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Case Report

A rare case of type 1 citrullinemia in newborn

Ashutosh Singh Rathore, Guntupalli Shravya L.*, Dhrumika Seth

Department of Pediatrics, Smt. B. K. S Medical Institute and Research Center, Sumandeep Vidhyapeeth Deemed to be University, Wagodhiya, Vadodara, Gujarat, India

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***Correspondence:**
Guntupalli Shravya L.,
E-mail: shravyaguntupalli94@gmail.com

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ABSTRACT

Citrullinemia type I (CTLN1) is a rare and lethal autosomal recessive genetic disorder. CTLN1 is caused by deficiency or absence of the enzyme arginino succinate synthetase (ASS). We reported a rare case of CTLN1 in a male full-term neonate. This report related to a full-term male child, born out of 3rd degree consanguineous marriage, admitted at our unit on DOL-3 with severe dehydration. ABG showed persistent severe metabolic acidosis despite of adequate treatment. So, suspecting an inborn error of metabolism (IEM) investigations were done in which we found high serum ammonia, serum lactate and urinary sodium. TMS and GCMS were done which observed a profile which can be seen in case of citrullinemia. CTLN1 is a rare and lethal genetic disorder. High index of suspicion is needed when patients present with such complex symptoms. Diagnosing and timely intervention helps in reducing the morbidity and mortality and with treatment, people with citrullinemia type 1 can have normal growth and development.

Keywords: Citrullinemia, ASS enzyme, IEM

INTRODUCTION

CTLN1 is a rare and life-threatening genetic disorder with autosomal recessive inheritence. CTLN1 is caused by decreased or absence of the enzyme ASS.[5] ASS has a major role in urea cycle through which, it helps in excretion of nitrogen from the body. Any deficiency or absence of ASS results in excessive accumulation of nitrogen, in the form of ammonia and leads to hyperammonaemia. We reported a rare case of CTLN type 1 in a male full-term neonate.

CASE REPORT

A full-term male child was delivered through LSCS for breech, born out of 3rd degree consanguineous marriage, with a birth weight of 2.43 kgs requiring no resuscitation at birth. He was breastfed and remained by mother's side until 2 days. Then he was admitted at our neonatal intensive care unit on DOL-3 with complains of refusal to feed, irritability and lethargy with 19% weight loss since birth. On admission child had signs of severe dehydration, acidotic breathing requiring minimal oxygen therapy. ABG was done which showed severe metabolic acidosis (pH-6.84, PCO_2-16.0 mmHg, HCO_3-2.6 meq/dl) with additional respiratory acidosis. Lab parameters showed serum sodium 154 mmol/l with normal urea and creatinine but deranged coagulation profile. Patient was treated for hypernatremic dehydration and sodium bicarbonate full correction was given. IV antibiotics were started empirically even when septic parameters were negative. On repeating, serum sodium normalized, but bicarbonate and CO_2 remained low, ABG (pH-7.12, $PC0_2$-11.8 mmHg, HCO_3-3.7 meq/dl), still showed no improvement in metabolic acidosis. Patient also continued to have acidotic breathing. On 2nd day of admission, patient started to have polyuria which showed no improvement with adequate IV fluid replacement. Sodium bicarbonate correction was continued. So, suspecting an inborn error of metabolism we sent the

work up and found serum ammonia (130 µmol/l), serum lactate (14 mmol/l) serum ketones (<5.0 mmol/l). Urinary sodium was done which was also raised. ABG (pH-7.19, HCO_3-5.4 meq/dl, PCO_2-14.5 mmHg) showed no improvement. So, TMS and GCMS were sent on 4th day of admission. Patient condition deteriorated further. Patient had to be intubated and was put on ventilator. Patient started developing third space loss due to acute kidney injury. Urine output had significantly reduced, 1 episode of RT bleed was noted and on repeating the investigations, severe thrombocytopenia (18,000 /µl), deranged coagulation profile (PT-42.2 sec, INR-3.95, aPTT-68.8 sec), hypernatremia (149 mmol/l) was noted, creatinine (2.1 mg/dl) was raised and ammonia (129 µmol/l) and lactate (14 mmol/l) were still high. 1-unit FFP and 1-unit patelet concentrate were transfused. No improvement was found in the patient clinically. In the next 2 days child developed bleeding manifestations (purpura rash) over the chest and abdomen. Patient had a progressive worsening of sensorium, frequent tonic posturing despite phenobarbitone. On DOL-8 TMS and GCMS screening report came out to be positive. TMS report showed increased levels of citrulline (>250 µmol/l; normal (<70 µmol/l) which was seen in CTLN. In view of this citrulline/arginine ratio (78.8; cut off-4) was done and found to be elevated and was interpreted as type I/II/ liver dysfunction. GCMS report showed increased excretion of lactic acid, glycerol, glycerol 3-phosphate and 4-hydroxyphenyllactic acid, LCMS analysis of provided DBS sample was s/o CTLN type I/II. The observed profile can be seen in case of CTLN type I/II/mitochondrial disorder/liver dysfunction. Parents were counselled regarding the condition of the child and molecular genetic testing: ASS1/SLC25A13 genes (clinical exome sequencing) was suggested. As parents were not willing for the test due to social issues, exome sequencing couldn't be done. On DOL-10 child went in to refractory shock requiring inotropes and patient's condition deteriorated further and patient succumbed on DOL-11. An EDTA sample was preserved for future genetic analysis.

