Clinical Pediatric Dermatology
ISSN: 2472-0143

Open access Case Report

Acrodermatitis Dysmetabolica in an Infant with a Methylmalonic Acidemia

F El Hadadi[1*], L Mezni[1], M Meziane[1], N Ismaili[1], K Senouci[1], O El Bakkali[2]

[1]*Department of Dermatology and Venerology, University Mohammed V Souissi, Rabat,Morocco*

[2]*Department of Pediatrics, University Mohammed V Souissi, Rabat, Morocco*

ABSTRACT

Combined Malonic and Methylmalonic Aciduria (CMAMMA), also called combined malonic and methylmalonic acidemia is an genetic metabolic disease characterized by elevated levels of malonic acid and methylmalonic acid. Some researchers have hypothesized that CMAMMA might be one of the most general forms of methylmalonic acidemia and possibly one of the most general inborn errors of metabolism. Due to being infrequently diagnosed, it most often goes undetected.

Keywords: Methylmalonic acidemia; Disease; Acrodermatits enteropathica; Infant

INTRODUCTION

Methylmalonic Acidemia (MMA) is a rare autosomal reces - sive disease with an incidence rate of 1 in 50,000 to 80,000 newborns, it was first reported in 1967 as a lethal, severe and multi-systems injured disease of abnormal metabolism. The cutaneous manifestations of MMA are grouped under the term of acrodermatitis dysmetabolic or acrodermatits enteropathica like syndrome. According to our literature research, this is the 1st Moroccan case of an 18 months infant who suffered from MMA [1].

Methylmalonic and Propionic Acidemia (MMA/PA) are autosomal recessive disorders of propionate catabolism caused by weakness in the enzymes methylmalonyl CoA mutase (MUT) or Propionyl-CoA Carboxylase (PCC) characterized by accumu-lation of metabolites of branched chain amino acid catabolism including as 3-hydroxypropionic acid, methylcitric acid and/or methylmalonic acid in plasma, urine and other body fluids [2].

CASE PRESENTATION

A 18 M old term boy with history of first degree consanguinityfour siblings deaths in the early neonatal period, psychomotor development retardation and a failure to thrive [3]. At the age of 3 months he developed a generalized hypotonia, diarrhea, seizures with a severe metabolic acidosis. Biological examination showed hypoglycemia, a normal plasma zinc level and urine organic acid analysis revelead elevated levels of methylmalonic acid and methylcitric acid suggestive of methylmalonic acidemia [4]. The genetic study of the methylmalonyl CoA mutase gene mutation was not available in our coun-try. He was subsequently administered larginine, lcarnitine, folic acid, vitamin b12 injections and a low-protein diet and metronidazole [5]. At the age of 18 months he was admitted to the pediatric department for an upper respiratory infection, vomitting, hyperamonemia. With an echocardiogram, dilated cardiomyopathy, he started furosemid, captopril and acetyl-salicylic acid [6]. 1 week after initiating these treatments, he developped an acrodermatitis enteropathica like skin lesions **(Figure 1)**: An extensive superficial scaled skin predominantly of the skin folds associated with erosive fissured erythematous dermatitis of the buttocks and erythematous weeping lesions of the neck folds, cheeks and occipital region. Alopecia, cheilitis

Received:	02-Dec-2020	**Manuscript No:**	IPCPDR-20-3695
Editor assigned:	07-Dec-2020	**PreQC No:**	IPCPDR-20-3695 (PQ)
Reviewed:	21-Dec-2020	**QC No:**	IPCPDR-20-3695
Revised:	09-Nov-2022	**Manuscript No:**	IPCPDR-20-3695 (R)
Published:	15-Dec-2022	**DOI:**	10.36648/2472-0143.9.3.21

Corresponding author F El Hadadi, Department of Dermatology and Venerology, University Mohammed V Souissi, Rabat,Morocco; E-mail: farahelhadadi1234@gmail.com

Citation Hadadi F El, Mezni L, Meziane M, Ismaili N, Senouci K, et al. (2022) Acrodermatitis Dysmetabolica in an Infant with a Methylmalonic Acidemia. Clin Pediatr Dermatol. 9:21.

tis and perleche were also noticed [7]. 2 days after the patient died due to a severe acute respiratory infection complicated by a septic shock [8].

Figure 1: Acrodermatitis dysmetabolica: a) Superficial scaled skin with erythematous weeping lesions of the upper and lower limbs; b) Perleche and cheilitis with a weeping, fissured lesions of the neck folds; c) Occipital region; d) Alopecia; e) Bilateral and periorificial dermatitis with erosive erythema of the buttocks.

RESULTS AND DISCUSSION

MMA is a rare inborn error of metabolism characterized by ac-cumulation of methylmalonic acid due to deficiency of methylmalonyl CoA mutase (MUT), this enzyme (MUT) catalyzes the conversion of methylmalonic CoA to succinyl CoA, which requires Vitamin B12 (cobalamin).

Patients with a complete enzyme deficiency present in the first days to weeks of life with acute deterioration of their general clinical condition, metabolic acidosis and hyperammonemia, progressing to coma and death, if untreated. Late-onset cases of MMA may present at any age: Infancy (our case), childhood or even later with a more heterogeneous clinical picture.

Mental outcome tends to be worse in PA and late complications include chronic kidney disease almost exclusively in MMA and cardiomyopathy mainly in PA. The completely outcome remains poor despite the existence of apparently effective therapy with a low protein diet and carnitine except for vitamin B12 responsive forms of MMA (mainly cblA type MMA), which have a better outcome if diagnosed timely and treated adequately.

