Magna Scientia Advanced Research and Reviews

eISSN: 2582-9394

Cross Ref DOI: 10.30574/msarr

Journal homepage: https://magnascientiapub.com/journals/msarr/

(CASE REPORT)

Check for updates

Seizure solver- pyridoxine dependent seizures

Vijay Ganesh [1, *], Manish Taneja [2] and Sangeetha [3]

[1] *Junior Resident, Department of Pediatrics, Base Hospital, Delhi Cantt, New Delhi, India.*
[2] *Neonatologist and Head of Department, Department of Pediatrics, Base Hospital, Delhi Cantt, New Delhi, India.*
[3] *Professor, Department of Pediatrics, Base Hospital, Delhi Cantt, New Delhi, India.*

Magna Scientia Advanced Research and Reviews, 2024, 12(01), 130–132

Publication history: Received on 26 August 2024; revised on 04 October 2024; accepted on 07 October 2024

Article DOI: https://doi.org/10.30574/msarr.2024.12.1.0156

Abstract

Pyridoxine dependency is a rare cause of seizures. Pyridoxine dependent seizures (PDS) occur despite normal vitamin B6 levels and is due to defective binding of pyridoxine to its apoenzyme, glutamate decarboxylase, which converts glutamic acid to gamma aminobutyric acid (GABA). Pyridoxine-dependent seizure is a rare autosomal recessive disorder that usually presents with neonatal intractable seizures. Parenteral pyridoxine injection test is a highly effective and reproducible test in confirming the diagnosis. Hunt, et al.(l) described the first case of PDS with autosomal recessive inheritance. Since then, several cases have been reported with onset of seizures after neonatal period (2-6). Pyridoxine-dependent epilepsy – *ALDH7A1* (PDE-*ALDH7A1*) is characterized by seizures not well controlled with anti-seizure medication that are responsive clinically and electrographically to large daily supplements of pyridoxine (vitamin B_6). This is true across a phenotypic spectrum that ranges from classic to atypical PDE-*ALDH7A1.* Intellectual disability is common, particularly in classic PDE-*ALDH7A1*. (7)

Keywords: Pyridoxine deficiency; Refractory neonatal seizures; Status epilepticus; Whole exome sequencing; Neonatology

1. Introduction

This case report presents a 4-day-old neonate with multi focal seizures initially suspected of sepsis. Despite antiepileptic drug therapy and ventilation for respiratory failure, seizures persisted for over 72 hours. A trial of pyridoxine resulted in dramatic seizure cessation, leading to the diagnosis of pyridoxine-dependent seizures (PDS). Subsequent whole exome sequencing confirmed the diagnosis by identifying a genetic deficiency. Early recognition and intervention in such cases are crucial to prevent adverse outcomes.

2. Methodology

After taking informed consent from parents, we reviewed this case who presented in a tertiary care hospital (level III NICU) with the complaints of persistent abnormal body movements noticed by parents and reduced feeding since postnatal day 3. The baby was subsequently diagnosed as a case of PDS after confirmation from genetic sequencing report.

3. Case description

A 4-day-old male neonate, born to a healthy primigravida mother with birth weight (3400gms) and gestation (37wks 4days) with no history of birth asphyxia and no other significant medical history, was delivered vaginally with no

* Corresponding author: Vijay Ganesh

reported complications. Antenatal scans were unremarkable during all three trimesters. The baby transitioned smoothly post-partum, established breastfeeding, and was discharged after 48 hours of life. At 4 days of life, the neonate presented with multifocal generalized seizures characterized by involuntary jerking movements involving both sides of the body. He also displayed shock-like features (hypotension with hyperlactatemia), including oxygen desaturation, delayed capillary refill time (CRT), and bradycardia. Additionally, he exhibited hypoglycaemia. The neonate received immediate resuscitation measures to address the shock and hypoglycemia. He was stabilized, and intravenous fluids containing dextrose were administered to manage the hypoglycaemia. Despite initial improvement with glucose administration and 2nd line AEDs, the seizures persisted for more than 48hrs. Given the clinical picture and unresponsive to treatment, a trial of intravenous pyridoxine was administered (100mg) was administered. Seizures dramatically ceased within minutes.

This prompted further investigations, including:

- Metabolic screen: Normal.
- MRI Brain: Normal study for age.
- Electroencephalogram (EEG): Abnormal burst spike patterns (>25hz) consistent with seizures and stopped after pyridoxine administration.
- CSF analysis: Non meningitis (RBC- Nil, WBC-5cells, Proteins-50mg/dl, CSF culture and PCR- no organism detected)
- Genetic testing: ALDH7A1 mutation (homozygous)

Analysis for the variant (c.187G>T) in the *ALDH7A1 (*Exon 1) gene.		
#	Variation detected in NGS	Sanger validation result*
1.	***ALDH7A1*, chr5:125930704C>A; c.187G>T (HOM); (p.Gly63Ter)**	**Present (Homozygous)**

* The variant analysis in Sanger sequencing is based on the *ALDH7A1* reference sequence NM_001182.5 (GRCh37) [1]. The exon number and nucleotide numbers will differ based on the reference file chosen andthe database used.

