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Severe Hyperkalemia Immediately After Birth

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Study Design A
Data Collection B
Statistical Analysis C
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Patient: Male, newborn
Final Diagnosis: Hyperkalemia
Symptoms: Respiratory distress • ventricular tachycardia
Medication: —
Clinical Procedure: Exchange transfusion
Specialty: Pediatrics and Neonatology

Objective: Unknown ethiology

Background: Hyperkalemia is an important cause of arrhythmias and a medical emergency that requires urgent treatment. The etiology is usually multifactorial. It is most frequently caused by impaired potassium secretion, followed by transcellular potassium shifts and an increased potassium load.

Case Report: A male newborn developed monomorphic ventricular tachycardia 2 hours after birth. He was born in the 35th week of gestation by urgent C-section following placental abruption. Laboratory results showed hemolytic anemia (Hb 99 g/L, Hct 0.31) with increased bilirubin levels and reticulocytosis, thrombocytopenia (39×10^9/L), hypoglycemia (0.8 mmol/L), and severe hyperkalemia (9.8 mmol/L). Umbilical artery blood gas analysis showed hypoxemia with acidosis (pO_2 3.8 kPa, pH 7.21, pCO_2 7.84 kPa, HCO_3 23.3 mmol/L, BE –5 mmol/L). Creatinine (102 µmol/L) and urea (9.8 mmol/L) were mildly elevated. Inflammatory markers were also increased (CRP 26 mg/L, blood leukocyte count 24×10^9/L). Early-onset sepsis, caused by *Candida albicans*, was confirmed approximately 24 hours after birth. Non-invasive ventilation with 35–40% O_2 was necessary due to transient tachypnea. The neonate received a transfusion of packed red blood cells, a 10% glucose infusion, and empirical antibiotic therapy. Hyperkalemia accompanied by arrhythmias was treated with calcium gluconate, insulin, Sorbisterit enema, and, finally, by exchange transfusion.

Conclusions: We report a case of severe hyperkalemia in a newborn immediately after birth. Making a decision as early as possible regarding exchange transfusion is essential in patients with hyperkalemia with electrocardiogram changes and hemodynamic instability.

MeSH Keywords: Hyperkalemia • Intensive Care Units, Pediatric • Neonatology • Pediatrics

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Background

The serum potassium concentration is tightly maintained within the range of 3.5–5.0 mmol/L [1]. The threshold may be considerably higher in neonates (up to 6.5 mmol/L), especially if they are born prematurely [2]. The serum potassium level is the concentration of potassium measurable in the extracellular space, where only 2% of potassium circulates. The other 98% is distributed intracellularly, approximately 75% of it intramuscularly [3,4]. Hyperkalemia is a common electrolyte disorder and is the most arrhythmogenic [5].

Hyperkalemia is usually caused by the concurrence of various factors: increased potassium intake, excretion disorders, and/or transcellular shifts [6–8]. In neonates, inborn errors of metabolism (congenital adrenal hyperplasia) are a leading cause of severe hyperkalemia [8,9]. Hyperkalemia destabilizes myocardial conduction by decreasing the resting membrane potential, leading to increased cardiac depolarization and myocardial excitability [10]. It can cause an spectrum of adverse ECG abnormalities, from peaked T waves, beginning with levels above 6.5 mmol/L, to shortened QT intervals, prolonged PR intervals, heart conduction blocks, depressed P waves, and wide QRS complexes, which tend to merge with the peaked T wave into 'sine-wave' activity [11]. Severe hyperkalemia (above 8 mmol/L) can precipitate fatal arrhythmias such as ventricular tachycardia and fibrillation, leading to asystole [9,11–14].

