A Methylmalonic Acidemia Case Presenting with Acrodermatitis Enteropathica

Hesaneh Izadyar¹, Peyman Eshraghi²

¹Student research committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.  
²Department of Pediatric Endocrinology, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract

We encountered a patient with methylmalonic aciduria associated with skin lesions resembling acrodermatitis enteropathica. This child was being fed with a low-protein diet when the skin disorder developed. A deficiency in plasma levels isoleucine, was confirmed. Supplementation of a high-caloric, protein-rich diet led to a prompt improvement of skin lesions. We assume that in our patient the skin lesions were the result of malnutrition, rather than being primarily associated with the underlying metabolic disease. To our knowledge, few reports are so far available concerning methylmalonic aciduria complicated by skin eruptions.

Keywords: Acrodermatitis Enteropathica, Children, Methylmalonic acidemia.

Introduction

Methylmalonic acidemia (MMA) is a rare autosomal recessive disease in which there is a deficiency in conversion of methylmalonic CoA to succinyl CoA. Vitamin B12 is needed to convert the methylmalonyl CoA to succinyl CoA. Some inherited conditions or B12 severe deficiency can lead to this disease (1). The principle way of methylmalonyl-coA production includes the metabolism of isoleusin, valine, threonine and methionine; so any deficiency of these amino acids can also cause MMA (2). The incidence rate of MMA is 1 in 50,000 to 80,000 newborns (3), but it is more common in countries with high amount of consanguinity and countries with no systematic newborn screening, like developing countries (4). Its typical presentations in children's first year of life are neurological symptoms like seizure, encephalopathy, and stroke. Lethargy, weak muscle tone, developmental delay, hepatomegaly, and poor eyesight are other MMA demonstrations. Inability to eat and mental disorders are patient's complains in long-term (5-7). MMA may cause coma and then death in some cases, if it remains untreated (8).

Metabolic syndromes like MMA are screened by MS/MS¹ test; but definitive diagnosis of MMA is performed by urine organic acid test (9).

*Corresponding Author:

Peyman Eshraghi, MD, Assistant Professor of Pediatric Endocrinology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.  
Email: eshraghip2@mums.ac.ir.  
Received date: Jan 15, 2014  
Accepted date: Apr 2, 2014

¹Mass Spectrometry
Treatment consists of low protein and high calorie diet, specified medications, antibiotics and sometimes organ transplantation (10). In rare cases, the MMA patients present with acrodermatitis enteropathica presentations (11).

Acrodermatitis enteropathica is an autosomal recessive disease, which is characterized by zinc malabsorption due to a mutation of the ligand protein for zinc (12-14). Acrodermatitis acidemica is a term for skin eruption that is similar to acrodermatitis enteropathica, that is also observed in some inborn errors of metabolism such as methylmalonic academia, propionic academia, and maple syrup urine disease, Glutaric aciduria type I, ornithine transcarbamylase deficiency and citrullinemia (15,16).

This disease causes diarrhea, alopecia, and skin inflammation in extremities (digits) and around cavities (anus, mouth, etc), due to malabsorption of zinc (17). In this study a three-month old infant boy who suffered from MMA with skin eruptions typical for acrodermatitis enteropathica is reported.

Case Report

In this study, we report a three-month old infant boy, who referred to pediatrics department of Qaem Hospital in Mashhad-Iran, due to skin lesions and lethargy. His parents were cousins. The patient has had polydactyly in upper limbs, frequent periods of respiratory distress from birth (like 3 previous children in his family, bilateral conjunctivitis and seizure.

Due to the death of three previous children in his family (at the ages of 9 days, 5 days and two years old) with presumptive diagnosis of metabolic disorders, tandem mass spectrometry was performed for him when he was 3 days old. The results of the screening showed elevated levels of propionylcarnitine (7.09 µmol/L) and significantly elevation in propionylcarnitine/ acetylcarntine ratio (0.65) which were associated with three differential diagnosis: propionic acidemia (Propionyl CoA carboxylase deficiency), Methylmalonic acidemia (methylmalonyl-CoA mutase deficiency) and cobalamin deficiency. So the urine organic acids test was requested and the results showed an elevation in LACTIC ACID (2955 mmol/mol creatinine) and Methylmalonic acid (2870 mmol/mol creatininie) and a slightly elevated Methylicitric Acid (46.1 mmol/mol creatinine). So diagnosis of methylmalonic acidemia was performed at 25 days of age and the diet with MMA formula and small amount of breast milk along with related medication was recommended. We could not performing genetic tests and adenosylcobalamin test for determining subtype of MMA but because of normal level of serum hemocysteine normal level of serum glycine and ammonia and acceptable clinical response and development after medications with no need to hospitalization, our case probably is mutase or adenosylcobalamin deficient.

However, a week before hospitalization, at the age of three months anemia (Hb 6.9, Hct: 22.4 MCV: 84.2, MCH: 25.9), symmetrical vesiculobullous eczematous, dry, scaly skin lesions of the mouth, diaper and also desquamation of the palms and soles was observed (Fig.1).

Fig1: A patient with methylmalonic aciduria associated with skin lesions resembling acrodermatitis enteropathica.
Clotrimazole had no effects and these symptoms were exacerbated. Skin biopsy was not permitted but after consultation with a dermatologist, acrodermatitis enteropathica-like lesions was confirmed by clinical signs. Because of normal level of serum zinc and low level of isoleucine, deficiency of isoleucine in his powder milk and diet consumed the cause of these lesions.

Discussion
A rash similar to that of acrodermatitis enteropathica has also been reported in infants fed breast milk that is low in zinc and in those with maple syrup urine disease (MSUD), organic aciduria, methylmalonic acidemia, biotinidase deficiency, essential fatty acid deficiency, severe protein malnutrition (kwashiorkor), and cystic fibrosis (18).

Acrodermatitis enteropathica was first described by Brandt (19) in 1936 and was named by Danbolt in 1951 with characteristic eczematous, bullous cutaneous lesions on periorificial and acral sites and all of these clinical features are caused by zinc deficiency (20). Diagnosis of acrodermatitis enteropathica is made primarily by clinical manifestations and a low serum zinc level is confirmative. However, if the serum zinc level is normal, with characteristic clinical features and a rapid response to zinc supplementation, the diagnosis can be established (21). Many metabolic disorders, such as MMA, propionic acidemia, MSUD, Glutaric aciduria type 1, Ornithine transcarbamylase deficiency, and citrullinemia, may present with cutaneous lesions on periorificial and acral sites and all of these clinical features are caused by zinc deficiency (20). Diagnosis of acrodermatitis enteropathica is made primarily by clinical manifestations and a low serum zinc level is confirmative. However, if the serum zinc level is normal, with characteristic clinical features and a rapid response to zinc supplementation, the diagnosis can be established (21). Many metabolic disorders, such as MMA, propionic acidemia, MSUD, Glutaric aciduria type 1, Ornithine transcarbamylase deficiency, and citrullinemia, may present with acrodermatitis enteropathica.

Conclusion
This finding indicates that serum zinc level is not an absolute value in diagnosis of acrodermatitis enteropathica. Also, aminoacidopathies in inborn errors of metabolism plays the major role in physiopathology of this kind of skin eruption especially in methylmalonic acidemia so replacement of related deficient amino acid will effectively cure the rash.

References


