ZKTB

OLGU SUNUMU

Severe Fulminant Form Of Neonatal Citrullinemia: A Case Report

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ÖZET:

Sitrüllinemi nadir görülen otozomal resesif bir bozukluktur. Sitrüllinemi tanısı amonyak, sitrüllin, glutamin, ve orotik asit düzeylerinin kan, plazma, ve idrardaki biyokimyasal analizde artışına dayanmaktadır. Hasta, bilinen herhangi bir metabolik bozukluğu olmayan ve aralarında akrabalık ilişkisi bulunmayan bir ailenin ilk çocuğu olarak doğdu. Hasta doğumunun 6. saatinde dispne, taşipne gastrointestinal kanama ve konvülsiyonlarının başlaması üzerine yenidoğan yoğun bakım ünitesine alındı. Metabolik taramada hiperamonyemi (908 µmol/L) ve sitrüllin düzeylerinde belirgin bir artış vardı. Hastaya sitrüllinemi tanısı konuldu. Proteinden fakir beslenme, arjinin takviyesi, ve sodyum benzoat tedavisi başladı. Yaşamının 38. gününde hasta kaybedildi. Sitrüllinemi vakalarında hiperamonyemi, üre siklüs bozukluğuna veya prüvat karboksilaz eksikliğine bağlı enerji metabolizmasındaki bozukluğa bağlı olarak ortaya çıkabilir. Ülkemizde akraba evlilikleri sık olarak görüldüğünden metabolik hastalıklar ciddi bir sağlık problemidir. Bu vakayı nadir görülen bir hastalık olan sitrüllineminin önemini vurgulamak amacıyla sunduk.

Anahtar kelimeler: *sitrüllinemi, yenidoğan, metabolik hastalıklar*

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ABSTRACT :

Neonatal Sitrüllineminin Ağır Fulminan Formu: Bir Olgu Sunumu

Citrullinemia is a rare autonomic recessive disorder. The diagnosis of citrullinemia is based on biochemical analysis of blood, plasma, and urine, revealing increased levels of ammonia, citrulline, glutamine, and orotic acid. The patient was born as the first child of a non-consanguineous family without any known metabolic disorders. The patient was hospitalised in NICU because of dyspne, tachypnea, gastrointestinal bleeding and convulsions. A clear increase in ammonia (908 µmol/L) and citrulline levels was observed in metabolic screening. The patient was diagnosed as citrullinemia. The treatment was started with total potential nutrition without protein, and supplementation of arginine, and sodium benzoat. The patient died on the 38th day of life. Hyperammonemia in citrullinemia can occur either from a disorder of energy metabolism due to an absence of pyruvate carboxylase or from a disorder of the urea cycle. In our country, metabolic disease are serious health problems due to the high incidence o of consanguineous marriages. This case is reported to emphasize the importance of citrullinemia which is seen rarely.

Anahtar kelimeler: *citrullinemia, newborn, metabolic disorder*

INTRODUCTION

Citrullinemia is a rare autosomal recessive disorder of the urea cycle with estimated incidence of 1 out of 57,000 live births(1). The diagnosis of citrullinemia is based on biochemical analysis of blood, plasma, and urine, revealing increased levels of ammonia, citrulline, glutamine, and orotic acid. Argininosuccinate synthetase (ASS) enzyme activity can be assayed in liver samples and cultured fibroblasts(2). Three clinical presentations: neonatal, infantile and late onset (adult) are described. In neonatal period the disease is presented with vomiting, lethargy and rapidly progressing respiratory insufficiency and coma(2,3).

Case Report Case Report

CASE REPORT

The patient was born as the first child of a non-consanguineous family without any known metabolic disorders. On the third day, the child is admitted to the emergency room due to poor feeding and vomiting. Lack of sucking, hepatomegaly and lethargy was found during physical examination. Dyspnea, tachypnea, gastrointestinal bleeding, and convulsions started on the 6th hour of admission to NICU. Metabolic screening revealed hyperammonemia (908 μmol/L). Citrullin levels were high. The patient was diagnosed with citrullinemia The patient's diet was devoid of protein. Supportive treatment with arginine and sodium benzoate was started.
Plasma ammonium level returned to normal. Therefore, peritoneal dialysis wasn't done. Genetic analysis was planned but family of patient didn't accept genetic analysis. Follow-up developed respiratory failure and sepsis. On the 38th day the patient died.

