, effectively ruling out systemic infection.

Chest radiograph did not reveal any significant abnormalities. Two-dimensional echocardiography demonstrated dilatation of the right atrium and right ventricle, mild tricuspid regurgitation, and features suggestive of mild pulmonary arterial hypertension, with preserved biventricular systolic function. Neuroimaging with MRI brain and electroencephalography (EEG) were normal.

The infant was managed with supportive care, including oxygen therapy, intravenous fluids, and empirical intravenous antibiotics pending exclusion of sepsis. Antiepileptic therapy (levetiracetam) was initiated as a precautionary measure. In view of the clinical presentation, absence of infection, and suspicion of nutritional deficiency, thiamine supplementation was initiated for both the infant and the mother.

A marked clinical improvement was observed within 48 hours. The infant was successfully weaned off oxygen support by the second day of hospitalization. Enteral feeding was gradually established via orogastric feeds, and intravenous fluids were tapered and discontinued.
Repeat echocardiography showed persistent but improved mild pulmonary hypertension with good ventricular function. The infant remained hemodynamically stable and was discharged with advice for continued nutritional supplementation.
At one-month follow-up, the infant was asymptomatic, thriving well, and demonstrated no evidence of neurodevelopmental delay.

Discussion

TRAPHEI represents a clinical manifestation of cardiac beriberi, an often overlooked consequence of thiamine deficiency. Despite being a preventable and treatable condition, it remains underdiagnosed due to its nonspecific presentation and overlap with more common pediatric conditions such as sepsis, pneumonia, and congenital heart disease.
The pathophysiology of TRAPHEI is rooted in impaired oxidative metabolism due to deficiency of thiamine-dependent enzymes. This leads to accumulation of pyruvate and lactate, resulting in metabolic acidosis. Additionally, myocardial energy depletion results in ventricular dysfunction, while pulmonary vasoconstriction contributes to elevated pulmonary arterial pressures.
Infants are particularly vulnerable due to:

- Limited thiamine stores at birth
- High metabolic demands
- Dependence on maternal breast milk

Maternal dietary practices, especially consumption of polished rice devoid of thiamine, significantly increase the risk.
The diagnosis of TRAPHEI is primarily clinical and should be suspected in infants presenting with:

- Acute onset respiratory distress
- Echocardiographic evidence of pulmonary hypertension
- Absence of structural heart disease or infection
- History suggestive of maternal nutritional deficiency

A rapid clinical response to thiamine administration is considered a key diagnostic criterion and often confirms the diagnosis retrospectively.
Management involves prompt administration of thiamine along with supportive measures such as oxygen therapy, fluid management, and treatment of complications. The response is typically dramatic, with rapid resolution of symptoms and hemodynamic stabilization.
Failure to recognize this condition may lead to serious outcomes, including refractory cardiac failure, neurological damage, or death. Therefore, a high index of suspicion is essential, particularly in resource-limited settings where nutritional deficiencies are prevalent.

Conclusion

TRAPHEI is an important and reversible cause of pulmonary hypertension in early infancy that should not be overlooked. This case highlights the critical role of clinical suspicion and maternal nutritional history in identifying this condition.
Early diagnosis and prompt administration of thiamine can lead to rapid clinical recovery and prevent potentially fatal complications. Given its preventable nature, public health measures such as maternal nutritional education, thiamine supplementation during pregnancy and lactation, and food fortification strategies are essential.
Increasing awareness among healthcare providers can significantly improve outcomes and reduce the burden of this treatable condition.

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