Affective Disorder as the First Manifestation of Methylmalonic Acidemia: A Case Report

Fatemeh Sheikhmoonesi*[1], MD; Arefeh Shafaat[1], MD; Shirin Moarefian[2], MD; Talieh Zaman, MD

1. Psychiatry and Behavioral Sciences Research Center, Mazandaran University of Medical Sciences, Sari, Iran
2. Iranian Inherited Metabolic Diseases Association
3. Department of Pediatric, Tehran University of Medical Sciences, Tehran, Iran

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Methylmalonic acidemia (MMA) is the most common organic acidemia in Asian cases**.** We report a 14-year-old boy who was admitted to psychiatric clinic with affective symptoms. MMA was diagnosed after extensive laboratory tests. This emphasizes that even a typical psychiatric disorder can actually represent part of the spectrum of an underlying systemic disorder. MMA is an autosomal-recessive inborn error of metabolism. The incidence might be as high as 1 in 25,000[1]. It is believed that this disease is more prevalent in the Middle East because of consanguineous marriages[2]. MMA usually presents clinically with nonspecific symptoms such as seizure, poor feeding, loss of consciousness, psychomotor retardation. As a consequence, patients often undergo extensive work-up before the correct diagnosis is made[3,4].

MMA is usually diagnosed in the first year of life[2], however, this report deals with a patient whose disease could not be diagnosed until the age fourteen.

H. is a 14-year-old male who was referred to child and adolescent psychiatry clinic without previous psychiatric history.

At that time, he exhibited irritability, labile mood, irrelevant speech, distractibility, agitated psychomotor, poor concentration, poor attention, self crying, self laughing, hypersomnia and hyper sexuality. His behavior had changed since 3 days ago suddenly without any significant stressor. He was admitted for inpatient treatment. On detailed history taking and assessment, it was found that he did not use any substance or drug, past medical history and familial history were negative. Furthermore, it was realized that his parents were cousins.

Routine lab tests showed normal results. Brain CT-scan (Computerized tomography) and brain MRI (Magnetic resonance imaging) with contrast were normal. Moreover, Electroencephalography (EEG) and LP (Lumbar puncture) findings were normal.

He was drug free for three days and the symptoms disappeared gradually, therefore, his parents requested to discharge him against physician`s advice. Two months after the onset of the psychiatric syndrome, he was admitted again. Reason of admission was symptoms such as mood fluctuations, hypersexuality, hypersomnia, visual and olfactory hallucination, which started two days before this admission.

A preliminary diagnosis of bipolar mood disorder with psychotic feature was made according to DSM-IV-TR by psychiatrist. So, H. received lithium 1500 mg/day and Na-Valproate 800 mg/day and propranolol 30 mg/day for two months without satisfactory outcome. He was referred to the Institute of Study for Inborn Errors of Metabolism. Laboratory tests were carried out, through which the following results were found:

Plasma Ammonia: 86 micmol/l (NL:10-47), Plasma Lactate: 16mg/dl(NL<20), Plasma Pyruvate: 0.7 mg/dl (NL:0.3-0.7), Plasma Acyl-Carnitin Profile revealed high C3/C2 ratio: 5.12/12.05=0.42 (NL<0.2), High C3: 5.12 micmol/l (NL:0.98-3.09), High normal C4DC:0.89 micmol/l (NL:0.22-0.89). Plasma Aminoacid Profile revealed high Branched chain aminoacids (Valin, Isoleucin and Leucin) as a result of low level of their metabolic activity. However, Homocystin and methionine were within normal ranges.

So the patient was treated as Methylmalonic Acidemia with L-carnitin 100mg/Kg of body weight and biotin 5 mg BID and oral B_{12} 1000mic/day. A three year follow-up evaluation indicated a clinically stable patient.

Edwin and his colleague have suggested that a low serum concentration of vitamin B_{12} may cause mental illness[4]. It is known that defects in methylmalonyl-CoA mutase or its coenzyme, cobalamin (vitamin B_{12}) will lead to the

* **Corresponding Author; Address:** Department of Psychiatry, Zare Hospital, Sari-Neka Road, Sari, Iran
E-mail: fmoonesi@mazums.ac.ir

accumulation of methylmalonic acid and a clinical picture of MMA[2].

Another case report showed acute extrapyramidal symptoms in methylmalonic acidemia and the authors assumed metabolic stroke in MMA. It was believed the accumulation of toxic organ acid metabolites was responsible for these lesions[5].

The most common phenotype features appear during infancy. Rare patients may present as adolescents or adults with CNS disease[6]. Our patient had episodes of confusion and mood lability which could be related to metabolic decompensation episodes.

When a patient has been labeled as having a psychiatric illness, other general medical conditions (especially rare diseases) might be ignored. This emphasizes that even a typical psychiatric disorder can actually represent part of the spectrum of an underlying systemic disorder.

Key words: Adolescent; Metabolic Disorder; Methylmalonic Acidemia; Affective Disorder; Psychiatric Disorder

References

1. Mahoney MS, Bick D. Recent advances in the inherited methylmalonic acidemias. *Acta Paediatr Scand* 1987;76(5):689-96.
2. Radmanesh A, Zaman T, Ghannati H, et al. Methylmalonic acidemia: brain imaging findings in 52 children and a review of the literature. *Pediatr Radiol* 2008;38(10):1054-61.
3. Scriver CR, Beaudet AL, Valle S. The metabolic and molecular basis of inherited disease. New York: MC Graw-Hill. 2001.
4. Edwin E, Holten K, Norum KR, et al. Vitamin B_{12} hypovitaminosis in mental disease. *Acta Med Scan* 1965; 177: 689-99.
5. Heidenreich R, Natowicz M, Hainline BE, et al. Acute extrapyramidal syndrome in methylmalonic academia: "Metabolic stroke" involving the globus pallidus. *J Pediatr* 1988;113(6):1022-7.
6. Kanaumi T, Takashima S, Hirose S, et al. Neuropathology of methylmalonic acidemia in a child. *Pediatr Neurol* 2006;34(2):156-9.