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Case report

NEWBORN TREATED WITH CONTINUOUS RENAL REPLACEMENT THERAPY FOR CITRULINEMIA-TYPE 1

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Abstract: **Introduction:** Hyperammonemia occurs as a result of the inability to convert ammonia, a metabolic toxin, into urea due to a block in the urea cycle, and there resulting neurotoxicity is responsible for the pathogenesis.

Case Presentation: Our patient was 7 days old when followed up in an external center for 3 days with a preliminary diagnosis of neonatal sepsis. Lethargy, vomiting, tachypnea, and convulsions, which are frequently seen in the first neonatal forms of urea cycle disorders, were also present in our patient. He was referred to us as a result of high ammonia levels when he was examined in terms of congenital metabolic diseases. He was intubated due to the rapid development of respiratory failure. When he was admitted to our intensive care unit with hyperammonemia, light reflex could not be obtained, and widespread cutis marmaratus was developed. Continuous renal replacement therapy was started in our patient and administered intermittently for 120 hours. The glucose infusion rate was followed by high fluid. When it orally tolerated, it is supported with sodium benzoate and sodium stearyl fumarate to reduce ammonia. Nutrition was limited to protein with Basic P.

Conclusion: After staying in the intensive care unit for 30 days, our patient was discharged with the recommendation of outpatient follow-up by the pediatric metabolism physician. When our patient came for his check up after two months,there was no nystagmus and no seizures.

Keywords: hyperammonemia, newborn, sepsis.

INTRODUCTION

Hyperammonemia, which occurs as a result of the inability to convert ammonia, a metabolic toxin, into urea due to a block in the urea cycle, and there resulting neurotoxicity is responsible for the pathogenesis. Hyperammonemia can be seen due to transient neonatal hyperammonemia, hereditary causes, severe systemic diseases in the newborn, urea cycled effects, fatty acid oxidation disorders, and organic acidemias (1).

Ammonia levels should be requested from the patients who present with the clinic of decreased nutrition, respiratory failure, groaning, vomiting, and sepsis in the neonatal period (2).

In this study, we aimed to present our patient who presented with hyperammonemia, which is one of the metabolic diseases that is frequently confused in the neonatal period, and whose ammonia level was rapidly reduced with continuous renal replacement therapy, and who was diagnosed with Citrullineemia by metabolic panel tests and discharged safely.

CASE REPORT

On the 7th day of his life, our male patient was admitted to our pediatric intensive care unit (PICU) 3 days ago due to the development of respiratory failure during the follow-up of the patient, who was considered to have neonatal sepsis in the external center with complaints of sleepiness, vomiting, and rapid breathing.

We learned that he was followed up prenatally with no issues. He was born at 37 weeks with a cesarean section (C/S) with 3320 grams and was discharged after 24 hours. Parents are first-degree cousins. On PICU admission, his fever was 37.5°C, heart rate was 140 beats/min, blood pressure was 55/30mmHg, respiratory rate was 40 breaths/min, and oxygen saturation was 90% under respiratory support with a mechanical ventilator in pressure control mode. Neither pupil was reactive to light. The patient had decreased hypotony,

weakness, cold extremities, and skin pallor. In his examinations, metabolic alkalosis and lactate elevation were present. Patient's blood pressure (30/20mmHg). Rhythmic tonic-clonic movements were observed in our patient, and levetiracetam was started as an antiepileptic. Ampicillin-cefotaxime intravenous 3x50 mg/kg/dose treatments, which are broad-spectrum antibiotics started with a preliminary diagnosis of sepsis in our patient in another center, were continued.

Hospitalization tests were also noted as Ammonia (µ/dL2102, Lactate dehydrogenase (unit/L) 1712, PRO-BNP (pg/ml) 21392, Aspartate aminotransferase (unit/L) 290, Lactate (mmol/L) 9.4. Table 1 shows the examinations taken on the first day of the patient's hospitalization. A left subclavian hemodialysis catheter was placed in our patient. To initiate continuous renal replacement therapy (CRRT), the circuit was filled with cross-matched blood mixed with isotonic liquid and 5.000 units/L heparin with 30% hematocrit. Our patient's ammonia level was very high, and dialysis was started at the recommended rate of 8.000 ml/h/1.73 m^2 dialysate and replacement fluid. Our dialysis rate decreased according to the follow-ups. DIALİSAN CVVHD BG2D K2 was used as CRRT solution and its electrolyte content was revised according to the patient's electrolyte imbalance and blood gas values. The patient was intubated and followed up with prediagnoses of coagulopathy, respiratory failure, cardiogenic shock due to inotropic need, and sepsis. Adrenaline infusion was started because the patient was hypotensive; Milrinone infusion was started because heart failure was seen on echo; erythrocyte suspension, random thrombocyte, and fresh frozen plasma were given due to anemia, thrombocytopenia, and

