Respiratory Distress Revealing Severe Hyperkalemia in the Neonatal Period

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Abstract: Hyperkalemia in neonates is defined by a potassium level greater than 6 mmol/L, being classified as severe if it exceeds 7 mmol/L. It most commonly occurs in very preterm infants born at less than 28 weeks of gestation and is rarer in term infants. Clinical signs during the neonatal period are non specific and often manifest as bradycardia or tachycardia. The causes are numerous, with some of the rarer causes including type 1 pseudohypoaldosteronism (PHA1), which is characterized by mineralocorticoid resistance leading to a severe early salt-wasting syndrome with life-threatening risks. We report the case of a neonate who presented with early respiratory distress syndrome and severe hyperkalemia at 48 hours of life. Laboratory examinations suggested a salt-wasting syndrome. Hormonal assessments revealed normal 17-OHP levels, with elevated renin and aldosterone. A diagnosis of type 1 pseudohypoaldosteronism was established. Treatment for hyperkalemia involved a full therapeutic escalation; however, unfortunately, the newborn died at 10 days of life.

Index terms: Term neonate, respiratory distress syndrome, dehydration, hyperkalemia, hyponatremia, salt-wasting syndrome, metabolic acidosis, aldosterone, renin, pseudohypoaldosteronism.

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I. Introduction

Hyperkalemia in neonates is defined as potassium levels greater than 6 mmol/L, and it is considered severe if it exceeds 7 mmol/L. It occurs most frequently in preterm infants born at less than 28 weeks of gestation, and less commonly in full-term neonates. Clinical signs during the neonatal period are non specific and often manifest as bradycardia or tachycardia. There are multiple causes, one of the rarer causes being type 1 pseudohypoaldosteronism (PHA1), which is characterized by resistance to mineralocorticoids.

Aldosterone is a hormone secreted by the adrenal glands and works with the renin-angiotensin system to maintain the balance of circulating blood volume.

Despite elevated levels of aldosterone and plasma renin, type 1 pseudohypoaldosteronism (PHA1) presents with neonatal salt loss, hypotension, hyperkalemia, hyponatremia, and metabolic acidosis. It is often misdiagnosed as congenital adrenal hyperplasia (CAH). It presents in primary (genetic) and secondary (or transient) forms.

The primary form has two clinical entities :

- A less severe autosomal dominant (AD) variant with isolated renal involvement (renal PHA1).
- A severe generalized variant (generalized PHA1), which is autosomal recessive (AR) with involvement of multiple target organs, often leading to a poor prognosis and death due to cardiac arrhythmias.

We report the case of a neonate who presented with respiratory distress syndrome and hyperkalemia at 48 hours of life.

Case: This is a female neonate, admitted to the neonatology unit at 4 hours of life for respiratory distress syndrome.

There is a noted consanguinity of the second degree, and she is the first child of the couple, with the mother having no significant medical history.

The pregnancy was monitored and carried to 35 weeks and 5 days of amenorrhea, complicated by pregnancy-induced hypertension for which she was treated with magnesium and later with methyldopa, and gestational diabetes for which she was treated with insulin.
The premature birth was unexplained, via vaginal delivery, with a birth weight of 2700 grams and a good Apgar score.
Immediately after birth, the neonate exhibited mild respiratory distress, which then worsened, leading to her transfer to the neonatology unit. Clinical examination revealed signs of dehydration, no melanoderma, male-type genitalia, and normally positioned gonads. The biological assessment showed hyperkalemia at 11 mmol/L (normal values: 3.5-5), hyponatremia at 111 mmol/L (normal values: 134-144), and decompensated metabolic acidosis. Renal function was normal: plasma creatinine was 4 mg/L, and renin levels were normal. Hormonal assessment revealed 17 OHP and cortisol levels without abnormalities, and elevated aldosterone (Table 1).
Thus, a renal cause and congenital adrenal hyperplasia were excluded. The diagnosis of type 1 pseudohypoaldosteronism was retained based on the clinical and biological signs.

Table 1: Additional Exams Assessment

Biological assessment	Results
Plasma Na (mmol/l) (Normal Range: 134-144)	111 mmol/L
Plasma K (mmol/l) (Normal Range: 3.5-5)	11 mmol/L
Blood creatinine (mg/l) (Normal Range: 2.4-8.5)	4 mg/l
Urinary Na (mmol/l) (Normal Range: < 20 mmol/l)	65 mmol/l
Blood pH	7.17
HCO3 (mmol/l) (Normal Range: 22-29)	8 mmol/l
Blood cultures	Negative
Plasma renin (Normal Range: 1-2 ng/ml/h)	27 ng/ml/h
Cortisol (µg/dl) (Normal Range: 6-17)	45.3 µg/dl
Aldosterone (Normal Range: 8-172 pg/ml)	181 pg/ml
Electrocardiogram	Arrhythmia
Echocardiography	Normal

*Normal Range (based on age)

A treatment regimen was initiated consisting of ion exchange resin , calcium gluconate, insulin infusion, and nebulized salbutamol, along with a continuous infusion of isotonic saline at 0.9% in the absence of 3%, fludrocortisone at a dose of 100 µg/day, and sodium bicarbonate to correct metabolic acidosis.
Hyperkalemia was refractory to treatment despite therapeutic escalation and worsened, leading to tachycardia followed by ventricular fibrillation. The newborn experienced several cardiac arrests and died at 10 days of life.