The standard treatment protocol for severe hyperkalemia includes a combination of intravenous calcium chloride (or gluconate) to antagonize the ECG changes, insulin to redistribute the potassium into cells, sodium bicarbonate to reduce the metabolic acidosis, and oral (or rectal) sodium polystyrene sulfonate (suspended in sorbitol) to bind and remove potassium through the gastrointestinal tract [11]. Other treatment options include potassium-eliminating loop diuretics (e.g., furosemide) when renal function is sufficient. Alternatively, potassium elimination by hemodialysis or exchange transfusion is recommended when other measures fail [9–11,15].

Case Report

A male infant was delivered in the 35th week of gestation by urgent C-section after placental abruption. This was the mother's second pregnancy and second delivery. The mother was 35 years old at the time of delivery and her blood type was A RhD positive. Prenatal screenings for congenital infections revealed an old infection with *Toxoplasma gondii*. The indirect Coombs test was negative. The mother was treated with Euthyrox for Hashimoto's thyroiditis. The pregnancy was uncomplicated until the 35th week of gestation when the mother was hospitalized due to a severe vaginal bleed that necessitated an urgent C-section. The baby's birth weight was 3230 g, birth length 51 cm, and head circumference 34 cm. After delivery, the male infant was pale, icteric, and bradycardic and had decreased muscle tone (Apgar score 5/9). A generalized petechial rash was observed. He was tachy-dyspneic, with increased work of breathing and an SpO_2 of 80% breathing air. To achieve adequate saturation, 35–40% O_2 was needed. Non-invasive ventilation (nasal continuous positive airway pressure – CPAP) was necessary for 2 days due to transient tachypnea. Immediately after birth, the neonate was transferred to the neonatal ward. Laboratory tests revealed anemia (Hb 99 g/L, Hct 0.31), thrombocytopenia (39x10^9/L), hypoglycemia (0.8 mmol/L), and severe hyperkalemia (>9 mmol/L). To correct the anemia, a concentrated erythrocyte transfusion was given (35 ml of A positive RhD positive blood). Due to hypoglycemia, a bolus of 10% glucose was administered, followed by a continuous infusion of 10% glucose. After transfusion, the neonate's breathing and circulation stabilized and blood glucose levels increased. A mild tremor was occasionally observed, but he did not have any convulsions.

Due to his poor physical appearance, the neonate was transferred to the intensive care unit, where monomorphic ventricular tachycardia was recorded on the ECG. A blood sample from the umbilical vein again showed severe hyperkalemia (9.8 mmol/L). Calcium gluconate, sodium bicarbonate, rapid-acting insulin, and a Sorbisterit rectal enema were administered. Due to the persistently elevated levels of potassium, an exchange transfusion was performed, after which the potassium levels normalized.

Other laboratory values were also abnormal: CRP was increased (26 mg/L), with leukocyte count still within the normal range for newborns (24×10^9/L). Blood cultures were performed, and intravenous antibiotic therapy was started with ampicillin, gentamicin, and cefotaxime. All 3 antibiotics were discontinued after 5 days, when hemocultures and lumbar puncture sample were confirmed negative for bacterial growth. However, *Candida albicans* was isolated from the blood cultures, so treatment with fluconazole was initiated approximately 24 hours after birth and terminated after 7 days, when control blood cultures were negative. All subsequent blood cultures were negative, and the levels of inflammatory markers decreased.

Along with persistent anemia (Hb 96 g/L, Hct 0.32 on the second day), a marked reticulocytosis (reticulocyte percentage 20%, reticulocyte count 735×10^9/L) was also noted on day 10. Hyperbilirubinemia was present (serum bilirubin 304 µmol/L 24 hours after exchange transfusion). Due to severe thrombocytopenia (lowest platelet count 9×10^9/L, the average around 40×10^9/L in the first week of life), he also received multiple platelet transfusions during hospitalization.

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Kidney function on the first day of life revealed elevated blood creatinine (102 µmol/L) and urea (9.8 mmol/L). The mean serum creatinine values in healthy newborn population studies were found to be around 55 µmol/L on day 1, with the highest values around 90 µmol/L (97th percentile) [16]. Renal failure is indicated by serum creatinine levels higher than 15 mg/L (133 µmol/L) [17]. Adrenal gland insufficiency was excluded because our patient had an isolated high serum potassium level immediately after birth, without any additional electrolyte imbalance.