DISCUSSION

In our case, once hypoglycaemia was ruled out as the cause of lethargy, sepsis was considered although there were no antecedents for early onset sepsis. On seeing the results (negative septic screen) sepsis was unlikely so hypernatremia dehydration was considered. What was unexplained initially was the normal urea despite dehydration, weight loss. The normal urea with a disproportionately raised creatinine, even in the later days was probably due to defective synthesis of urea. Respiratory alkalosis due to hyperventilation was the key feature in urea cycle disorders and the low bicarbonate seen in our patient could be due to the metabolic compensation for the low PCO_2 in respiratory alkalosis.

CTLN1 is an autosomal recessive genetic disorder that included an acute form (classic) seen in neonates, a milder late onset form, a form that occurred during or after pregnancy and an asymptomatic form.[8,9] The classical form was more often seen with higher degree of consanguinity. It had been estimated that about 1 in 44,300 to 1 in 200,000 individuals worldwide have CTLN1.[10] CTLN1 was caused by deficiency or absence of the enzyme ASS.[5] ASS had a major role in urea cycle through which, it helped in excretion of nitrogen from the body. Any deficiency or absence of ASS resulted in excessive accumulation of nitrogen, in the form of ammonia and led to hyperammonaemia in the body. The classic form might present with vomiting, refusal to feed, lethargy and signs of raised intracranial pressure.[8,9] A large number of infants with initial ammonia concentration >300 µmol/l had cognitive impairment and residual neurological damage.[3,4] The treatment of CTLN1 was focused on preventing excessive ammonia from being formed or from removing excessive ammonia during a hyperammonaemia episode. Hemodiafiltration was the therapy of choice in severe hyperammonaemia encephalopathy and if not available haemodialysis or hemofiltration should be performed rapidly to prevent permanent neurological damage.[2] It was noted that levels of serum citrulline remained highly elevated even with long-term therapy. Medications that assisted in the removal of nitrogen through alternative methods were available which included buphenyl, ammonul and raviciti as well as arginine.[7,10]

Dietary restrictions were aimed at restriction of amount of protein intake to avoid the formation of excess ammonia. However, enough protein intake was required for proper growth. Infants were placed on a low protein, high calorie diet supplemented by essential amino acids. A combination of a high biological value natural protein such as breast milk or cow's milk formulations, an essential amino acid formula and a calorie supplement without protein was often used.[6]

CONCLUSION

CTLN1 is a rare and lethal genetic disorder. High index of suspicion is needed when patients present with such complex symptoms. Diagnosing and timely intervention helps in reducing the morbidity and mortality and with treatment, people with CTLN1 can have normal growth and development. However, episodes of high ammonia can cause brain and nerve damage that cannot be repaired. This type of brain damage can cause permanent learning and intellectual disabilities as well as problems with muscle control and coordination.

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REFERENCES

1. Sander J, Janzen N, Sander S, Steuerwald U, Das AM, Scholl S, et al. Neonatal screening for citrullinemia. Eur J Pediatr. 2003;162(6):417-20.
2. Häberle J, Boddaert N, Burlina A, Chakrapani A, Dixon M, Huemer M, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. Orphanet J Rare Dis. 2012;7:32.
3. Bachman C. Outcome and survival of 88 patients with urea cycle disorders: a retrospective evaluation. Eur J Paediatr. 2003;162(6):410-6.
4. Bachman C. Long term outcome of patients with urea cycle disorders and the question of neonatal screening. Eur J Pediatr. 2003;162(1):29-33.
5. Korea Disease Control and Prevention Agency. Rare disease information citrullinemia. Cheongju Korea Dis Control Prevent Agency. 2021.
6. Chong MF, Shaw V, M. Lawson. Clinical Paediatric Dietetics. Oxford: Blackwell Publishing; 2007: 604.
7. Citrullinemia. Screening, Technology and Research in Genetics (STAR-G). Updated Feb. 18, 2016
8. Citrullinemia type 1. National Organization for Rare Disorders (NORD).
9. Quinonex SC, Thoene JG. Citrullinemia type I. Gene Reviews. Seattle (WA): University of Washington; 1993.
10. Wasim M, Awan FR, Khan HN, Tawab A, Iqbal M, Ayesha H. Aminoacidopathies: prevalence, etiology, screening, and treatment options. Biochem Genet. 2018;56(1-2):7-21.

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