Indian Journal of Pediatrics (January 2024) 91(1):88
https://doi.org/10.1007/s12098-023-04818-z

SCIENTIFIC LETTER

An Extremely Rare Cause of Hyperammonemic Encephalopathy in an Infant

R. Ganesh[1] · **R. Karthik Narayanan**[2]

Received: 21 June 2023 / Accepted: 1 August 2023 / Published online: 23 August 2023

To the Editor: A 3-mo-old girl, previously well, presented with vomiting, lethargy for 1 d and an episode of generalized seizures. There was no fever/loose stools. She is first born to non-consanguineous parents and on examination, she was encephalopathic [Glasgow coma scale (GCS): E2V1M4], had effortless tachypnea (RR: 72/min). Abdomen examination showed moderate hepatomegaly. Central nervous system (CNS) examination showed normal tone. Investigations revealed normal blood counts, sugar, electrolytes, negative C-reactive protein (CRP), hyperammonemia (460 Umol/L), metabolic acidosis (pH: 7.36, pCO_2: 7.2 mmHg, HCO_3^-: 8 mmol/L), lactate: 8.3 mmol/L (0.7–2.1), ketonuria (4+), elevated aspartate aminotransferase (AST)-135 U/L and alanine transaminase (ALT)- 85 U/L. She was ventilated, started on fluids, sodium benzoate & carnitine and peritoneal dialysis was performed with bicarbonate-based fluid. With the above measures her sensorium improved in 36 h, ammonia levels dropped to 17 Umol/L and lactate 2.5 mmol/L. In the meanwhile, MRI brain, plasma aminoacids, acyl carnitine and urine organic acids done were normal. She was discharged on sodium benzoate, carnitine and gene testing revealed pathogenic homozygous missense mutation in exon 6 of CA5A gene confirming carbonic anhydrase VA (CA-VA) deficiency. At 1.6 y of age, she is biochemically and developmentally normal.

CA-VA deficiency is a very rare, autosomal recessive disorder due to homozygous mutation in CA5A gene with 26 children reported till date, about 71% from Indian subcontinent [1, 2]. CA-VA supplies bicarbonate for 4 mitochondrial enzymes namely carbamoyl phosphate synthetase-1, propionyl-CoA carboxylase, pyruvate carboxylase and 3-methylcrotonyl-CoA carboxylase and therefore, its deficiency impairs urea cycle, TCA cycle and gluconeogenesis. CA-VA deficiency is characterized by a triad of hyperammonemia, hyperlactatemia and ketonuria. Low pCO_2 in blood gas, overshooting the expecting compensation, points towards CA-VA deficiency. About one-third can have recurrent metabolic decompensation while majority have a good neurological outcome [2, 3] which might be due to the overlapping function of CA-VB that produces some bicarbonate aiding the intra-mitochondrial enzymes to function normally [4]. Long term treatment includes sodium benzoate, carnitine, timely recognition & treatment of metabolic crisis and avoiding valproate, acetazolamide, topiramate, zonisamide & steroids [4].

Declarations

Conflict of Interest None.

References

1. van Karnebeek C, Häberle J. Carbonic Anhydrase VA Deficiency. 2015 Apr 2 [Updated 2021 Aug 26]. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2023. Available at: https://www.ncbi.nlm.nih.gov/books/NBK284774/.
2. Marwaha A, Ibrahim J, Rice T, et al. Two cases of carbonic anhydrase VA deficiency- An ultrarare metabolic decompensation syndrome presenting with hyperammonemia, lactic acidosis, ketonuria, and good clinical outcome. JIMD Rep. 2020;57:9–14.
3. Olgac A, Kasapkara CS, Kilic M, et al. Carbonic anhydrase VA deficiency: a very rare case of hyperammonemic encephalopathy. J Pediatr Endocrinol Metab. 2020;33:1349–52.
4. Singanamalla B, Saini AG, Attri SV, Suthar R, Mukhopadhyay K. Carbonic anhydrase-VA deficiency: a close mimicker of urea cycle disorders. Ann Indian Acad Neurol. 2021;24:820–1.

✉ R. Ganesh
ganeped79@rediffmail.com

[1] Department of Pediatric Inherited Metabolic Diseases, Rainbow Children's Hospital, Chennai 600015, Tamil Nadu, India

[2] Department of Pediatric Critical Care, Rainbow Children's Hospital, Chennai 600015, Tamil Nadu, India