DISCUSSION

Citrullinemia has two clinically and genetically distinct form. The classic form (type 1) is caused by argininosuccinate synthetase deficiency that functions in the urea cycle metabolism It is inherited as an autosomal recessive trait. ASS1 and SLC25A13 mutations cause citrullinemia. It has variable clinical manifestation depending on the amount of enzyme deficiency. The neonatal form is very severe and can lead to death during acute attacks. In the differential diagnosis of the disease, other conditions caused by the enzymatic defets in the urea cycle should be suspected. The defects of carbamoyl phosphate synthetase (CPS), ornithine transcarbamylase (OTC), argininosuccinate synthetase (citrullinemia), argininosuccinic acid lyase (argininosuccinic aciduria), arginase (hyperargininemia), and N-acetylglutamate synthetase enzymes cause urea cycle disease. Citrullinemia is differentiated from the other enzyme deficiencies, with decreased arginine and significantly increased citrulline level. Urinary orotic acid level increases moderately.Hyperammonemia accompanied by citrullinemia can occur either from a disruption of energy metabolism due to an absence of pyruvate carboxylase or from a defect of the urea cycle(4). As in other urea cycle disorders, the inability to produce urea leads to hyperammonemia and glutamine accumulation, causing astrocyte swelling and encephalopathy(2,3,5). In the neonatal form, the acute presentation occurs within first few days or hours of life and is characterized by progressive neurologic deterioration(5). The symptoms of citrullinemia can be similar to the symptoms of other diseases, like septisemia in neonatal period or hypoxic ischemic encephalopathy. The prognosis depends on form, the time of onset and early diagnosis of the disease. Early treatment can be life saving(6). The complications are cerebral edema, elevated intracranial pressure, herniation and hyperammonemic coma potentially leading to death. Neurodevelopmental outcome of neonatal urea cycle defect is disappointing and is related to the duration of hyperammonemia(6,7). A series of 23 cases, were reported from Turkey among which 14 patients died (7). A case from Adana and two cases from İstanbul were also reported who had respiratory distress as clinical manifestation (6,8).
In this case, the patient was diagnosed early and the prompt treatments were started after diagnosis. Because of the long duration of hyperammonemic coma, hydrocephaly, periventricular leucomalasia and cortical atrophia has been observed in the cranial ultrasound.
In our country, metabolic disorders are serious health problems because of the high incidence of consanguineous marriages. We would like to report this case to emphasize the importance of citrullinemia in Turkey.

REFERENCES:

1) Brusilow SW, Horwich AL. Urea cycle enzymes. In: Scriver C, Beaudet A, Valle D, Sly W, eds. Metabolic and Molecular Bases of Inherited Disease. 8 ed. New York: McGraw Hill; 2001:1909-63

2) Maestri NE, Clissold DB, Brusilow SW. Long-term survival of patients with argininosuccinate synthetase deficiency. J Pediatr 1995;127:929-35.

3) Summer M, Tuchman M. Proceedings of a consensus conference for the management of patients with urea cycle disorders. J Pediatr 2001; 138:6-10.

4) Karnik D, Thomas N, Jacob J, Oommen A. Hyperammonemia with Citrullinemia. Indian Pediatr. 2004;41:842-4

5) Majoie CB, Mourmans JM, Akkerman EM, Duran M, Poll-The BT. Neonatal citrullinemia: comparison of conventional MR, diffusion-weighted, and diffusion tensor findings. AJNR Am J Neuroradiol. 2004;25(1):32-5.

6)Gulcan H, Bicak U, Akinci A. Citrullinemia associated with congenital hypothyroidism. Ege Tıp Dergisi. 2004:43(3):197–9

7)Tokatli A, Coskun T, Ozalp I. Citrullinemia. Clinical experience with 23 cases. Turk J Pediatr 1998; 40:185-193.

8)Ataoglu E, Ozkul AA, Guney I, Buyukavci A, Elevli M. Sepsis bulguları ile başvuran iki sitrüllinemi olgusu. Haseki tıp bülteni, 2008;46:117-9