Case Report

A rare case of familial methylmalonic acidemia presenting with Acrodermatitis Enteropathica type of lesion

Wali P. P[1], Parakh H[2], Reddy P[3]

[1]Dr. Pradnya P. Wali, Junior Consultant Neonatologist, [2]Dr. Hemant Parakh, Consultant Neonatologist, [3]Dr. Prashant Reddy, Consultant Pediatricians, Sunrise Children Hospital, Hyderabad, AP, India.

Address for Correspondence: Dr. Pradnya P. Wali, Email: drpradnyawali@gmail.com

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Abstract

Methylmalonic academia (MMA) is an inborn error of metabolism commonly presenting in newborns with an occurrence of 1 in 50,000 to 80,000 newborns. It has autosomal recessive mode of inheritance. It is a disorder of amino acid metabolism. MMA occurs due to defective conversion of methylmalonyl-coenzyme A (CoA) to succinyl-CoA. It presents early at around 1 month to 1 year of age. It has predominat neurologic manifestations such as seizures, developmental delay, encephalopathy, and stroke. However due to malabsorption of zinc and secondary deficiency of branched chain aminoacids it rarely presents as Acrodermatitis Enteropathica. Here we report a case of a 5 months old girl with familial MMA presenting with skin eruptions typical of Acrodermatitis Enteropathica.

Keywords: Methylmalonic Acidemia, Acrodermatitis Enteropathica, Inborn error of metabolism

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Case Report

A 5 month old baby girl presented to our hospital with history of loose stools lasting for 15 days. She was lethargic and noted to have skin lesions. On analyzing her history she was born out of second degree consanguineous parents. She lost her sibling at 4 months who was diagnosed as sepsis with developmental delay. There was history of two neonatal deaths in her paternal side with similar complaints.

On admission she was sick, dehydrated &lethargic. She had severe chelitis & prominent skin lesions over trunk, perioral & perianal region. She had poor weight gain, hypotonia & severe microcephaly; Head circumference being 35 cms at 5 months of age. She had developmental delay was present with partial neck holding & was not able to rollover.

Her initial investigations revealed anemia (Hb-6.8g/dl, Hct-20.7, TLC-5000/cu.mm, platelets-1.5 lakhs/cu.mm, hypernatremia Na+: 150mmol/L).

She was treated with intravenous fluids, antibiotics & other supportive measures. She was given blood transfusion. With history of consanguinity among her parents with family history of neonatal deaths, Inborn error of metabolism was suspected. Tandem Mass Spectroscopy & Gas Chromatography were planned. Mass Spectroscopy was positive for methylmalonic acidemia. Magnetic Resonance imaging of BRAIN was suggestive of neurometabolic disorder. She was started on carnitine supplementation, calorie rich diet, protein restriction, special metanutrition formula along with cobalamin supplementation.

Her skin lesions did not improve with clotrimazole. Acrodermatitis enteropathica like lesions were confirmed by clinical signs & she was started on zinc supplementation following which she showed signs of improvement. Genetic counseling was done. She is on follow up with good recovery.

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Discussion

Methylmalonic academia (MMA) is an inborn error of metabolism commonly presenting in newborns with an occurrence of 1 in 50,000 to 80,000 newborns [1]. It has autosomal recessive mode of inheritance. It is a disorder of amino acid metabolism. MMA occurs due to defective conversion of methylmalonyl-coenzyme A (CoA) to succinyl-CoA.

It presents early at around 1 month to 1 year of age. It has predominat neurologic manifestations such as seizures, developmental delay, encephalopathy, and stroke [2,3].

However due to malabsorption of zinc and secondary deficiency of branched chain aminoacids it rarely presents as Acrodermatitis enteropathica [4]. As Methylmalonyl-coA is associated with metabolism of isoleucine, valine, threonine and methionine, disorders of these aminoacids also affects Methylmalonyl-coA [5]. It is predominant in areas with high rates of consanguineous marriages [6]. MMA affects both males and females equally.

Genetics:

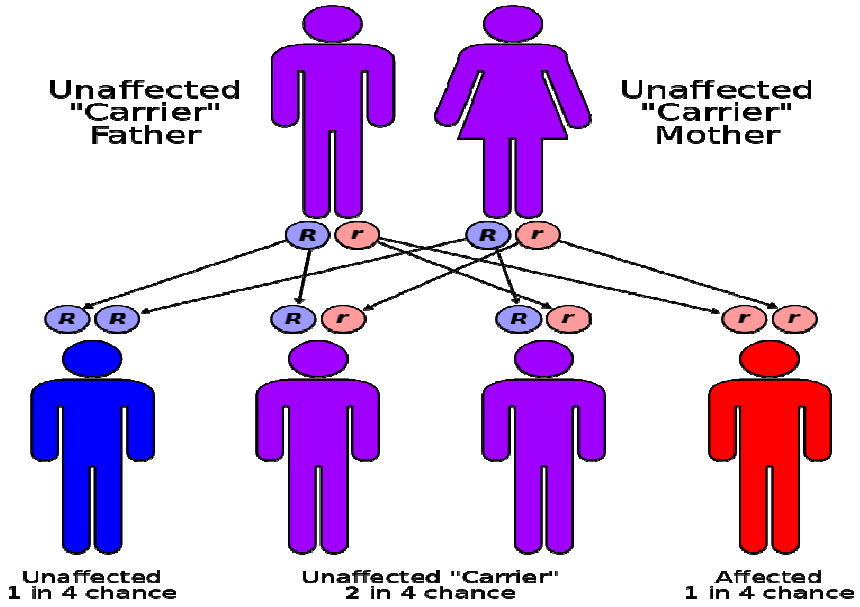

Fig 1: Autosomal recessive inheritance pattern in MMA

In our case there was strong family history with previous sibling death due to developmental delay & respiratory failure. Even two of the fathers cousins who had consanguinity had affected children who died in infancy due to similar complaints. All affected siblings were female. No genetic testing or detail metabolic analysis was done in those infants.

