P-139 - GLUTATHIONE SYNTHETASE DEFICIENCY PRESENTING AS METABOLIC ACIDOSIS AND NEONATAL HEMOLYTIC ANEMIA

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INTRODUCTION: Glutathione synthetase deficiency is a rare autosomal recessive disorder resulting in low levels of glutathione and an increased susceptibility to oxidative stress. Patients manifest with a range of symptoms including metabolic acidosis, hemolytic anemia, neurological problems and massive excretion of pyroglutamic acid (5-oxoproline) in the urine. Wide clinical variation has been reported. Treatment with antioxidants has been recommended in an attempt to prevent morbidity and mortality associated with the disorder.

CASE PRESENTATION: We present a 9 month old female patient referred to our hospital presenting metabolic acidosis and hemolytic anemia. She was born at term, after an uneventful pregnancy and delivery, at 2 days of life she presented with tachypnea and sleepiness. Blood gas analysis revealed a pH of 7.16, bicarbonate of 9 mmol/l and an anion gap of 31. Infectious causes were ruled out and she was transferred to our center. With the suspicion of a neonatal metabolic disorder she was studied and Urinary organic acids chromatography revealed a large peak of 5-oxoproline, the aminoacids showed <8 umol/l glutamate (range 8-179), 139 umol/l glycine (range 154-338) and 3.5 umol/l cystine (range 6-43). This profile brought the suspicion of a glutathione cycle defect. With the biochemical profile and clinical presentation Glutathione synthetase deficiency was considered and treatment with bicarbonate, vitamins C and E was initiated immediately with good response. Hemolysis was moderate, requiring some red blood cell transfusions. Non-conjugated bilirubin, lactate dehydrogenase and reticulocyte count were normal for age. Her red blood cell count remained stable only requiring transfusion on two viral respiratory tract infections and a gastrointestinal infection due to Salmonella and Adenovirus. Her bicarbonate is also stable but low, despite intense antioxidant treatment. Sequence analysis of GSS gene showed two Pathogenic variants, c.491G>A (p.Arg164Gln) and c.709C>T (p.Arg237*)

CONCLUSION: Glutathione synthetase deficiency and other erythrocyte metabolism defects should be considered in the initial assessment of neonates and infants with hemolytic anemia and/or metabolic acidosis. Early diagnosis and prompt treatment can improve long term outcomes.