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Methylmalonic acidemia with emergency hypertension

Acidemia metilmalónica con hipertensión de emergencia

Dear Editor,

Methylmalonic acidemia (MMA) is a heterogeneous disorder of propionate metabolism. MMA is caused by deficiency of the mitochondrial enzyme, methylmalonyl-CoA mutase-apoenzyme activity (MUT) or defective in adenosylcobalamin (coenzyme) synthesis.[1] The most patients with cblA and half patients with cblB forms of MMA are responsive to vitamin B12.[2,3] Clinical manifestation of MMA may be acute or chronic. The acute form of the disease occurs during infancy and even as early as the second day of life with poor feeding, vomiting, dehydration, weight loss, temperature instability, lethargy, hypotonia, seizure and progressing to coma. Laboratory findings include: metabolic acidosis, ketosis, hypoglycemia, hyperlactatemia, hyperammonemia, pancytopenia.[4]

Definitive diagnosis of isolated MMA is based on analysis of organic acids in plasma and/or urine; however genetic testing diagnosis in some condition is accessible to confirm the diagnosis of isolated MMA. Below, we describe the presentation and management of two cases of MMA with severe hypertention.

The first case was a 46-day-old girl, admitted to the emergency department because of generalized edema and severe hypertension. She was born from consanguineous parents at term with a birth weight 2.600 kg. She had frequent vomiting in 9th day of life. Edema of hands and feet appeared in 39th day of life. On admission, she had SBP 130 mmHg (above 99th), DBP 75 mmHg (above 99th), periorbital and legs pitting edema and respiratory distress. Laboratory findings included: microscopic hematuria, massive proteinuria, hypoalbominemia, pancytopenia and high anion gap metabolic acidosis.

The patient was managed by nephrologists with diagnosis of congenital nephrotic syndrome. Angiography of abdominal aorta and renal artery were normal. She had brain atrophy and supra and infra tentorial ventricolomegaly in brain CT scan and left ventricular hypertrophy in echocardiography. Abdominal sonography was normal but both kidneys were seen larger than normal. Bone marrow aspiration (BMA) was performed because of pancytopenia which was normal. Patient's hypertension did not respond to Losartan, Hydralazine, Captopril and Amlodipine. Metabolic consulting and then metabolic tests due to refractory metabolic acidosis was done. The patient with suspected organic aciduria was treated with hydroxycobalamin 1 mg daily, biotin 10 mg daily and L-carnitine 50 mg/kg/day. She had high level of glycine in blood amino acid chromatography but ammonia, lactate, serum B12 and hemocystein were normal. Methylmalonic aciduria confirmed with high level of urine methlmalonic acid and increased serum level of propionyl carnitine. We have increased the dose of B12 up to 2 mg IM daily but unfortunately, the patient died.

The second case was a 45-day-old boy admitted from the emergency ward with complaints of anemia, respiratory distress and severe hypertension. He was born from non-consanguineous parents at term with a birth weight 2.800 kg. The first baby of the family had died at the age of 5-months due to propionic aciduria. On examination he had respiratory distress (RR = 67), SBP 134 mmHg (above 99th) and DBP 78 mmHg (above 99th) and mild pitting edema in legs. Laboratory results included: high anion gap metabolic acidosis, pancytopenia, hypoalbominemia, proteinuria, and microscopic hematuria. Lactate, ammonia, serum B12, serum hemocystein and other electrolytes were normal but serum glycine was increased. Renal artery disorder has been excluded by Doppler sonography. Abdominal sonography was normal but both kidneys had upper normal size and increased cortical echogenicity. BMA was performed because of pancytopenia which was normal. According to the familial history and our previous case, after sending samples for urine organic acid, acylcarnitine profile and chromatography of serum amino acid, B12 2 mg IM daily, carnitine 50 mg/kg/day, biotin 10 mg daily and low protein diet was started for the patient. His blood pressure was refractory to all of anti-hypertensive drugs such as Hydralazine, Captopril, Labetalol. Methylmalonic aciduria confirmed by increased of urine methylmalonic acid and serum propionyl carnitine.

Despite early treatment of methylmalonic acid even without waiting for tests result, the patient died.

Chronic renal disease is a life-threatening complication of MMA and finally leads to dialysis or kidney transplantation. Renal impairment most occurs in patients with mut (0) and cblB mutation.[5] The mechanism of renal injury in MMA is still unknown. Proximal tubular disorder is a main pathogenic mechanism of MMA-associated kidney disease.[6] A recent case study has reported 2 cases of MMA associated with hemolytic uremic syndrome (HUS) association which revealed that probable pathogenesis of thrombotic microangiopathy could be related to the increase of plasma methylmalonic acid and homocysteine levels.[7]

In the current study, the two mentioned patients had MMA that confirmed with assessment of urine organic acid and acylcarnitine profile. They had just renal involvement that their symptom and signs were started during infancy that was refractory to all of the treatment and despite early treatment in the one of them, they died.

In summary, in each case with hematuria, proteinuria, nephrotic syndrome, unexplained hypertension or renal failure of unknown origin especially in pediatric patients, metabolic screening and urinary organic acid analysis should be carried out as soon as possible.

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Glomerulonefritis necrosante en el síndrome por consumo de cocaína y levamisol

Necrotising glomerulonephritis in levamisole-contaminated cocaine use

Sr. Director:

España es el país con mayor incidencia de consumo de cocaína en adultos[1,2], y en la última década se han incrementado las partidas de cocaína adulteradas con levamisol[2,3]. En relación con la toma de cocaína/levamisol (C/L) se describe un síndrome diferenciado por: 1) lesiones cutáneas purpúricas, necróticas o equimóticas, en tronco, extremidades y lóbulo de las orejas; el sustrato histológico es una vasculitis leucocitoclástica o una vasculopatía trombótica; 2) leucopenia y neutropenia, y 3) positividad de distintos parámetros inmunológicos[2,3] (tabla 1). La nefropatía por C/L se halla apenas documentada.

Describimos el caso de un paciente que desarrolló una glomerulonefritis necrosante, con insuficiencia renal y síndrome nefrótico, asociada al consumo de C/L. Hasta donde sabemos esta sería la primera publicación con biopsia renal en nuestro país.