Adenosine kinase deficiency presenting like Multiple Acyl-coA dehydrogenase deficiency

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INTRODUCTION
Adenosine kinase (ADK) deficiency is an ultra-rare inborn error of adenosine and methionine metabolism. It is caused by homozygous or compound heterozygous mutation in the ADK which encodes for the ADK enzyme. ADK enzyme converts adenosine to adenosine monophosphate (AMP). In ADK deficiency, adenosine accumulates and it impairs the methionine cycle. Biochemically, methionine, S-adenosylhomocysteine (AdoHcy), S-adenosylmethionine (AdoMet) are elevated with normal homocysteine. It presents with developmental delay, liver failure, epilepsy, and dysmorphic features. Here we present a case who presented with hypoketotic hypoglycemia.

CASE REPORT
A 2-year-old girl presented to our ER with lethargy and hypoketotic hypoglycemia (26 mg/dl). Plasma insulin level and carnitine-acylcarnitin profile was normal. On physical examination she had macrocephaly with frontal bossing and mild hepatomegaly. Previous history revealed neonatal hypoglycemia, indirect hyperbilirubinemia and mild global developmental delay. Parents were first-degree consuans and they reported a deceased 12-years-old boy due liver failure. While she was evaluated for hypoglycemia etiology at pediatric endocrinology outpatient clinic, she presented to ER with encephalopathy, hypoglycemia and liver failure (INR: 6.8; ALT: 8185 U/L; AST: 7899 U/L). Plasma ammonia level, blood gases and brain MRI were normal. Mild hypermethioninemia (46-366 mcml/L) was considered as part of liver failure. Urine organic acid analysis showed abnormal metabolites resembling Multiple acyl-CoA dehydrogenase deficiency (MADD). L-carnitine, CoQ10, riboflavin, moderate protein and fat restricted-diet was started. She recovered within one week and during one year follow-up period her clinical picture was stable with mild hepatopathy and coagulopathy. MADD was ruled out with molecular analysis and WES was performed which revealed a homozygous novel variant [c.1009A>T (p.Ile337Phe)] in ADK. Recently, she developed atomic seizures with head drop and EEG showed bilateral frontal epileptic activities.

DISCUSSION
ADK deficiency can present with MADD-like clinical and biochemical findings and should be considered in differential diagnosis of recurrent hypoglycemia, liver failure, global developmental delay, epilepsy and hypermethioninemia. Methionine restricted diet should be considered for treatment. In our case her protein restricted diet that was planned for MADD helped to reduce her encephalopathic and liver failure attacks.

References