Non-Ketotic Hyperglycinemia: A Rare Presentation with Neurological and Skeletal Abnormalities

Sir,

Non-Ketotic Hyperglycinemia (NKH), also known as glycine encephalopathy, is a disorder of glycine metabolism caused by reduced activity of glycine cleavage enzyme system resulting in excessive accumulation of glycine in tissue and organs, particularly in brain resulting in neurological problems.[1] NKH has autosomal recessive inheritance and is caused by a mutation in glycine decarboxylase and aminomethyl transferase genes.[2] Incidence of NKH is unknown, but it is more common in Finland where prevalence is estimated to be 1:55,000 newborns.[3] There are two types of NKH: severe and attenuated.[4] Neonatal form presents in first few days of life and is characterised by hypotonia, hiccups, seizures, encephalopathy, and lethargy progressively leading to coma and ultimately death.[5] Prognosis of NKH is poor with a 50% mortality rate in the first week of life. The case to be reported is a rare case of NKH in a newborn associated with agenesis of the corpus callosum and talipes equinovarus. Till date, no such case has been reported from Pakistan.

A newborn male, born to consanguineous parents, at 35 weeks gestation, with APGAR score of 5/10 at 1st minute and 6/10 at next 5 minutes required resuscitation by positive pressure ventilation (PPV). Maternal history revealed raised umbilical artery doppler indices and polyhydramnios. Upon examination, the baby had a heart rate of 134 beats per minute, respiratory rate of 52 breaths per minute, oxygen saturation of 97% on room air, and blood sugar of 82 mg/dL. Neurological examination revealed hypotonia and poor neonatal reflexes. Rest of the examination was normal. The baby was admitted to Neonatal Intensive Care Unit and managed on the line of hypoxic-ischemic encephalopathy as per protocol. Baseline investigations were normal.

On the second day of life, the patient had apnea followed by bradycardia. He was intubated and placed on mechanical ventilator. Keeping in view his rapidly deteriorating clinical condition despite optimum management, inborn errors of metabolism (IEM) were suspected. Baby was kept NPO. Inj Aminovel was discontinued from IV fluids and workup for IEM was sent. On 3rd day, protein-free formula milk was started *via* an orogastric tube. On 4th day of life, baby developed hiccups and refractory seizures. Antiepileptic and Inj Levetiracetam was started. IEM workup was traced. Urine analysis revealed organic acids within normal limits and no ketones were identified. Plasma HPLC (High Performance Liquid Chromatography) report suggested hyperglycinemia. Glycine levels were 1168 umol/L (Normal reference range: 154-338 umol/L). CSF for amino acid analysis was sent which showed glycine of 281 umol/L and CSF / plasma glycine ratio of 0.24 (normal: <0.02). CT scan brain showed widely spaced lateral ventricles running parallel to each other, with loss of normal bow tie configuration (racing car sign positive) along with colpocephaly and high riding third ventricle. These features suggested a disease with congenital absence of corpus callosum.

Based upon above mentioned investigations, diagnosis of NKH was made. Sodium benzoate was started. On 7th day, the baby's pupils became sluggish. No improvement in clinical condition was observed. Despite all management efforts, the condition of the patient deteriorated. Pupils progressively stopped reacting to light. Parents were counseled regarding poor prognosis of patient, nature of disease and genetic predisposition. Conservative management was continued. The baby expired on 16th day of life.

NKH is a serious metabolic disorder with a very high mortality. Early diagnosis is important and even with obvious neurological findings, one must keep the differential of metabolic disorder in mind and investigate it in clinically deteriorating patients. Prompt administration of sodium benzoate along with IV fluids and avoidance of protein-rich diet can prove to be beneficial in this regard. Despite the best possible management, the prognosis of NKH is poor and the mortality rate is high. The importance of diagnosis is also very pivotal for counselling parents regarding subsequent pregnancies.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
AT: Concept and designing of the work.
MA: Drafting and revision of intellectual content.
AK, EQ: Final proof reading and approval for publication.
ZA: Headed the research, revision of content, and approval for publication.
All authors approved the final version of the manuscript to be published.

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Andleeb Tariq[1], Menahil Asdaque[1], Arshad Khushdil[2], Ehsan Qadir[2] and Zeeshan Ahmed[2]

[1]Department of Paediatrics, Combined Military Hospital, Rawalpindi, Pakistan

[2]Department of Neonatology, Pakistan Emirates Military Hospital, Rawalpindi, Pakistan

Correspondence to: Dr. Menahil Asdaque, Department of Paediatrics, Combined Military Hospital, Rawalpindi, Pakistan
E-mail: menahil.asdaque@gmail.com

Received: June 04, 2023; Revised: September 20, 2023; Accepted: October 31, 2023
DOI: https://doi.org/10.29271/jcpsp.2024.03.375