PYROGLUTAMIC ACIDEMIA - A RARE CASE REPORT IN DY PATIL MEDICAL COLLEGE DPU VIDYAPEETH

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Abstract

Pyroglutamic acidemia or 5-oxiprolinemia is an under-recognized cause of high anion gap metabolic acidosis and increased excretion of pyroglutamic acid in urine which is a derangement of gamma- glutamyl cycle. Most common presentation would be vomiting, acidosis, increased anion metabolic acidosis. It is common in paediatric population with inherited autosomal recessive enzyme deficiencies. Here we report a case of 2-month-old female child presented with loose stools and vomiting since 4 days. Because of persistent metabolic acidosis a suspicion of IEM was made and GCMS TMS was sent which is suggestive of pyroglutamic acidemia and was further treated accordingly.

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1. Introduction

Organic acidemias (OAs), is a rare group of inherited metabolic disorder, manifesting in neonates or infants as acute, life threatening, severe metabolic decompensation, after a brief initial symptom free period for a few days (1)(2). The key feature of metabolic decompensation is the raise in the plasma ammonia levels above the toxic levels that needs to be addressed as it leads to life threatening neurological complications (3). Pediatricians have a challenging task in obtaining a timely diagnosis and initiating a treatment. There are almost more than 65 different types of Organic aciduria that have been described with an incidence rate of 1 in 3000 live births (4). Vomiting, poor eating, loose stools, dehydration and lethargy are non-specific signs and symptoms of metabolic decompensation that might mimic other illnesses such bacterial sepsis. (5). Elevated serum ammonia levels above 200mmol/L have a direct effect on neurological outcomes that are usually associated with drowsiness and lethargy (6,7). By gamma-glutamyl cycle the small intestines, kidneys, and liver produce glutathione (8). Gamma glutamyl cycle maximises the absorption of amino acids and is crucial for chemical detoxification (9). A condition known as pyroglutaric acidemia occurs when the body is unable to synthesise glutathione.. Risk factors for glutathione deficiency are advanced age, female gender, pregnancy, malnutrition, critical illness, chronic kidney or liver disease, alcohol abuse, antiepileptic drugs and chronic acetaminophen use (10). Chronic acidosis, injury to the central nervous system, and hemolytic anaemia are all consequences of high levels of gamma-glutamyl amino acids.. And as the levels increase, patient becomes more acidotic. (11,12). The hazardous intermediate of paracetamol, N-acetyl-p-benzoquinoeimine, permanently binds to glutathione, and its depletion causes a disturbance of the gamma glutamyl cycle, which worsens the acidosis. Due to the difficulty in measuring the serum 5-oxoproline level, this illness is probably underdiagnosed. (13).

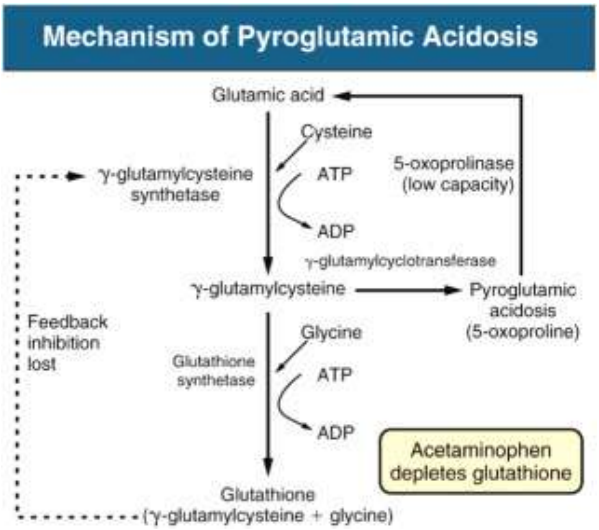

Fig. 1 (10)

Case presentation:

A 2-month-old female child born to a non-consanguineous couple via LSCS I/v/o PIH to a 25-year-old primi of with H/o pregnancy induced hypertension was on tablet labetalol and H/o hypothyroidism and was on tablet thyronorm 25mcg. Initially the baby was breast fed only for 2 weeks, later because of loose stools and excoriation the baby was started on formula feeds. The baby was thriving well on top up feeds and at 2 months of life initially had complaints of loose stools for 4 days, fever for 2 days and vomiting for 1 day, mother gives history of one episode of GTCS lasting for 5 mins after which the baby was admitted in private hospital. On admission the baby was irritable and was tachypneic for which baby was kept on o2 support and started on iv antibiotics and iv fluids. CBC was done which showed anemia, thrombocytopenia, and leukocytosis (lymphocytic). MRI brain was organized which was suggestive of viral encephalitis and started on acyclovir. CSF analysis was done which showed protein- 102, glucose-76, TLC- 10 and lymphocytic -100%. The baby is receiving treatment for viral encephalitis with acyclovir, ceftriaxone and paracetamol. Parents took DAMA after 4 days of treatment and took the baby home and baby was well for 4 days after which baby started having respiratory distress and was brought to DY Patil Medical College.

On examining the baby, acidotic breathing was present, tachypnea was present, and baby was requiring 02 support.
Temp: afebrile, Hr:162/min, Rr:68/min, Spo2: 100 % on bcpap, Bp: 98/66 mmhg, Pp: well felt
On systemic examination:
CVS: systolic murmur +, CNS: conscious, irritable, b/l pupils reactive to light, RS: Air entry bilaterally, b/l crepts +, deep breathing + , sub costal retractions +, P/A: soft, non-tender, hepatosplenomegaly

On admission samples were sent for septic screen and it showed elevated CRP (86), Hb(8.6), Platelet count(40,000),and on ABG high anion gap metabolic acidosis was present.
ABG was done in view of acidotic breathing which showed high anion gap metabolic acidosis.

On admission	After 2 days
PH: 7.21	PH: 7.24
PO2:154 on 5L O2 by bcpap	PO2:128
PCO2:18	PC02:16
HCO3- : 7.7	HC03-: 6.4
Na:145	Na: 138
Cl:118	Cl: 108
Anion gap: 29	Anion gap: 23

Antibiotics were upgraded to Inj.Meropenem and PCV transfusion was given, Inj.Soda bicarbonate was given in view of acidotic breathing.
This metabolic acidosis was persistent, and a suspicion of metabolic disorder was aroused. Then a metabolic workup was organized, which showed elevated ammonia (224) , elevated lactate(24). Further the feeds were withheld, and the ammonia levels repeated after 24 hrs, the levels were shown to be in decreasing trend.
A metabolic cocktail was started along with sodium benzoate and on re introducing the feeds the baby started having loose stools again, white in colour.
Hence GCMS/TMS was sent which was suggestive of pyroglutaric aciduria.
Further lactose was stopped and started on soyamilk formula and metabolic cocktail was started, the baby started getting better, loose stools reduced and then got discharged on soyamilk formula.

2. Conclusion

Pyroglutamic academia is still an under recognized cause of elevated anion gap metabolic acidosis. The main objective of this case is to raise awareness that there may be more than one contributing component to the cause, such as sepsis and malnutrition. Identifying and addressing the contributing factors should include stopping of any possibly contributing drugs (such as paracetamol and flucloxacillin) and treatment of any underlying diseases that have been identified as risk factors. Treatment involves Acetaminophen withdrawal, supportive care, and addressing risk factorts for glutathione insufficiency (14,15). Paracetamol (acetaminophen) and 5-oxoproline can be measured simultaneously in serum using a straightforward, affordable, and quick using capillary electrophoresis method with diode array detection (DAD) (13).

This paper is to emphasize that pyroglutamic acidemia is one of the common causes of High Anion Gap Metabolic Acidosis but goes unrecognized due to the rare presentation.

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