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Case Report

Metabolic Stroke Secondary to Propionic Acidemia Presented as Acute Encephalopathy in a Seventeen Months Old Indian Girl

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Abstract

Background: Propionic academia (PA) is disorder of branched-chain amino acid metabolism due to deficient activity of propionyl Co A carboxylase. We present a child with PA whose initial presentation was acute encephalopathy.

Case Report: This seventeen months old girl presented with acute onset encephalopathy of twelve hours duration. Central nervous system examination showed Glasgow coma scale of 6/15, pupils were symmetrical and reacting to light, hypotonia, depressed deep tendon reflexes, extensor plantar, respiratory system examination showed tachypnea. She had wide anion gap metabolic acidosis, hyperammonemia, blood sugar level of 43 mg/dl. The initial diagnosis of acute metabolic encephalopathy secondary to organic acidemia was considered. Her MRI brain showed bilateral fairly symmetrical areas of hyperintensities in lentiform nuclei which showed diffusion restriction. Gas chromatography and mass spectrometry (GCMS) of urine sample showed elevated levels of ketones (3-hydroxybutyric acid, Acetoacetic acid, 3-hydroxyisovaleric acid) with presence of 3-hydroxy propionic acid, carnitine, acylcarnitine analysis showed elevated levels of C2, C3 and C4-OH, suggesting a possibility of propionic acidemia.

Conclusion: Presentation of our case was acute onset encephalopathy. The report highlights neuroradiological presentation of a metabolic stroke secondary to propionic academia.

Keywords: *Encephalopathy; Metabolic Stroke; Propionic Acidemia*

Introduction

Propionic acidemia (PA) is a rare inborn errors of metabolism characterized by accumulation of propionic acid due to deficiency of mitochondria-located enzyme propionyl-CoA carboxylase (PCC). PA is one of the intoxication type organic acidemias. Patients present with acute deterioration, metabolic acidosis and hyperammonemia either in early neonatal period or at a later age with a more heterogeneous clinical picture, multiorgan involvement with frequent neurologic dysfunction that includes developmental delay, movement disorders/dystonia, seizures, stroke-like episodes, psychiatric symptoms, and basal ganglia lesions, leading to early death or to severe neurological handicap in many survivors. Standard treatment relies on the dietary restriction of propionate precursors combined with carnitine supplementation, which buffers mitochondrial propionate accumulation. To reduce propionate production by intestinal flora [1,2] chronic cyclic metronidazole (MTZ) administration is advised [3].

Case Report

Seventeen months old girl with normal birth and developmental history, she had potato chips, vegetable soup following which had vomiting and became drowsy. She presented with acute onset encephalopathy of twelve hours duration. On examination she was

tachypneic, her weight for height was in moderate acute malnutrition range, general examination was normal, detail central nervous system examination showed Glasgow coma scale was 6/15, pupils were symmetrical and reacting to light, deep tendon reflexes were depressed, plantars were extensor, possibility of severely decompensated metabolic encephalopathy was considered. She was put on mechanical ventilation. She had wide anion gap metabolic acidosis (Arterial blood gas Ph: 6.93, pCO_2: 20, HCO_3: 4, base excess: -27), hyperammonemia (blood ammonia 1477.6 mcg/dl), blood sugar level of 43 mg/dl, plasma lactate 1.3 mmol/L, serum pyruvate 1.33 mg/dl, CPK total 223 U/L. Patient was initiated on intravenous fluids with sodium bicarbonate, empirical L-Carnitine (100 mg/kg/day), Thiamine (20 mg/kg/day), Riboflavin (10 mg/kg/day), Biotin (10 mg/day), Sodium benzoate (400 mg/kg/day), arginine (450 mg/kg/day), metronidazole (24 mg/kg/day), oral lactulose. Magnetic resonance imaging (MRI) of brain showed bilateral fairly symmetrical areas of hyperintensities in lentiform nuclei which showed diffusion restriction. Possibility of Metabolic Stroke was considered. Gas chromatography and mass spectrometry (GCMS) of urine sample showed elevated levels of ketones (3-hydroxybutyric acid, Acetoacetic acid, 3-hydroxyisovaleric acid) with presence of 3-hydroxy propionic acid, suggesting a possibility of propionic academia, carnitine, acylcarnitine analysis showed elevated levels of C2, C3 and C4-OH, suggesting a possibility of propionic acidemia. Serial lab values were monitored. On day 5 of admission family went against medical advice and took discharge. The report highlights the clinical and neuroradiological presentation of a metabolic stroke secondary to propionic academia.

