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Autozygosity mapping using new panel of 19 STR markers linked to Methylmalonic Acidemia associated genes: Identification of a mutation

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Introduction

Methylmalonic acidemia is an autosomal recessively inherited disorder caused by defect in methylmalonyl-coenzymeA mutase (MCM) enzyme. MCM is encoded by MUT gene. Other types of MMA are cblA and cblB (encoded by MMAA and MMAB genes), which are involved in disrupting the synthesis of the methylmalonyl–coenzyme A cofactor. Common symptoms of this disease are encephalopathy, hyperammonemia, metabolic acidosis, neurologic deficits, vomiting, lethargy and hypotonia. One important cause of this disease is consanguinity marriage that is common in our country.

Methods

A 5 years old boy was referred to our center for genetic diagnosis of MMA disease. DNA was extracted from blood samples were taken from this family. 19 STR markers linked to the three genes of this disease were selected and two panels of multiplex PCR were designed to amplify 19 STR markers. DNA fragment analysis was performed by ABI 3130 genetic analyzer and defective gene in this patient was sequenced.

Results

homozygosity was observed in all STR markers of MMAB gene in this patient (fig 1). Exons of this gene were sequenced and we found a homozygous mutation c.197-1 G>T in affected child in exon 2 of MMAB gene. His parents are Heterozygous for this mutation (fig 2). The Pathogenicity of this mutation was confirmed because no other mutations were found in exons of this gene.

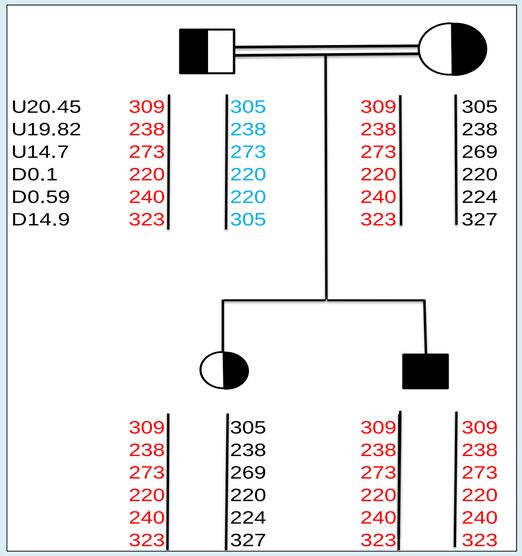
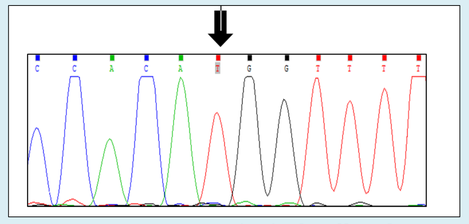
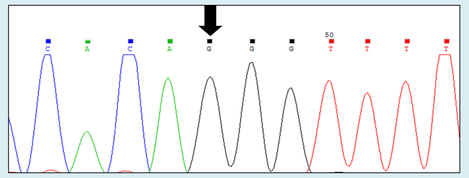


Fig1. haplotype of MMAB gene in this family. Patient showed homozygosity for this gene.



c.197-1 G>T mutation in the affected child



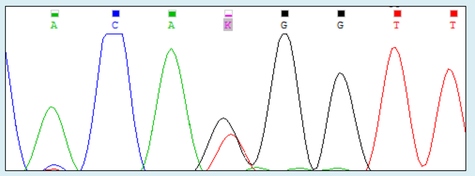


Fig2. his parents are heterozygote for this mutation

Discussion

Using STR markers and homozygosity mapping technique in polygenic disease is a rapid and cost effective method for detecting the defective gene. We hope that this study is useful for prenatal diagnosis of this disease.