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HYPERKALEMIA IN NEWBORN: CASE REPORT

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Abstract

Hyperkalemia can be a sign of many diseases; however, this condition is rare in children. We present and analyze the case of hyperkalemia in an infant born to the mother with SARS-CoV-2 infection in the third trimester. Hyperkalemia was an accidental finding in a child hospitalized for pneumonia. Despite prolonged elevated potassium levels, the typical clinical signs of hyperkalemia were absent; additionally, as the ECG changes were not representative of the magnitude of hyperkalemia. Among other findings, mild thrombocytosis was revealed; however, it did not correlate with hyperkalemia. Other possible causes of the hyperkalemia, including kidney diseases, aldosterone deficiency, drug exposure, endocrine disorders (diabetes and adrenogenital syndrome), familial disorders, neuromuscular disorders, acidosis, hypertension, or genetic syndromes were ruled out. In conclusion, many pathological conditions should be ruled out in the case of hyperkalemia in a newborn. The question of SARS-CoV-2 transmission from the pregnant woman to the fetus in the third trimester of pregnancy and possible effect of the infection on electrolyte balance in the newborn requires further study.

Keywords: *electrolyte balance, hyperkalemia, COVID-19, infants*

Introduction

An electrolyte imbalance accompanies many congenital and acquired childhood diseases and conditions [1-5]. Potassium is one of the most important microelements in the human body, involved in maintaining acid-base balance in the blood, water balance of intercellular and intracellular fluids, water-salt balance, and osmotic pressure [6]. Approximately 98% of potassium is contained in the cells.

Hyperkalemia, or higher than normal potassium level, can be a sign of many disorders, however, this condition is rare in children [7]. Hyperkalemia is also recognized as one of the major risk factors contributing to potentially life-threatening cardiac arrhythmic complications; thus, it is among indications for emergency medical care [8-10].

Hyperkalemia is defined as a serum or plasma potassium concentration is higher than 5.5 mmol/L, but in premature and young children the upper limit can reach 6.5 mmol/L [11]. Infants have a higher normal blood potassium level as a result of reduced urinary potassium excretion caused by relative insensitivity to aldosterone and decreased glomerular filtration rate [10].

Even though children are less likely to develop hyperkalemia than adults, childhood hyperkalemia is not uncommon, and severe hyperkalemia (K^+> 7 mmol/L) is a serious clinical problem that requires urgent measures to address [10].

The ongoing incidence of COVID-19 cases poses numerous challenges to medical professionals and researchers worldwide. Extrapulmonary symptoms and rare symptoms not characteristic of other respiratory infections continue being reported [12-13]. Therefore, unexplained symptoms in patients with COVID-19 require careful analysis to identify possible links to this insidious and multifaceted infection.

Herein we present and analyze the case of hyperkalemia in an infant born to the mother with SARS-CoV-2 infection in the third trimester.

Case presentation

A newborn boy, aged 22 days, entered the clinic with the mother reporting that he suffers from nasal congestion, cough, irritability, fever of 37.2-37.7° C, and poor appetite. The malaise began 10 days before the hospitalization, and the patient received symptomatic therapy (vasoconstrictor nasal drops), but since there was no improvement, he was referred to hospital.

The anamnesis shows that the boy was born from the second full-term pregnancy, via spontaneous vaginal delivery, with the weight of 3070 g. At 32-33 weeks of gestation the mother had COVID-19 (confirmed by positive PCR nasopharyngeal swab for SARS-CoV-2). The Apgar score was 8 at 1 minute and 9 points at 5 minutes after birth. The patient received BCG vaccination and was discharged from the maternity ward on the third day. Early neonatal period was non-contributory. Formula was used for feeding due to hypogalactia.

On examination, predisposition to tachycardia (heart rate 180-165 per min), respiratory rate – 46 breaths per minute, SpO2 – 97%, weight – 3950 g, blood pressure – 90/60 mmHg. Hyperemia of the pharynx, difficulty of nasal breathing and slight mucous secretion were seen. Heart tones were rhythmic. At auscultation over lungs the exhalations were extended, weakened breath in the lower parts on the right, at percussion – shortening in the sound in the lower parts on the right were observed. The abdomen was soft. The liver was +2 cm below the edge of the costal arch, the spleen was not palpable. Urination was free, diuresis was sufficient.

Complete blood count revealed normal level of leukocytes (6,750 – 10,640/μL) and mild thrombocytosis (559–621/μL).

Laboratory test for markers to SARS-CoV-2 in the infant by ELISA revealed elevated IgG antibodies, 11.24 IU (reference up to 1.1 IU), while IgM antibodies were normal, 0.064 IU (reference up to 1.0 IU). Biochemical blood test showed hyperkalemia (7.53 mmol/L), hypercalcemia (3.12 mmol/L), normal sodium (131.9 mmol/L), phosphorus (2.34 mmol/L), chloride (107.0 mmol/L) and magnesium levels (1.0 mmol/L). Laboratory indicators of liver and kidney function (urea, creatinine), hemostasis systems did not exceed normal level for the age.

