Case report

A case of 3-hydroxy-3-methyl glutaric CoA lyase deficiency in north of Iran descent.

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Abstract
The HMG-CoA lyase (HL) deficiency or 3-hydroxy-3-methylglutaric aciduria (MIM 246450) is a metabolic disease that is an inborn error of intermediary metabolism for the first time described in 1976. In this article we reported the clinical signs and symptoms and related lab test of this case to improve our knowledge. In this article our case was presented with persistent vomiting from a day before admission and oliguria. But this patient had three history of admission due to pneumonia at 5 month, hypoglycemia at 7 month and acidosis at 8 month of age.
Keywords: HMG-CoA lyase, deficiency

1. Introduction

The HMG-CoA lyase (HL) deficiency or 3-hydroxy-3-methylglutaric aciduria (MIM 246450) is a metabolic disorder Which is an inborn error of intermediary metabolism described in 1976 (1).It is rare worldwide and autosomal recessive disease caused by mutations in the HMGCL gene. These patients suffer from the absence of ketone bodies as alternative energy source of glucose and the accumulation of toxic metabolites of leucine catabolism (2).
HMG-CoA lyase (HL) deficiency is related with hepatomegaly, pancreatitis, seizures, and hyperammonemia (3). In the current article, we report the first case of HMG CoA lyase deficiency in north of Iran.

2. Case presentation:

A 9 month girl with HMG CoA lyase deficiency presented with persistent vomiting from a day before admission. The patient was oliguria and did not have diarrhea. The patient was the only and first child of family and her gestational age was 38 weeks and was born with birth weight of 3000 gram. Patient had three history of admission due to pneumonia at 5 month, hypoglycemia at 7 month and acidosis at 8 month of age. In her family history father and mother was cousin and the father was known case of minor B-thalassemia.
The temperature was 37.5, respiratory rate was 47/min. At the time of admission the weight was 8.5 kg on 50% percentile, height: 70 cm on 50% percentile and head circumference of 46 cm between 90 to 97 percentiles. She was initially treated with levo carnitine , iron and poly citrate.

The result of lab tests findings were summarized in table 1,2 and 3. The urine analysis of the patients indicated trace glycosuria but other parameters were normal. The tandem mass tests results were showed in table 4. Due to persistent vomiting several times of admission and metabolic acidosis patient was evaluated. The evaluation of amino acids and fatty acids revealed no disorders. But evaluation of organic academia showed The HMG-CoA lyase deficiency. The result of organic acid tests indicated there was mild elevation of C5OH (1.1, cut of <0.9) in acylcarnitine profile by tandem mass. In urine analysis by GC/MS there was huge elevation of 3-hydroxy-3-methylglutaric acid(1184.26%, cutoff<30.52%), 3-methylglutaconic acid(588.22%, cutoff<5.12%), 3-methylglutaricacid(226.26%,cutoff10.48%),and 3 hydroxy osovaleric acid (128.75%, cutoff<6.1%), these findings were diagnostic for HMG-CoA lyase (HL) deficiency

3. Discussion:

The symptoms of HMG-CoA lyase deficiency begin during neonatal and first year of life. HMG-CoA lyase deficiency results in periods of metabolic crisis,

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those are generally triggered by illness or infection, high protein intake, or fasting. Metabolic crises cause lethargy, behavioral alterations, hypotonia, fever, nausea, vomiting, diarrhea, hypoketotic hypoglycemia, metabolic acidosis, hyperammonia, hepatomegaly, and mistreatment causes breathing problems, seizures, coma, and death.

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Table 1. The biochemistry test results.

test	result	unit	Nl range	flag
Uric acid	8.5	Mg/dl	2.6-6	High
Cholesterol	63	Mg/dl	100-200	Low
Triglyceride	32	Mg/dl	34-166	low
Sodium	133	Meq/l	132-149	
Potassium	4.7	Meq/l	3.5-5	
Blood sugar	234	Mg/dl		
SGOT	6510	u/l	<40	high
SGPT	2610	u/l	<40	high
Alkaline	415	u/l	<645	
Chloride	65	µMol/l	97-107	low
Lactate	20	Mg/dl	2-20	
Pyruvate	1	Mg/dl	0.3-0.7	high
ammoniac	88	Umol/l	11-60	high

Table 2. the hematologic test assecment

test	result	unit	Nl range	flag
PT	37	SEC		
Prothrombin control	12	SEC		
Prothrombin activity	18	%		
INR	8.3	RATIO	1-1.3	HIGH
p.t.t	57	SEC	30-45	HIGH

Table 3. the hormone and immunology test analysis

test	result	unit	Nl range	flag
Cortisol 8 AM (C.L)	>2200	Nmol/l	124-662	low
GH(C.L)	0.68	Ng/ml	0-10	
insulin(C.L)	1.8	Iu/ml	2-22	low
ACTH fasting(C.L)	4.8	Pg/ml	5-55	low
Homocycteine(elisa)	15.5	Mcmo/l	5-15	high

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Table 4.tandem mass test results

test	result	unit	Nl range
TSH(CH)	0.6	µu/ML	<10
17-oh progesterone	9.9	Ng/Ml	FEMALE<4.1
Biotinidase	51	Dru	7-26 part def
			<7 total def
Galactose	0.2	Mg/Dl	<5.7
phenylalanine	1.6	Mg/Dl	<4.2
Immunoreactive	42.2	µg/L	<60.5

HMG CoA lyase catalyzes the last step in the catabolism of leucine and free fatty acids in ketogenesis . Commonly, ketones are a minor energy substrate for the myocardium [4,5]. Therefore in some case myocardial dysfunctions are seen.
In this study our case was presented with persistent vomiting from a day before admission and oliguria.
But this patient had three history of admission due to pneumonia at 5 month, hypoglycemia at 7 month and acidosis at 8 month of age. Our study showed that considering the patient signs and symptoms, to our knowledge, we must consider HMG-CoA lyase deficiency in these patients.

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