Umbilical artery blood gas analysis showed hypoxia with mild acidosis (pH 7.21, pO_2 3.8 kPa, pCO_2 7.84 kPa, HCO_3 23.3 mmol/L, BE -5 mmol/L). Venous blood gas analysis after non-invasive ventilation and transfusion showed persisting acidosis (pH 7.24, pCO_2 6.6 kPa, HCO_3 20.6 mmol/L, BE –6.8 mmol/L) with a pO_2 of 5.1 kPa and a mildly elevated lactate concentration (2.8 mmol/L).

Direct hyperbilirubinemia was present (219 µmol/L on the second day) and liver enzymes were elevated (ALT 7.2 µkat/L and AST 15.2 µkat/L, gamma-GT normal). Metabolic tests, performed to evaluate the direct hyperbilirubinemia, showed that plasma amino acids and acylcarnitine were within the normal range. Screening for organic acids in the urine found metabolites that could be explained by kidney or liver immaturity or liver damage. Due to persistently increased levels of bilirubin and liver enzymes, the neonate was followed up by a pediatric gastroenterologist and was treated with ursodeoxycholic acid up to 3.5 months of age, when the levels of liver enzymes and bilirubin normalized.

Heart ultrasound showed interventricular septal and right ventricular hypertrophy and a restrictive ventricular muscular defect, which was considered to be hemodynamically insignificant. Head ultrasound showed calcified blood vessels in the basal ganglia. The electroencephalogram was normal. Thoracic X-ray and abdominal ultrasound showed no anomalies. During hospitalization, bilateral congenital cataracts were diagnosed, without other ocular malformations. Surgery on both eyes was indicated at the age of approximately 1 year and 10 months.

The hemoglobin level was persistently decreased (78–98 g/L, Hct 0.23–0.35) during hospitalization and after discharge. Marked reticulocytosis (reticulocyte percentage up to 47%, reticulocyte count 1456×10^9/L) persisted at later outpatient visits. Thrombocytopenia did not reoccur. Mild hyperkalemia (up to 6 mmol/L) was detected at control visits. Severe hyperkalemia and arrhythmias did not reoccur. The peripheral blood smear showed moderate anisocytosis and poikilocytosis. Immune hemolytic anemias were excluded, glucose-6-phosphate dehydrogenase mutation was not identified, and the EMA (Eosin-5-maleimide binding) test for hereditary spherocytosis was negative. The etiology of the recurrent hemolytic episodes remained unknown.

Discussion

We report an interesting clinical case of a newborn with severe hyperkalemia that led to a life-threatening arrhythmia. Such severe hyperkalemia is rarely seen in newborns, especially immediately after birth. Since the newborn had multiple complications during delivery, we hypothesize that the cause of the severe hyperkalemia was multifactorial. Below, we discuss the most probable contributing factors.

Hemolysis

The baby had a low Hb (99 g/L) after birth, and anemia was constantly present during follow-up, despite repeated transfusions. Increased bilirubin levels, reticulocytosis, and blood smear findings led to a diagnosis of hemolytic anemia. Hemolysis was therefore the most obvious and probable cause of hyperkalemia, but the etiology of hemolysis remained unidentified. Both the mother and child had the same blood group (A, RhD positive), and indirect and direct Coombs tests were negative, which excluded immune hemolytic anemia. Erythrocyte enzyme deficiencies and membranopathies were also excluded. Recently, a blood sample for the RNA isolation and additional diagnostics of possible glucose 6-phosphate dehydrogenase deficiency was collected.