Following pyridoxine administration, the neonate's clinical condition improved significantly. Seizures ceased, and he remained seizure-free throughout his hospital stay and follow-up appointments. He was discharged on a maintenance dose of oral pyridoxine and continues to be monitored for long-term outcomes and possible developmental implications.

4. Discussion

Pyridoxine-dependent seizure is a rare autosomal recessive disorder localized to chromosome 2q31(8). So far pyridoxine dependent seizures have been reported in only 8 Indian children (9-13). This includes the 4 cases reported by Baxter (12). Although a regional variation in its incidence exists, pyridoxine-dependency has been said to be a rare cause of neonatal seizures. This case highlights the importance of considering pyridoxine deficiency in the differential diagnosis of neonatal seizures, even in the presence of seemingly unrelated symptoms like hypoglycemia. The shock-like features presented in this case are not typical of pyridoxine deficiency, but they underscore the diverse clinical manifestations that can occur. Early recognition of pyridoxine deficiency is crucial as prompt treatment with pyridoxine is highly effective in resolving seizures and preventing potential long-term complications. The elevated α-AA level was not noted on metabolic screen. Genetic screen played a key role in the diagnosis. This metabolite accumulates when the body cannot properly process pyridoxine, serving as a specific biomarker for pyridoxine deficiency. Certain genetic mutations can impair pyridoxine metabolism, leading to deficiency and its associated complications. This case also illustrates the importance of considering PDS in the differential diagnosis of refractory neonatal seizures. Epileptic seizure discharges subside within 2-6 minutes after the intravenous injection of 50-100 mg of pyridoxine. Rarely, the discharges can persist for several hours after injection. Parenteral pyridoxine injection test is a highly effective and reproducible test in confirming the diagnosis of pyridoxine dependency (8). Early treatment determines the prognosis. In the absence of early appropriate treatment, the prognosis is poor, all survivors being severely mentally retarded. Untreated children with pyridoxine-dependent seizures usually die with a severe seizure disorder.

5. Conclusion

This case report emphasizes the importance of maintaining a broad differential diagnosis for neonatal seizures, including rare but potentially treatable conditions like pyridoxine deficiency. Because of the high proportion of atypical cases, all children with early onset (younger than 3 years) intractable seizures or status epilepticus should receive a trial of pyridoxine whatever be the suspected cause. A prompt trial of pyridoxine therapy can be lifesaving and should be considered alongside routine investigations in such cases. WES can offer confirmatory genetic diagnosis and further insights into the underlying pathophysiology.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Hunt AD, Stokes J, McCrory WW, Stroud HH. Pyridoxine dependency: Report of a case of intractable convulsions in an infant controlled by pyridoxine. Pediatrics 1954, 13:140-145.

[2] Goutieres F, Aicardi J. Atypical presenta tion of pyridoxine dependent seizures: A treatable cause of intractable epilepsy in infants. Ann Neurol 1985, 17: 117-120.

[3] Krishnamoorthy KS. Pyridoxine depen dency seizure: Report of a rare presenta tion. Ann Nejjrol 1983, 13: 103-104.

[4] Coker SB. Postneonatal vitamin B6 deficiency epilepsy. Pediatrics 1992, 4: 499-501.

[5] Sehgal H. convulsions: Pyridoxine dependent A case report. Indian Pediatr 1977,19: 419-421.

[6] Minns R. Vitamin B6 deficiency and dependency. Dev Med Child Neurol 1980, 22: 795-799.

[7] Pyridoxine dependent epilepsy- ALDH7A1 Sidney M gospe Genereviews (2001)

[8] Mikati MA, Trevathen E, Krishnamoorthy KS, Lombroso CT. Pyridoxine-dependent epilepsy: EEG investigations and long-term follow-up. Electroencephalography Clin Neurophysiol 1991; 78: 215-222.

[9] Singh UK, Sinha RK. Pyridoxine dependent seizures. Indian Pediatr 1996; 33: 121-123.

[10] Sehgal H. Pyridoxine dependent convulsions. Indian Pediatr 1977; 14: 419-421.

[11] Raghavan KR, Rangnekar JV, Chabra S, Tyagarajan R, Fernandez AR. Pyridoxine dependent seizures in a newborn. Indian Pediatr 1990; 27: 747-750.

[12] Baxter P. Epidemiology of pyridoxine-dependent and pyridoxine responsive seizures in the UK. Arch Dis Child 1999; 81; 431-433.

[13] Gupta VK, Mishra D, Mathur I, Singh KK. Pyridoxine-dependent seizures: A case report and a critical review of the literature. J Pediatr Child Health 2001; 37: 592-596.