IgM antibodies to SARS-CoV-2 in the mother were 0.054 IU.

Serum potassium levels remained high, ranging from 7.53 mmol/L to 6.16 mmol/L, and returned to normal only on the 20th day of treatment. However, 3 months after discharge from the hospital, potassium levels increased again while platelets level during this period of follow-up was consistently high (Table 1).

ECG monitoring detected sinus tachycardia (a heart rate of 190 beats per minute), and peaked T waves. Starting on day 5 of hospitalization the heart rate decreased to 154 beats per minute. Chest X-ray detected focal right pneumonia.

Diagnostic search for the cause of hyperkalemia included determining blood glucose, 17-hydroxyprogesterone (17-OHP), aldosterone (ALD), thyroid-stimulating hormone (TSH), and free thyroxine (FT4). The results did not exceed respective reference values, ruling out the hormonal origin of hyperkalemia in this child. Urine and blood pH was normal.

Abdominal ultrasound, with an emphasis on the adrenal glands, echocardiography, and neurosonography were performed, allowing to rule out damage to the internal organs and central nervous system.

The treatment included antibiotics (ampisulbin) and symptomatic therapy. In order to reduce cardiotoxic effect of severe hyperkalemia ($K^+ > 7.00$ mmol/L), 10% glucose IV solution was administered; however, a good hypokalemic effect was induced by 0.9% sodium chloride solution administered orally.

Gradually, concurrent with ongoing treatment, the serum potassium level has normalized. The child was discharged from the hospital in satisfactory condition to family doctor observation on the 20th day after admission.

Discussion

Hyperkalemia in children may be fictitious and true [6, 10]. Fictitious or pseudohyperkalemia because of hemolysis, tissue lysis due to blood sampling was ruled out considering that repeated blood samples were obtained using standard methods.

True hyperkalemia in children is most commonly associated with renal failure, acidosis, and hormonal defects, including mineralocorticoids, aldosterone or insulin [14].

We searched for and subsequently ruled out the following possible causes of hyperkalemia in the patient: kidney diseases, aldosterone deficiency, drug exposure, endocrine disorders (diabetes, adrenogenital syndrome), familial disorders, neuromuscular disorders, acidosis, hypertension, and genetic syndromes.

Kidney diseases were ruled out as urea, creatinine levels were normal. There were no changes in urine tests, as well as in clinical presentation. The patient had not taken any medication before, except of short course of vasoconstrictor nasal drops.

The patient was repeatedly examined by an endocrinologist with the appointment of a series of tests to exclude endocrinological conditions associated with hyperkalemia. Adrenogenital syndrome was ruled out considering normal levels of 17-OHP during newborn screening and further investigations.

Normal urine and blood pH and normal level of aldosterone allowed to rule out hyperkalemic renal tubular acidosis or tubular hyperkalemia.

This clinical case presented some challenging questions. First, whether the IgG antibodies to SARS-CoV-2 detected in the infant were transplacental maternal antibodies or whether placental and neonatal SARS-CoV-2 transmission possible? The second question is what caused hyperkalemia in the newborn and whether was related to the intrauterine SARS-CoV-2 infection?

Cases of SARS-CoV-2 transmission from the mother to the fetus through the placenta, although infrequent, have been reported [15-17]. For instance, a case of transplacental transmission of SARS-CoV-2 infection at 35 weeks of gestation manifested by neurological disorders in the newborn was described [18]. Studies suggest that maternal viremia causes infection of the placenta, which leads to an inflammatory reaction and subsequently to neonatal viremia.

An unequivocal confirmation of mother-to-fetus transmission of SARS-CoV-2 relies on the virus detected by either PCR or in culture in the amniotic fluid collected prior to membrane rupture, in the blood collected within the first 12 hours of birth, or in the cord blood [19]. Unfortunately, in our case,

none of these fluids were examined for the viral infection within the relevant time frame. Similarly, neither cord blood nor neonatal blood collected within the first 12 hours of birth was tested for the presence of IgM antibodies.

Published reports showed that children born to mothers infected with COVID-19 in the first and second trimesters of pregnancy had IgG antibodies to SARS-CoV-2 after birth, but no IgM antibodies [20]. Moreover, maternal antibodies to SARS-CoV-2 were shown to be transmitted through the placenta after both asymptomatic and symptomatic infection, and their concentration in the cord blood correlated with the concentration of maternal antibodies and duration between the onset of infection and childbirth.

However, in our case, more than 2 months has passed from the time of COVID-19 infection in the mother to the test for IgM antibodies in the child, so this may explain why no IgM antibodies were detected in the child.