It is unusual for hemolysis alone to cause such a significant increase in the serum potassium concentration. It is difficult to determine the impact of hemolysis on the serum potassium level. Some articles have mentioned that even small extracellular potassium shifts (1% of the intracellular potassium) can cause severe hyperkalemia [9]. Goyal and Schmotzer [18] studied the degree of hemolysis (HI, hemolytic index) and its contribution to elevation of the serum potassium concentration. They showed that the highest levels of hemolysis (HI grade 7, free Hb 0.5–1 g/L) can cause serum potassium concentrations of 8–9 mmol/L. Unfortunately, the HI could not be determined in our case since it is defined by the concentration of free Hb in the serum. Free Hb is not as specific for hemolysis in neonates compared to older children and adults, therefore the levels of free Hb were not checked in any of the blood samples.

The reticulocyte count is thought to be significantly correlated with the degree of hemolysis when erythrocyte survival is less than 11 days (severe hemolysis) [19]. In a study by Fehr et al. [19], patients with severe hemolysis had reticulocyte counts from 188×10^9/L to 1030×10^9/L. In our case, the reticulocyte count was 735×10^9/L on day 10 and it peaked at 1456×10^9/L during outpatient follow-up. Such a high degree

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of hemolysis could probably cause severe hyperkalemia, but it is evident that severe hemolysis was also present throughout the patient's hospitalization and follow-up, without any recurrence of severe hyperkalemia, even when the reticulocyte count peaked at the age of 3 months (1456×10^9/L, 47%). Therefore, we believe that there were other cofactors after birth that contributed to hyperkalemia.

Hypoxemia and acidosis

Acidosis can cause an extracellular shift of potassium (due to hydrogen ion exchange). However, there is an inconsistent response to respiratory acidosis and a limited response to organic acidosis (i.e., lactic acidosis), as organic acids tend to move across membranes with the hydrogen ion [3,8,11]. Hyperkalemia can be caused by mineral acidosis [11,20], which was not present in our case.

Non-oliguric hyperkalemia has been defined as a serum potassium of 7 mmol/L during the first 72 hours of life in the presence of a urinary output of >1 mL/kg/h [21]. The incidence of non-oliguric hyperkalemia is high in preterm infants (up to 52%) [21,22]. This may partly be due to a shift of potassium from the intracellular space to the extracellular space associated with immature functioning of Na/K ATP (adenosine triphosphate)ase activity [23]. Non-oliguric hyperkalemia due to Na/K ATPase pump immaturity was unlikely in our case, since it is almost exclusively present in extremely preterm infants, and potassium levels usually rise in the first 24 hours after birth [22,24].

Some animal studies have found that an increase in serum potassium is correlated with the severity of the ischemic insult [25,26]. Several authors have investigated the rise in serum potassium during ischemic events (e.g., cardiac arrest, sepsis, hypoperfusion states, and hemorrhagic shock) and suggested that Na/K ATPase is inhibited due to hypoxia, which decreases the influx of potassium [26,27]. Other researchers have suggested that ATP-sensitive potassium channel activation is the main mechanism through which the efflux of potassium causes hyperkalemia during muscle cell ischemia. ATP-sensitive potassium channels are found in many tissues, including skeletal muscle cells, red blood cells, pancreatic cells, and nonvascular and vascular smooth muscle cells. These channels are increasingly activated when the cellular ATP/adenosine diphosphate ratio is decreased, as seen in hypoxic conditions [28–30].

Our patient suffered hypoxia due to placental abruption. At birth, secondary apnea was present and non-invasive ventilation was necessary to initiate breathing. Umbilical artery blood gas analysis showed hypoxia with acidosis (pO_2 3.8 kPa, pH 7.21, pCO_2 7.84 kPa, HCO_3 23.3 mmol/L). Perinatal hypoxia might have partially contributed to hyperkalemia in our patient.

Conclusions

We report a case of severe hyperkalemia in a newborn immediately after birth. It is essential to make a decision as early as possible regarding exchange transfusion in a patient with hyperkalemia with electrocardiogram changes and hemodynamic instability.

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Conflict of interest

None.

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