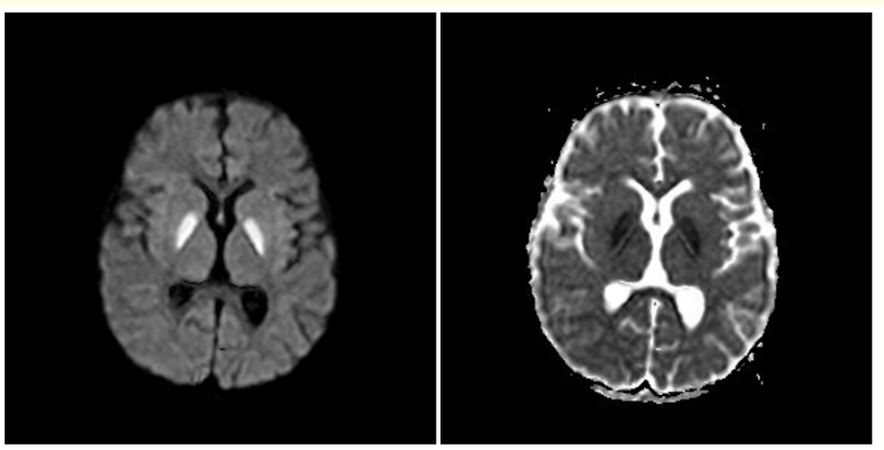

Figure 1 ***Figure 2***

Figure 1 and 2: *Magnetic resonance imaging (MRI) of brain showing diffusion restriction (Figure 1), with corresponding hypointensity on apparent diffusion coefficient map (Figure 2) in bilateral lentiform nuclei.*

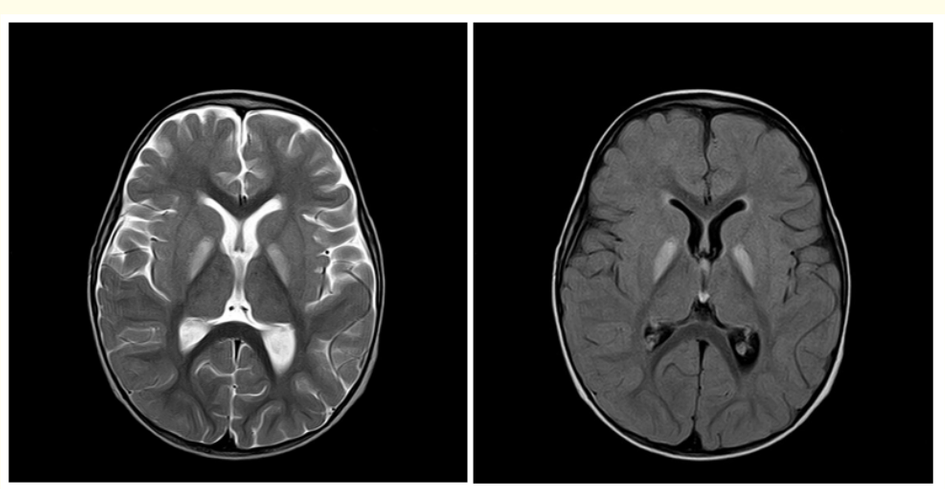

Figure 3 ***Figure 4***

Figure 3 and 4: *Magnetic resonance imaging (MRI) of brain showing T2 hyperintensity (Figure 3), T2 FLAIR hyperintensity (Figure 4) in bilateral lentiform nuclei.*

Discussion

Organic acidemias usually present as life threatening episodes of metabolic decompensation [1,2]. Propionic academia (PA) is disorder of branched-chain amino acid metabolism due to deficient activity of propionyl Co A carboxylase (PCC). Breakdown of propionyl-CoA to methylmalonyl-CoA depends on propionyl-CoA-carboxylase, which needs biotin as a cofactor. PA may be caused either by a lack of propionyl-CoA carboxylase or by biotin deficiency. In PA, build up of propionic acid and other propionyl CoA derived metabolites results in episodes of vomiting, dehydration, hyperammonemia and severe metabolic acidosis. PA phenotype varies from severe early/neonatal-onset form with high mortality and poor outcome to milder forms with a later onset and varying presentations [2,4]. Early-onset PA patients may also present with sepsis resulting from immune deficiency, failure to thrive, pancreatitis. Individuals with PA, develop worsening metabolic acidosis in the presence of physiological stress from increased catabolism during episodes of fever, infection, vomiting, trauma, and psychological or physiological stress. Our patient had episodes of vomiting followed by lethargy. At these times, individuals are thought to have higher metabolic rates than they can tolerate and they require prompt therapy (similar to that used in new onset patients) to mitigate complications, morbidity, and mortality [5]. Hypoglycemia has been described in patients with organic acidemia presenting in crisis [6]. Hyperglycemia is rare and has only been reported in a few PA patients in crisis. Lehner., *et al*. reported a newborn with PA who had severe hyperglycemia and presented with hyperexcitability, drowsiness, vomiting and hypotonia. Lab analysis during acute attack of PA shows severe metabolic acidosis with wide anion gap, ketosis, neutropenia, thrombocytopenia, hypoglycemia, hyperammonemia, elevated glycine concentration in all body fluids (blood, urine, and spinal fluid), decrease in plasma levels of branched-chain amino acids (leucine, isoleucine, valine), markedly elevated concentrations of propionic acid and methylcitric acid in the plasma and urine. 3-Hydroxypropionic acid, propionyl glycine, and other intermediate metabolites of isoleucine catabolism, such as tiglic acid, tiglylglycine, and 2-methyloacetoacetic acid, are also found in urine. Moderate elevations in blood levels of ammonia, glycine, and previously mentioned organic acids usually persist between the acute attacks. CT scan and MRI of the brain may reveal cerebral atrophy, demyelination, and abnormalities in the globus pallidus and basal ganglia as the evidence of a metabolic stroke. Confirmation of PA diagnosis is by detection of biallelic pathogenic variants in *PCCA* or *PCCB* genes or of deficient PCC enzymatic activity. Basal ganglia are sensitive to metabolic disturbances that affect oxidative metabolism. Neuropathologic basis of disease in basal ganglia has been reported in propionic acidemia [3]The finding of basal ganglia lesions, as slitlike high-T2 intensity lentiform nuclei, shrunken caudate heads, or acutely swollen basal ganglia, always should prompt evaluation for possible · underlying metabolic disease, so that appropriate therapy can be started to avoid further brain damage. Basal ganglia changes in PA may be caused by specific toxic effects from different metabolites or basal ganglia structures might be metabolically most active in PA crises, and therefore are most vulnerable to anoxia and metabolic insults.

