

THE ANTENATAL COURSE OF A PATIENT WITH INFANTILE BARTTER SYNDROME AND GESTATIONAL DIABETES, A CASE STUDY.

Background

Bartter syndrome is an inherited renal tubular disorder characterized by a defect in salt reabsorption in the thick ascending limb of the loop of Henle⁽¹⁾, which results in salt wasting, hypokalemia, and metabolic alkalosis⁽²⁾. It is a rare disorder that affects around 1 in 1,000,000 of the population. It is reported that the relationship between phenotypes and genotypes are poor⁽³⁾. The rarity of the syndrome and the lack of genetic characterization meant that there is lack of high-quality studies that can address treatment of each subtype. Consequently, management is usually based on clinical experience of nephrologists and understanding of the renal system rather than treatment based on robust evidence. Most types are autosomal recessive with hypokalaemia and hypokalaemic alkalosis⁽³⁾. Antenatally, fetuses with Bartter syndrome were associated with polyhydramnios, and prematurity⁽⁴⁾. Some Subtypes were characterized by hypochloremic alkalosis⁽³⁾, nephrocalcinosis⁽⁵⁾, sensorineural hearing loss⁽⁶⁾ and Hypocalcaemic hypercalciuria and failure to thrive⁽⁴⁾.

Case Study

We present a 25-year-old white Caucasian woman in her second pregnancy who was diagnosed with infantile Bartter syndrome at the age of 9 months. She has no family history of Bartter syndrome or obstetric cholestasis. Her mother had gestational diabetes.

The patient was born at 34 weeks due to polyhydramnios which was attributed to gestational diabetes. After 9 month of multiple reviews. The patient was diagnosed with Bartter syndrome and started on indomethacin treatment which controlled the symptoms. Daily 32 mmol of potassium supplementation and 1 mg of calcium supplementation was started. The patient struggled with compliance to medication in childhood. She had several admissions to the pediatric ward for potassium replacement. As she grew up her compliance increased, and she maintained a stable level of potassium with no other complications. She is currently on 32 mmol / Day.

On Examination, She was fully grown with a normal height of 1.66 m and 70 Kg of weight at booking. She remained normotensive throughout her pregnancies, but her blood pressure increased due to PET. There was no increasing need for potassium supplementation during pregnancy.

The patient did not have any other medical conditions and her diabetes resolved completely in between pregnancies. She had one episode of pyelonephritis at the age of 23 in which her potassium was up to 4.8 mmol/L and her renal function deteriorated but recovered with antibiotics.

At the age of 19, she had her first pregnancy, which was complicated by obstetric cholestasis and gestational diabetes, but there was no deterioration in kidney functions or electrolytes disturbances. She had a late preterm vaginal delivery at 36+5 weeks and with no complications. Between pregnancies, she had stable kidney functions and no diabetes mellitus. Her mean potassium during her first pregnancy was 3.33 mmol/L. Her mean Sodium was 137.36 mmol/L, mean Chloride was 97.0 mmol/l. and mean Creatine was 98.81 µmol/L. Her inter-pregnancy average creatine level was 101 µmol/L. Owing to the adaptation of the renal system in pregnancy a stable creatine may indicate a decline in renal functions.

This pregnancy was complicated by gestational diabetes, which required insulin starting at 14 weeks. She maintained a stable level of kidney functions until 28 weeks of pregnancy. During this period, Her mean creatine was 98.75 µmol/L, Her average potassium was 3.325 mmol/L. Her mean sodium was 138.6 mmol/L and her was Chloride 99.25 mmol/L. Her mean sodium was 138.6 mmol/L and her was Chloride 99.25 mmol/L. In the third trimester, her Creatinine increased to from 110 to 178 µmol/L. Her potassium was 3.5 (3.2-4.2) mmol/L She tested positive for protein in urine and her PCR ratio was 135mg/mmol. In line with this picture of worsening kidney functions and superimposed preeclampsia, her blood pressure spiked at 160/100. It was controlled by labetalol till delivery. Her liver functions started to be affected at 31+5 weeks. Her ALT increased to 56 U/L from 8 U/L and her platelet dropped to 128 x109/L from 197 x109/L. She received two doses of steroids and delivered at 32 weeks. She was delivered by Category III Caesarean section due to low lying placenta. Her blood pressure normalized post delivery. Her creatine levels continued to worsen post delivery 202 µmol/L before recovering to 126 µmol/L on day 5.

Discussion

Due to the rarity of the syndrome, most evidence is based on case studies. There are case studies that mention the occurrence of diabetes mellitus in Bartter syndrome^(7, 8). Additionally, Bartter syndrome like phenotype in diabetes mellitus⁽⁹⁾. There is no mention of a link between gestational diabetes and Bartter syndrome. It is unclear whether these associations are coincidental or causal. However, experimental potassium deficiency was proven to induce glucose intolerance by the means of decrease in plasma insulin response to sustained hyperglycemia⁽¹⁰⁾. The association between obstetric cholestasis with Bartter syndrome in pregnancy has not been reported before and is most likely coincidental.

There are few cases of Bartter syndrome in pregnancy reported⁽¹¹⁻¹⁵⁾. The association between chronic kidney disease and preeclampsia is well established⁽¹⁶⁾. However, The association between Bartter syndrome and preeclampsia was not specifically cited in the few case studies of barter syndrome in pregnancy except for one case report that mentioned pregnancy induced hypertension⁽¹⁷⁾. This association might be attributed to the secondary hyperaldosteronism and activation of the renin-angiotensin-aldosterone system (RAAS). In our case the patient developed early onset pre-eclampsia with a mild form of HELLP syndrome at 31 weeks on top of worsening kidney functions. Previous studies mentioned the increased need for potassium supplementation^(13, 14). That was not the case in our patient who maintained the same pre-pregnancy potassium levels without increase in daily potassium dose.

Conclusion

There are very few cases published in literature regarding Bartter syndrome in pregnancy and it is very rare. A larger study might not be feasible. However, a larger sample might demonstrate or refute a link between gestational diabetes, hypokalemia and Bartter syndrome in pregnancy. In practice, nausea and vomiting in early pregnancy and Hyperemesis Gravidarum should be treated more thoughtfully in these cases as it can exacerbate hypokalemia. Avoidance of dehydration and contraction alkalosis is important. As for all patients with chronic kidney disease, low dose aspirin is important to reduce the risk of pre-eclampsia. For parturient patients with Bartter syndrome, strict fluid balance charting and avoidance of dehydration or fluid overload should be prioritized, and caesarean sections reserved for obstetric reasons.

References

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There are no conflicts of interests to declare.