CASE REPORT

# Maternal Pseudo-Bartter Syndrome Associated with Severe Perinatal Brain Injury

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**Background:** Maternal electrolyte imbalance is rarely reported as causative factor of severe perinatal brain injury. **Case characteristics:** This case outlines a unique maternal and neonatal pseudo-Bartter syndrome presented with metabolic alkalosis and hypochloremia due to maternal severe vomiting. **Observation:** Neonatal MRI brain revealed extensive brain hemorrhages with porencephalic cysts. Subsequent investigation workup points towards maternal severe metabolic alkalosis as its cause. **Message:** Careful medical attention should be paid to pregnant women with excessive vomiting to ensure a healthy outcome for both the mother and the baby.

**Keywords:** *Metabolic alkalosis, Perinatal stroke, Dyselectrolytemia.*

Severe intracranial hemorrhage is an important cause of neonatal mortality and morbidity in premature infants [1]. Metabolic and electrolyte abnormalities during pregnancy, if left untreated, may lead to significant maternal and fetal morbidity [2]. Although there are many obstetric risk factors for perinatal brain injury, the association between maternal metabolic alkalosis and severe perinatal intracranial hemorrhage is not well known. We relate the case of maternal and neonatal pseudo-Bartter syndrome characterized by severe metabolic alkalosis and hypochloremia following maternal vomiting as likely the cause of severe neonatal brain injury.

## Case Report

A 31-year-old, gravida 7 para 5 woman with 32+3weeks of gestation and bodyweight of 59 kg prior to pregnancy, was admitted with bouts of vomiting, abdominal cramps and upper limb parasthesia for 2 days. She had no complaints of fever, diarrhea, or abdominal distension. She had no past history of anorexia nervosa, bulimia or drug intake. She continued to have persistent vomiting and diagnosed as having gastroenteritis for which she was treated with intravenous fluid, electrolyte replacement and antibiotics therapy. Her blood chemistry analysis showed severe persistent hypokalemia and moderate hypochloremia. She was seen at obstetric outpatient department one week prior for her routine check-up and had fetal growth scan which was unremarkable. Her pregnancy was uncomplicated and her medical and personal history were unremarkable.

In view of maternal complaints of reduced fetal movement and fetal heart rate monitoring showing variable and late decelerations, emergency caesarean section was performed for non-reassuring fetal status.

A baby girl was delivered with birth weight of 2.2 kg and Apgar score of 3 and 3 at 1 and 5 minutes, respectively. Baby was born flat at birth with bradycardia and apnea requiring intermittent positive pressure ventilation *via* endotracheal tube. She responded well to resuscitative measures, her heart rate and oxygen saturations improved gradually, baby was transferred to neonatal intensive care unit and was put on mechanical ventilation. Umbilical blood gas analysis, baby's first arterial blood gas values and renal panel showed persistent metabolic alkalosis with severe hypokalemia and hypochloremia, (***Table* I**) likely reflecting maternal and fetal alkalotic state. Her electrolyte imbalance was corrected and renal panel normalizes within 48 hours of life with intravenous fluid and electrolyte replacement therapy. Over the course of first few days, baby showed no spontaneous breathing effort, absent reflexes and brain stem response and was severely hypotonic. Day 1 cranial ultrasound scan was suggestive of multiple porencephalic cysts with frontal and parietal bleeding. Amplitude-electroencephalograph showed severe encephalopathic changes with burst suppression pattern. Magnetic resonance imaging (MRI) showed extensive hemorrhagic changes in the brain (intraventricular, periventricular, thalami, cerebral peduncle, posterior pons and cerebellar hemorrhages) and left orbit of eye

**TABLE I** MATERNAL AND NEONATAL BLOOD CHEMISTRY AND GAS ANALYSIS

| *Parameter* | *Umbilical artery* | *Umbilical vein* | *Maternal blood (at delivery)* | *Neonatal blood (at birth)* | *Neonatal blood (at 48 h of life)* |
|---|---|---|---|---|---|
| pH | 7.38 | 7.35 | - | 7.39 | 7.32 |
| pCO2 (mm Hg) | 58.9 | 61.1 | - | 49.9 | 45.6 |
| pO2 (mmHg) | 13.1 | 9.4 | - | 66.5 | 59.8 |
| Base Excess (mmol/L) | 7.6 | 5.5 | - | 1.6 | -2.1 |
| Bicarbonate (mmol/L) | 34.8 | 33.1 | 29.0 | 29.8 | 21.2 |
| Lactate (mmol/L) | 5.71 | 5.5 | - | 8.7 | 2.1 |
| Sodium (mmol/L) | - | - | 138.0 | 139.0 | 138 |
| Potassium (mmol/L) | - | - | 2.4 | 2.3 | 3.9 |
| Chloride (mmol/L) | - | - | 81.0 | 87.0 | 103 |
| Urea (mmol/L) | - | - | 2.9 | 2.6 | 7.8 |
| Creatinine (µmol/L) | - | - | 76.0 | 54 | 51 |

with retinal detachment. The upper cervical cord appeared swollen with hemorrhagic changes and there was intradural extramedullary hemorrhage in lumbar spine. Parents were counselled for poor prognosis and the baby died on day5 of life. Mother responded symptomatically to medical treatment with improvement in episodes of vomiting and abdominal cramps. Her blood counts, abdominal ultrasound scan and coagulation studies were normal and she was discharged well from the hospital on post-operative day 8. Neonatal workup for infection, viral studies, bleeding disorders, metabolic screen and placental histopathology were unremarkable with no causative factor for severe neonatal encephalopathy and extensive brain hemorrhages. List of investigations carried out for baby and their result interpretation are summarized in ***Web Table* I**.