Severe nutritional deficiency of vitamin B_{12} can also result in similar features like MMA [7]. MMA presents usually in first year of life. Clinical features include Vomiting, dehydration, lethargy, recurrent infections, failure to thrive, hepatosplenomegaly, seizures, encephalopathy, stroke.

Skin eruptions similar to acrodermatitis enteropathica may occur in MMA [8, 9] causing skin inflammation in extremities, perioral & perianal region. Low protein diet strictly limited in branched chain aminoacids, mostly isoleucine may result in cutaneous lesions.

Complete blood cell (CBC) counts, Serum Electrolytes, RFT, ABG are the initial line of investigations. TMS & GCMS confirms the diagnosis. Neutropenia, anemia, thrombocytopenia & metabolic acidosis are noted. There is raised levels of ammonia, glycine, and methylmalonic acid. Urinary levels of methylmalonic acid, methylcitrate, propionic acid & 3-hydroxypropionate levels are high.

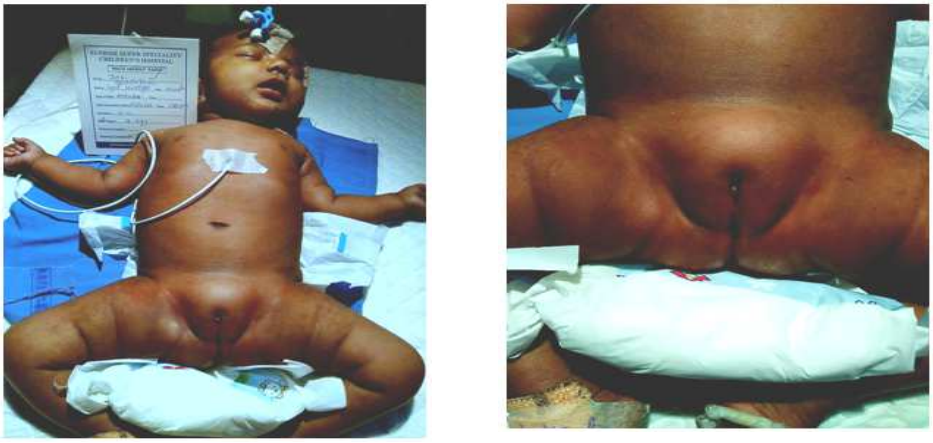

Fig 2: Picture showing cutaneous lesions similar to Acrodermatitis enteropathica in a child with MMA.

Magnetic resonance imaging (MRI) studies show bilateral lesions of the globus pallidus in patients with methylmalonic academia [10-13] along with delayed myelination, immature gyral pattern, microhemorrhages and periventricular white matter lesions.

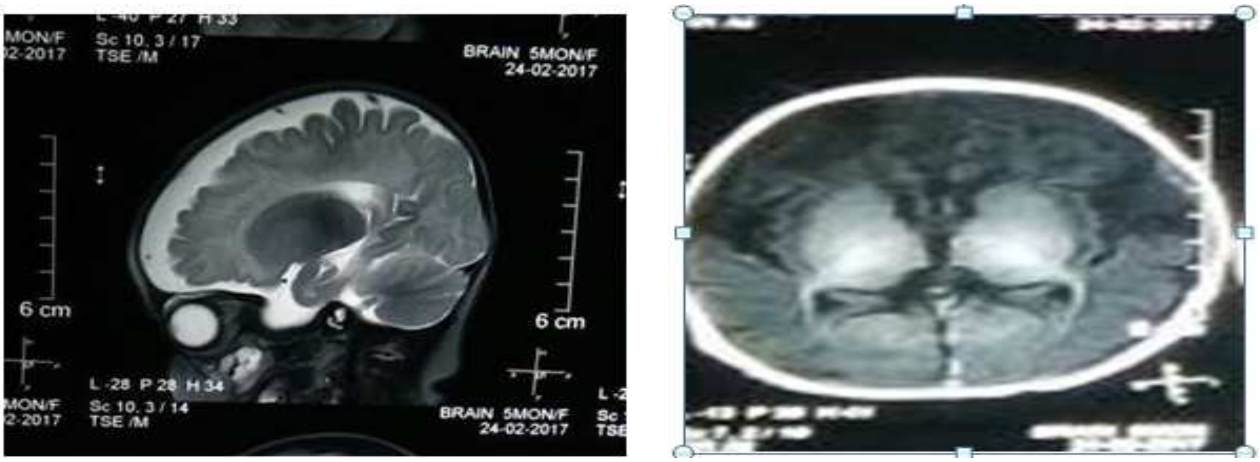

Fig 3: MRI Brain Showing Prominence of Extraventricular CSF Spaces Mainly in Fronto-temporal area & Restricted diffusion in corpus callosum genu seen.

Medical management of methylmalonic acidemia includes protein-restricted diet with L-carnitine and cobalamin supplementation. Treatment of underlying infections is mandatory. Prognosis varies with the type of defect. There are 6 recognized defects in methylmalonate metabolism. *cblA* has the best prognosis whereas mut0 has the worst prognosis [14,15]. Patients with cobalamin-responsive disease may have better long-term prognosis. It is noted that early-onset cobalamin-nonresponders have the worst outcomes, with median survival of 6 years [16].

Conclusion

Prompt diagnosis with good clinical acumen of disorders of metabolism helps in better outcome.

Understanding rare manifestations of such disorders with appropriate management is the cornerstone of management of metabolic disorders.

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