DISCUSSION

Causes of hyperkalemia are multiple and can be of renal, hematological (acute hemolysis), or hormonal origin. The most frequent hormonal causes are adrenal insufficiency and congenital adrenal hyperplasia, with the latter presenting as a salt-wasting syndrome occurring after a symptom-free interval of 7 to 20 days, and the 17 OHP levels are elevated.

A much rarer cause of salt-wasting syndrome is pseudohypoaldosteronism [2]. It was first described by Cheek and Perry [9] in 1958 in an infant with severe salt-wasting syndrome; since then, only isolated cases have been reported, rarely case series in the literature [10].

We distinguish [11] :

-Renal PHA type 1, which follows an autosomal dominant inheritance pattern with heterogeneous mutations on the gene coding for the mineralocorticoid receptor, resulting in the absence of aldosterone binding to the receptor. Salt loss is confined to the kidneys and, biologically, is characterized by salt wasting, hyponatremia, hyperkalemia, and metabolic acidosis, with elevated plasma levels of renin and aldosterone. While treatment often involves oral salt supplementation, the clinical expression of this condition can vary significantly. It generally has a benign course, followed by spontaneous remission over time. The spontaneous resolution of symptoms after early childhood in patients with renal PHA type 1 may be attributed either to a dietary shift from low-sodium human breast milk to a saltier diet or to the maturation of renal tubular sodium reabsorption with age.
- Generalized pseudohypoaldosteronism type 1 is a systemic form that results in generalized receptor resistance to mineralocorticoids, following an autosomal recessive inheritance pattern due to homozygous or compound heterozygous mutations in the SCNN1A, SCNN1B, and SCNN1G genes coding for the ENaC protein (epithelial sodium channel). This is a very rare condition, with a prevalence of about 1 in 80,000 births; clinical expression is variable and presents during the neonatal period as a salt-wasting syndrome with dehydration and weight loss. The biological profile shows hyponatremia, refractory hyperkalemia, metabolic acidosis, and elevated natriuresis. Diagnosis is confirmed by measuring aldosterone, which is very high, alongside elevated renin, as was the case with our patient [12][13].
The clinical presentation may mimic congenital adrenal hyperplasia due to enzyme blockage, which should be systematically investigated, although the absence of a free interval makes it very unlikely, along with conditions such as hypoaldosteronism due to aldosterone deficiency or Bartter syndrome presenting in the neonate.
The treatment for the acute phase consists of administering high doses of sodium to correct sodium losses, which could not be accomplished in our patient due to the unavailability of hypertonic saline. Additionally, measures to correct hyperkalemia and acidosis are taken. Treatment with hydrocortisone or fludrocortisone may be initiated while awaiting diagnostic confirmation.
Ion exchange resins, which act as "potassium binders," are widely used in managing hyperkalemia. The most commonly used potassium binders are sodium polystyrene sulfonate (Kayexalate^{R}) and calcium polystyrene sulfonate. However, sodium-containing resin is preferred over calcium-containing resin as it simultaneously corrects hyponatremia as well as hyperkalemia [14]. The dose of Kayexalate is 1 g/kg every 6 hours as needed. Oral use is not recommended in neonates, and only the rectal route is advised.
Ideally, genetic counseling should be implemented based on genetic studies of the index case so that the family can benefit for future births.
PHA type 1 is considered severe due to adverse effects on the respiratory tract, salivary glands, colon, and sweat glands in addition to the renal system [15]. Children with viable forms have an increased vulnerability to respiratory and skin infections, experience recurrent diarrhea episodes, and show growth delays.

Conclusion :

Although very rare, generalized pseudohypoaldosteronism type 1 remains a cause of neonatal hyperkalemia that must be quickly considered, hence the importance of systematically conducting hormonal assessments that could be responsible for a salt-wasting syndrome. While congenital adrenal hyperplasia (CAH) remains the most common endocrine cause of salt-wasting syndrome that should be considered in principle, pediatricians need to be capable of identifying much rarer causes, especially in the absence of a free interval, with the occurrence of severe hyperkalemia within the first 24 hours, to establish an early diagnosis. Hyperkalemia is challenging to treat and can lead to severe arrhythmias and then death. PHA type 1 differs from other types of pseudohypoaldosteronism by its early, generalized, and severe nature; genetic testing enables diagnostic confirmation and genetic counseling that will be invaluable to the family.

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