## DISCUSSION

Obstetric risk factors for severe neonatal intracranial hemorrhage include fetal bleeding disorders, twin to twin transfusion, fetal hypoxia, maternal trauma and non-immune hydrops fetalis. Maternal excessive vomiting and fetal metabolic alkalosis as a cause of brain injury is uncommon in the literature [3,4]. Our case is unusual that the newborn had already shown severe intracranial and spinal hemorrhage with porencephalic cysts and metabolic alkalosis at birth. Both mother and her fetus presented with the same significant metabolic abnormalities at the time of delivery, thereby mimicking a Bartter syndrome.

Pseudo-Bartter syndrome presents with the biochemical findings of severe hypokalemic metabolic alkalosis, hyponatremia and hypochloremia, suggestive of Bartter syndrome but without showing any primary renal tubule abnormalities [5]. Although we did not look at maternal arterial blood gases, the blood venous levels of electrolytes were suggestive of metabolic alkalosis, with causative agent likely being excessive vomiting. Chloride and hydrogen ion depletion from severe vomiting is the origin for both maternal and fetal hypokalemic metabolic alkalosis [6]. We hypothesize that, the same mechanism of renal potassium depletion induced by hypochloremia seen in mother, does also exist in the fetus.

As evident from umbilical cord gases, changes in fetal acid-base status could have occurred secondary to maternal alterations in pH. It has been proved that though transplacental diffusion of charged bicarbonate anion occurs slowly, significant transfer occurs when condition persists in excess of few hours. Therefore, it is likely that excessive vomiting lead to significant maternal and, secondarily fetal alkalosis [7].

We were unable to find reported obstetric and peripartum causes of such a severe perinatal brain injury. There was no evidence of peripartum infection, intra-uterine infection, bleeding diathesis, maternal trauma, placental insufficiency or severe perinatal asphyxia. Mother's personal history was unremarkable and she was antenatally well with normal fetal scans. Workup of baby to find cause of severe perinatal insult was mostly unremarkable.

It is known that a change in pH of cerebral spinal fluid (CSF) happens in equilibration with arterial pH and this in turn regulates cerebral blood flow (CBF). An elevation in pH (metabolic alkalosis) causes contraction of cerebral vasculature making it prone for bleeding as well as has a

direct effect on vascular endothelium, nerves and astrocytes [8]. Being rare, little has been reported about the patterns of electronic fetal heart rate monitoring in fetal alkalosis. In our case, loss of variability and late decelerations might have reflected the fetal alkalosis and brain injury, though they are not specific. EEG has been shown as useful tool for assessment of neonatal brain injury [9]. As our case had shown severe EEG abnormalities in form of burst suppression and cranial scan suggestive of porencephalic cysts, shortly after birth, the timing of cerebral insult was considered perinatal in origin.

In conclusion, our case is unique suggesting that maternal excessive vomiting could have contributed to fetal alkalosis and pseudo-Bartter syndrome, and severe perinatal brain injury. We recommend that any acid-base imbalance in pregnant women should be monitored carefully and corrected optimally to ensure the fetal well-being.

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All authors approved the final manuscript. SV will be the guarantor.
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**WEB TABLE I** LIST OF INVESTIGATIONS PERFORMED ON NEONATE WITH RESULT INTERPRETATION

| *Tests performed* | *Investigations* | *Results* | *Interpretation* |
|---|---|---|---|
| Hematological tests | FBC, PS | Low hemoglobin, hematocrit<br>Normal WBC, platelet count<br>Elevated reticulocyte count<br>Normocytic, normochromic RBC hemolysisNo evidence of infection | Evidence of anemia and hemolysis, no evidence of infection |
| Biochemical tests | Renal panel, LFT | Within normal limits | Normal studies |
| Microbiological tests | Blood culture<br>Ear swab<br>Placental swab | No bacterial growth | No evidence of infection or colonization |
| CSF examination | CSF profile, Gram stain<br>Bacterial culture<br>Viral PCR | Packed with RBC,<br>normal WBC and protein and low glucoseNo bacterial or viral growth on culture and PCR | Evidence of intraventricular hemorrhage, no evidence of bacterial or viral meningitis |
| Coagulation profile | BT, PT, APTT,<br>D-dimer quantitation | Initially deranged PT which improved with Vitamin K and FFP replacement | No significant evidence of bleeding tendency or coagulation abnormalities |
| Intrauterine infections infection | TORCH studies | No IgG / IgM antibodies detected | No evidence of intrauterine infection |
| Viral studies | Throat swab, Rectal swab | No virus detected | No evidence of viral infection |
| Metabolic studies | IEM studies, Serum ammonia | No significant abnormalities seen | Normal metabolic workup |
| Genetic tests | Chromosomal studies | Normal female karyotype with no abnormalities detected | Normal genetic testing |
| Radiological examination | CXR, AXR, Abdominal US | Normal radiological findings | No evidence of intraabdominal or intrathoracic bleeding |
| Histopathologicaltest | Placental examination | No evidence of chorioamnionitis, abruptio placentae or vasculitis | No significant placental abnormalities |

*Abbreviations: FBC – Full Blood Count, PS – Peripheral Smear, WBC – White Blood Cells, RBC – Red Blood Cells, LFT – Liver Function Test, CSF – Cerebro Spinal Fluid, PCR – Polymerase Chain Reaction, BT – Bleeding Time, PT – Prothrombin Time, APTT – Activated Partial Thromboplastin Time, FFP – Fresh Frozen Plasma, TORCH – Toxoplasmosis, Rubella, Cytomegalovirus, Herpes, IEM – Inborn Error of Metabolism, CXR – Chest X-ray, AXR – Abdominal X-ray, US – Ultrasound Scan.*