The main symptoms include; acidosis, ketosis, hyperammonemia, hypoglycemia, hyperglycemia and neutropenia are main symptoms of MMA. Major secondary complications are the developmental delay (variable), a tubulointerstitial nephritis with pro-gressive renal failure, “metabolic stroke” (acute and chronic basal ganglia involvement), disabling movement disorder with choreoathetosis, dystonia and para/quadriparesis, pancreatitis, growth failure, functional immune impairment and optic nerve atrophy.

The cutaneous manifestations, also called acrodermatitis dysmetabolica/acrodermatitis acidemia or acrodermatitis entheropathica like skin lesions can occur a short time (4-15 days) after the onset of the acute decompensation or simultaneously, they can recur in each acute episode, as they can appear during a 2nd or 3rd outbreak.

Patients presents a superficial scalded skin over erythematous underling tissue and superficial desquamation initially limited to the skin folds and pressure points (head, perineum) with a progressive extension to the whole body. Blisters and superficial erosions can be present as well as the Nikolsky’s sign.

Gradually over a few weeks, painful, weeping, erosive erythema appears principally on the buttocks neck folds and the face, erythematosquamous plaques with circinate margins, have also been described in the lower limbs and the trunk. Lesions of the mucous membranes are mild (stomatitis, ulceration cheilitis, perlech). The clinical picture is very similar to that observed in acrodermatitis enteropathica. Alopecia appeared gradually, the hair loss is mainly from the posterior part of the scalp and the remaining hair is fine, dull and brittle.

Some authors report the possibility of a skin rash similar to staphylococcal scald syndrome, generalized desquamative erythroderma, necrolytic migratory erythema and a morbiliform punctiform erythema. Metabolic disorders can be present at birth and many can be recognize by routine screening. If a metabolic disorder is not identified early, then it may be diagnosed later in life, when symptoms appear. Specific blood and DNA tests could be done to diagnose genetic metabolic disorders.

The gut microbiota, which is a population of microbes that live in the human digestive system, also have an important part in metabolism and generally have a positive function for its host. In terms of pathophysiological/mechanism interactions, an abnormal gut microbiota can valid a role in metabolic disorder related obesity. Differential diagnoses arise mainly with other metabolic disorders summarized in **Table 1**.

Table 1: Metabolic disorders, associated with Acrodermatitis enteropathica.

Metabolic enzymes deficiency	Disorder
Amminoacidopathies	Maple syrup urine disease, Phe-nylketonuria, Hartnup disease, Non-ketotic hyperglycinemia, Congenital isoleucine degrada-tion disorder
Organic acidemias	Methylmalonic acidemia, Propi-onic acidemia, Glutaric acidemia type I, Biotinidase deficiency
Urea cycle disorders	Ornithine transcarbamylase defi-ciency, Citrullinemia, Carbamoyl phosphate synthetase deficiency, Essential fatty acid deficiency, Necrolytic migratory erythema associated with glucagonoma

Treatments is based on a special diet: An adequate energy and avoiding endogenous protein catabolism, through low protein intake with limited doses of isoleucine, valine, threonine and methionine. Standard therapy of long term management includes: L carnitine; antibiotics to reduce intestinal flora; vitamin B12 in responsive MMA patients; low protein diet; precursor free amino acid and/or isoleucine/valine supplementation; vitamin and mineral supplementation; caring for special situations and provision of an emergency regimen in recurrent illnesses.

CONCLUSION

The prognosis depends on the underlying genetic mutation that causes the metabolic alteration, but also the metabolic complications such as: Ketoacidosis, hypoxia and irreversible brain damage; repeated or chronic hyperammonemia, causing neuronal death and mental retardation, pancytopenia, predisposing to potentially fatal infections.

MMA is a severe genetic disease with poor prognosis. The skinlesions are probably due to several factors of a metabolic, nu-tritional and genetic nature. Therefore, lifelong follow-up by a multidisciplinary team (pediatricians, dermatologists, endocri-nologist) is required.

REFERENCES

1. Hörster F, Hoffmann GF (2004) Pathophysiology, diagnosis, and treatment of methylmalonic aciduria-recent advances and new challenges. Pediatr Nephrol 19: 1071-4.
2. Lindblad B, Lindblad BS, Olin P, Svanberg B, Zetterström R (1968) Methylmalonic acidemia a disorder associated with acidosis, hyperglycinemia and hyperlactatemia. Acta Paediatr 57: 417-24.
3. Oberholzer VG, Levin B, Burgess EA, Young WF (1967) Methylmalonic aciduria. An inborn error of metabolism leading to chronic metabolic acidosis. Arch Dis childh 42: 492.
4. Baumgartner MR, Hörster F, Dionisi-Vici C, Haliloglu G, Karall D, et al. (2014) Proposed guidelines for the diagnosis and management of methylmalonic and propionic acide-mia. Orphanet J Rare Dis 9: 1-36.
5. Zhou X, Cui Y, Han J (2018) Methylmalonic acidemia: Current status and research priorities. Intractable Rare Dis Res 7: 73-8.
6. Bodemer C, de Prost Y, Bachollet B, Poggi F, Teillac-Hamel D, et al. (1994) Cutaneous manifestations of methylmalonic and propionic acidaemia: A description based on 38 cases. Brit J Dermatol 131: 93-8.
7. Bartralot-Soler R, García-Patos V, Rodríguez-Cano L, Mollet-Sánchez J (2006) Acrodermatitis acidémica. Piel 21: 1888-92.
8. Gupta N, Jain P, Kabra M, Gulati S, Sethuraman G (2015) Acrodermatitis dysmetabolica-report of two cases. Indian J Pediatr 82: 869-70.