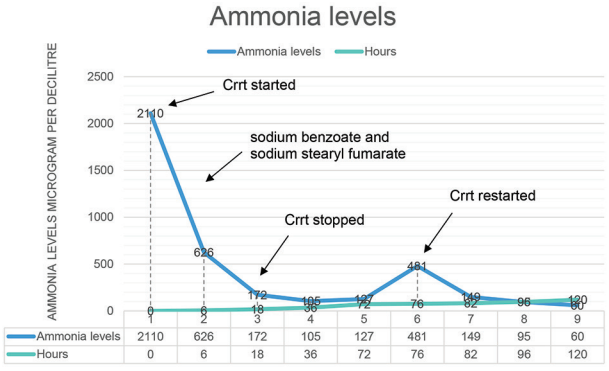

Figure 1. *Serum ammonia levels from the time of admission to the resolution of hyperammonemia. Serum ammonia levels substantially decreased with the addition of CRRT to sodium benzoate and sodium stearyl fumarate. Although both therapies effectively decreased serum ammonia levels, CRRT rate settings in the case were: blood flow of 50 ml/min, dialysate flow of 400 ml/h, and replacement flow of 400 ml/h*

Table 1. *First day of hospitalization (Biochemical and Hematologic Findings of the patient)*

White blood cell (per µL)	18400
Lymphocyte (per µL)	12000
Neutrophil (per µL)	6000
Platelet (per µL)	48.000
Hemoglobin (g/dL)	15
C reactive protein (mg/L)	1
Procalcitonin (ng/mL)	26
Urea (mg/dL)	8,6
Creatinine (mg/dL)	1.34
Aspartate aminotransferase (unit/L)	290
Alanine aminotransferase (unit/L)	162
Lactate dehydrogenase (unit/L)	1712
Ammonia (µg/dL)	2102
pH	7.5
pCO2	23
Lactate (mmol/L)	9,4
HCO3	21
PRO-BNP (pg/ml)	21392
D-dimer (ng/mL)	9.4
APTT (sec)	58
INR	2.99
Fibrinogen	104

increased INR in the tests. Thiamine was administered as 2x100 mg due to high lactate.

The dialysate and replacement fluid flow rate were started at 8000 cc/1.73 m^2/day, and the control 6-hour ammonia value quickly decreased to 626µg/dl. The ammonia levels were reduced to 2000 cc/1.72 m^2/day and dialysis was stopped when ammonia dropped below 60µg/dl. Biochemical parameters and blood gas values were monitored 4 times a day and ammonia level was observed every 6 hours. After 120 h of CRRT, each ammonia level was < 60 µg/dl, and CRRT was stopped. The ammonia values of our patient are shown in Figure 1.

Ammonia levels decreased rapidly with CRRT, and ammonia level was maintained by giving oral sodium benzoate and sodium stearyl fumarates up port and fluids with a high glucose infusion rate.

In their follow-up, he did not need inotropes on the second day; light reflex was acquired, hypotonicity decreased; blood gas values improved; On the 4th day, the patient was extubated.

Enteral nutrition of the patient whose ammonia levels decreased with sodium benzoate, sodium stearyl fumarate, and high dextrose fluid was started on the 5th day as basic-p.

The patient, who was followed up in the intensive care unit for 30 days, developed septicemia and was discharged with the recommendation of a pediatric metabolism physician.

DISCUSSION

It presents with neurological symptoms associated with hyperammonemia in the neonatal period (2). Often, 24-72 hours after feeding, the findings of acute hyperammonemia form is the main clinical picture of the patient. Lethargy, hypotonia, convulsions, coma, feeding difficulties, vomiting, dehydration, hepatomegaly, and hyperammonemia initially cause tachypnea or hyperpnea because it stimulates the respiratory center, followed by apnea and respiratory failure with respiratory center suppression (3). Hyperammonemia is a metabolic emergency and should be considered in the differential diagnosis of sepsis (4). A significant increase is observed between high ammonia levels and mortality in newborns. Unfortunately, hemodialysis in newborns is difficult due to the difficulty of vascular intervention and the High ratio of circulating blood volume to the baby's blood volume in the dialysis setting. At the same time, rebound hyperammonemia was observed after dialysis was stopped in studies, and ammonia increased again in our patient, and the need for dialysis again (5). Respiratory and cardiac failure and cardiac collapse findings developed in our patient.

