1 例肉碱棕榈酰转移酶1A 缺乏症的临床特点及CPT1A 基因突变分析

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摘要:

目的:分析1 例肉碱棕榈酰转移酶1A(CPT1A)缺乏症患儿的临床和基因突变特点,提高对该病的认识。方法:收集该患儿的临床资料,血液串联质谱分析酰基肉碱谱。抽取患儿及其父母的外周静脉血3 mL,提取DNA,通过测序技术,对CPT1A 基因所有外显子及相邻内含子(侧翼区域)序列进行直接测序,检测突变。结果:患儿临床表现为腹泻、发热、抽搐,随后出现意识障碍,发育倒退。血生化示转氨酶、心肌酶升高,低血糖,血氨增高,血液相串联质谱仪分析示游离肉碱(C0)193.61(参考值10.00 ~90.00),棕榈酰肉碱(C16)0.06(0.20 ~ 3.00),棕榈烯酰肉碱(C16:1)0.01(0.02 ~ 0.30),十八碳酰肉碱(C18)0.07(0.10 ~1.50),十八碳烯酰肉碱(C18:1)0.04(0.20 ~2.80),十八碳二烯酰肉碱(C18:2)0.02(0.10 ~1.10),C0/ (C16+C18) 为1 595.54(6.50 ~100)。基因检测示CPT1A 基因存在c.281+1G>A(Intron3)剪接突变与15-18 号外显子杂合缺失,患儿母亲携带CPT1A 基因c.281+1G>A(Intron3)剪接突变,患儿父亲携带CPT1A 基因15-18 号外显子杂合缺失。父母亲均为杂合突变,临床表型正常,为该突变的携带者。结论:CPT1A 缺乏症临床表现为低酮性低血糖、肝损伤伴肝大、高血氨、凝血功能异常、惊厥、昏迷等,其临床表现多样且缺乏特异性,易误诊。血酰基肉碱谱分析、基因检查有助于早期明确诊断。

关键词: 肉碱棕榈酰转移酶1A 缺乏症 串联质谱 肝损害 基因突变
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Clinical Characteristics of One Case of Carnitine Palmitoyltransferase 1A Deficiency and Analysis of CPT1A Gene Mutation

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Abstract:

Objective: To analyze the clinical and gene mutation characteristics of a child with carnitine palmitoyl transferase 1A (CPT1A) deficiency, and to improve the understanding of the disease. Methods: Clinical data of the child was collected. Acyl carnitine spectrum was analyzed by blood tandem mass spectrometry. DNA was extracted from 3 mL peripheral venous blood of the child and the child爷s parents. Exons CPT1A and adjacent introns (flank region) sequence were sequenced directly by gene-sequencing techniques for detecting mutations. Results: The clinical manifestations of the child were diarrhea, fever, convulsions, followed by disturbance of consciousness and developmental regression. The blood biochemistry showed the increase of myocardial enzyme and transaminase, hypoglycemia and increase of blood ammonia. Blood phase seris mass spectrometer analysis showed that free carnitine (C0) 193.61 (reference value from 10.00 to 90.00), palmitoylcarnitine (C16) 0.06 (from 0.20 to 3.00), palmitenyl carnitine (C16:1) 0.01 (from 0.02 to 0.30), octadecanoyl carnitine (C18) 0.07 (from 0.10 to 1.50), octadecaenoylcarnitine (C18:1) 0.04(from 0.20 to 2.80), octadecadienoylcarnitine (C18:2) 0.02 (from 0.10 to 1.10), C0/ (C16+C18) 1,595.54 (from 6.50 to 100).Gene detection showed that the CPT1A gene had c.281+1G>A (Intron3) splicing mutation and heterozygous deletion of exon 15-18. The mother carried the CPT1A gene c.281+1G>A (Intron3) splicing mutation, the father carried the heterozygous deletion of exon 15-18 of the CPT1A gene. Both were heterozygous mutations with normal clinical phenotype and carriers of the mutation. Conclusion: The clinical manifestations of CPT1A deficiency are hypoglycemia of low ketone, liver injury with hepatomegaly, high blood ammonia,abnormal coagulation function, convulsion, coma, etc. The clinical manifestations are diverse and lack of specificity, which is easy to be misdiagnosed. Analysis of serum acyl carnitine spectrum, gene detection is helpful for early diagnosis.

Key words: carnitine palmitoyltransferase 1A deficiency tandem mass spectrum liver injury gene mutation