Acute management of PA includes mechanical ventilation, intravenous fluid (10% dextrose 120 - 150 ml/kg/day with electrolytes), stop all sources of protein, intralipids (if available- 3 g/kg/day) vasopressors if necessary, normal saline fluid boluses, antibiotics (after drawing cultures), hemodialysis, intravenous carnitine boluses (100 mg/kg/dose 3 - 4 times per day), in undiagnosed patients if hyperammonemia is present then manage with sodium benzoate/sodium phenylacetate, in known patient of PA start N-carbamylglutamate, monitor ammonia, electrolyte and blood gases, reintroduce protein within 24 - 36h, eeg monitoring [7]. Biotin at 10 - 20 mg/day is suggested as additional therapy. Long term management includes L-Carnitine supplementation (200 mg/kg per dose twice daily) to prevent deficiency due to excretion of acylcarnitines, gut flora control regimen, prevention of constipation, Metronidazole (20 mg/kg per day during 10 - 15 days a month) reduces propionate production in gut, chronic treatment with sodium benzoate (150 - 250 mg/kg per day) to correct both chronic hyperammonaemia and hyperglycinaemia, screening studies including echocardiogram, electrocardiogram (EKG), hearing screen, optic fields (if cerebral edema), dilated ophthalmologic exam, physical therapy, occupational therapy, and referral to early intervention (in the neonates) [7,8]. Special diet has been tried in PA, with variable outcomes from fair-excellent to severe neurological handicap, with strict dietary compliance were noted.

Disabling movement disorder, optic nerve atrophy, cardiomyopathy, severe muscle lipidosis, worse intellectual outcome could be sequela in PA patients [8]. Every PA patient and their siblings should receive the childhood immunization schedule, all patients, their

caregivers and household members should receive the inactivated influenza vaccine annually [7]. Mannitol, 5-pentanoic acid, lactated ringers, systemic steroids and valproic acid these medications are contraindicated in PA patients [7]. Poor developmental outcomes are reported in most of the largest series. Therefore, reversal of catabolism and removal of toxic compounds are lifesaving measures. PA patients have high morbidity with acute and chronic neurological involvement and various visceral complications that are incompletely prevented by transplantation [8].

Conclusion

Presentation of our case was acute onset encephalopathy. The report highlights neuroradiological presentation of a metabolic stroke secondary to propionic academia.

Bibliography

1. Dionisi-Vici C., *et al.* "Classical' organic aciduria, propionic aciduria methylmalonicaciduria and isovaleric aciduria: long-term outcome and effects of expanded newborn screening using tandem mass spectrometry". *Journal of Inherited Metabolic Disease* 29 (2006): 383-389.

2. Deodato F., *et al.* "Methylmalonic and propionic aciduria". *American Journal of Medical Genetics. Part C: Seminars in Medical Genetics* 142C (2006): 104-112.

3. Harding BN., *et al.* "Propionic acidaemia: a neuropathological study of two patients presenting in infancy". *Neuropathology and Applied Neurobiology* 17 (1991): 133-138.

4. Ozand PT., *et al.* "Unusual presentations of propionic acidemia". *Brain and Development* 16 (1994): 46-57.

5. MA Dixon and JV Leonard. "Intercurrent illness in inborn errors of intermediary metabolism". *Archives of Disease in Childhood* 67 (1992): 1387-1391.

6. Henriquez H., *et al.* "Emergency presentations of patients with methylmalonic acidemia, propionic acidemia and branched chain amino acidemia (MSUD)". *Brain and Development* 16 (1994): 86-93.

7. Chapman KA., *et al.* "Acute management of propionic acidemia". *Molecular Genetics and Metabolism* 105 (2012): 16-25.

8. De Baulny HO., *et al.* "Methylmalonic and propionic acidaemias: management and outcome". *Journal of Inherited Metabolic Disease* 28 (2005): 415-423.

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