In the study of Joanna M. Spinale et al., two newborns, 5 and 6 days old, were followed up with hyperammonemia; As in our case, high-dose CRRT treatment was applied, and the ammonia values at the beginning of dialysis were 1454 and 1000 µmol/L, and at the 6th hour of dialysis, the ammonia values decreased below 200 µmol/L. Our patient was 2110 µmol/L at the beginning of dialysis, and it could decrease to 626 µmol/L at the 6th hour of dialysis (6).

In the study of Christopher Markham et al. in 2 newborns with a diagnosis of hyperammonemia, the predialysis ammonia value was 1,382 µg / dl, and although it was reduced below 60 µg / dl at the 10th hour of dialysis, rebound hyperammonemia developed after dialysis was terminated, just like in our case. The family decided to redirect her goals of care to comfort measures and the patient died the next day. Her diagnostic postmortem work-up revealed a diagnosis of citrullinemia. In other cases, the initial ammonia value was 623 µg/dl, metabolic acidosis was present in the blood gas, and at the 15th hour, the ammonia value was reduced below 100 µg/dl and he was discharged with the diagnosis of organic acidemia. Although the ammonia level was still measured as 186 µg/dl at the 15th hour of our patient, the initial ammonia values were lower in both cases than in our case.

CONCLUSION

After 120 h of dialysis, each ammonia level was <60 µg/dl and CRRT was stopped. Ammonia levels decreased rapidly with dialysis, and ammonia level was maintained by giving oral sodium benzoate and sodium stearyl fumarate support and fluids with a high glucose infusion rate. The urea cycled effect was considered in the foreground because of the absence of acidosis in the blood gas of our patient and the high result of the serum amino acid citrulline level. The patient who became neurologically active was discharged after 30 days of intensive care hospitalization, and his treatments were arranged. When our patient came for the control in the 2nd month of his life, it was observed that he had head control. There was no nystagmus and no seizures.

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Data Availability State

All patient data are stored in our hospital's data recording system.

Availability of data and material: The authors approve that all the necessary papers regarding this report can be offered upon request.

Consent to participate: Informed consent form for approved participation was obtained from the parents.

Consent for publication: Informed consent form for approved participation was obtained from the parents.

Author contributions

The manuscript has been read and approved by all the authors.

Licensing

Sažetak

NOVOROĐENČE LEČENO KONTINUIRANOM TERAPIJOM ZAMENE BUBREŽNE FUNKCIJE ZA CITRULINEMIJU-TIP 1

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Uvod: Hiperamonijemija nastaje kao rezultat nemogućnosti pretvaranja amonijaka, metaboličkog toksina, u ureu zbog blokade u ciklusu uree, a nastala neurotoksičnost je odgovorna za patogenezu.

Prikaz slučaja: Naš pacijent je imao 7 dana kada je bio praćen u drugom centru 3 dana sa preliminarnom dijagnozom neonatalne sepse. Letargija, povraćanje, tahipneja i konvulzije, koji se često javljaju kod prvih neonatalnih oblika poremećaja ciklusa ureje, takođe su bili prisutni kod našeg pacijenta. Kod nas je upućen zbog visokog nivoa amonijaka otkrivenog u sklopu pregleda zbog urođenih metaboličkih bolesti. Intubiran je zbog brzog razvoja respiratorne insuficijencije. Kada je primljen na naše odeljenje intenzivne nege sa hiperamonijemijom, nije mogao da se dobije svetlosni refleks uz razvijene promene na koži po tipu cutis marmorata.

Kod našeg pacijenta je započeta kontinuirana terapija zamene bubrežne funkcije i primenjivana je sa prekidima tokom 120 sati. Brzina infuzije glukoze je praćena visokim nivoom tečnosti. Kada se toleriše oralno, podržava se natrijum benzoatom i natrijum stearil fumaratom kako bi se smanjio nivo amonijaka. Ishrana je bila ograničena na protein.

Zaključak: Nakon 30 dana boravka na odeljenju intenzivne nege, pacijent je otpušten uz preporuku ambulantnog praćenja od stane pedijatra. Na kontrolnom pregledu posle 2 meseca, pacijent je bio bez nistagmusa i epi napada.

Ključne reči: hiperamonijemija, novorođenče, sepsa.

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