At the same time, another case study showed that in some neonates whose mothers suffered from COVID-19 in the third trimester, both IgM and IgG antibodies to SARS-CoV-2 were detected, while other neonates had only IgG. However, in that study the levels of inflammatory cytokine IL-6 were elevated in all infants, despite the absence of visible clinical signs of infection and the absence of IgM [21]. Therefore, we cannot completely rule out the impact of SARS-CoV-2 on the fetus during maternal infection. Thrombocytosis detected after the birth is a condition that often has been found during the residual period of COVID-19 infection, and it can also be a sign of transferred intrauterine infection [22].

Thrombocytosis itself could be a cause of hyperkalemia, although while previously we observed elevated platelet count in children after COVID-19, this was the only instance of hyperkalemia we detected. Additionally, there was no correlation between platelet count and potassium concentration. We observed a decrease and even a temporary normalization of potassium levels, even though platelets remained high.

Hyperkalemia in patients with COVID-19 is most often associated with kidney damage, which is one of the main target organs of SARS-CoV-2 infection; kidney damage often underlies severity of the symptoms and produces sequelae of the disease [23, 24]. However, electrolyte imbalance, including hyperkalemia is common in patients with SARS-CoV-2 infection, even without acute kidney injury and is associated with high cell turnover [12].

Despite the prolonged increase in serum potassium concentration in our patient, characteristic clinical signs of hyperkalemia, such as severe weakness, hypoactive or absent bowel sounds, indicating dynamic intestinal obstruction, and neurological disorders were not detected; ECG changes did not correlate with the severity of hyperkalemia. This is consistent with the literature, which also reports asymptomatic course of hyperkalemia in the majority of pediatric patients [6, 25].

So called transient hyperkalemia usually has short duration, and results from reduced urinary potassium excretion associated with a low glomerular filtration rate in neonates, as well as adaptation in tubular transport along the nephron [26]. Although in our case the hyperkalemia was an accidental finding in a child hospitalized for pneumonia, it lasted for more than one month from the date of birth.

The impact of SARS-CoV-2 infection in pregnant women on renal function and electrolyte balance in the fetus and newborn cannot be completely ruled out, so the role of COVID-19 in pregnant women in the development of neonatal hyperkalemia remains controversial and requires further study.

Conclusions

Several pathological conditions should be ruled out in the case of hyperkalemia in a newborn. The question of transmission of SARS-CoV-2 from a pregnant woman to the fetus in the third trimester of pregnancy and its possible effect on electrolyte balance in the newborn requires further study.

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References

1. Naseem, F., Saleem, A,, Mahar, I.A., Arif F. (2019). Electrolyte imbalance in critically ill

paediatric patients. *Pak J Med Sci*, 35(4), 1093-1098.
2. Boyarchuk, O., Dmytrash, L. (2019). Clinical Manifestations in the Patients with Primary Immunodeficiencies: Data from One Regional Center. *Turkish Journal of Immunology,* 17(3), 113-119.
3. Brodsky, N.N., Boyarchuk, O., Kovalchuk, T., et al. (2020). Novel compound heterozygous variants in NHLRC2 in a patient with FINCA syndrome. *J Hum Genet,* 65(10), 911-915.
4. Boyarchuk, O., Volyanska, L., Dmytrash, L. (2017). Clinical variability of chromosome 22q11.2 deletion syndrome. *Cent Eur J Immunol,* 42(4), 412-417.
5. Boyarchuk, O., Balatska, N., Chomomydz, I. (2019). Evaluation of warning signs of primary immunodeficiencies. *Pediatria Polska – Polish Journal of Paediatrics,* 94(6), 337-341.
6. Lehnhardt, A., Kemper, M.J. (2011). Pathogenesis, diagnosis and management of hyperkalemia. *Pediatr Nephrol,* 26(3), 377-384.
7. Hollander, R., Mortier, G., van Hoeck K. (2016). Hyperkalemia in young children: blood pressure checked? *Eur J Pediatr*, 175(12), 2011-3.
8. Bianchi, S., Aucella, F., De Nicola, L. et al. (2019). Management of hyperkalemia in patients with kidney disease: a position paper endorsed by the Italian Society of Nephrology. *Journal of Nephrology,* 32(4), 499-516.
9. Collins, A.J., Pitt, B., Reaven, N. et al. (2017). Association of serum potassium with all-cause mortality in patients with and without heart failure, chronic kidney disease, and/or diabetes. *Am. J. Nephrol,* 46, 213-221.
10. Masilamani, K., van der Voort, J. (2012). The management of acute hyperkalaemia in neonates and children. *Arch Dis Child,* 97(4), 376-380.
11. Shaffer, S.G., Kilbride, H.W., Hayen, L.K., Meade, V.M., Warady, B.A. (1992). Hyperkalemia in very low birth weight infants. *J Pediatr*, 121(2), 275-279.
12. Gupta, A., Madhavan, M.V., Sehgal, K. et al. (2020). Extrapulmonary manifestations of COVID-19. *Nat Med*, 26, 1017–1032.
13. Sancho-Shimizu, V., Brodin, P., Cobat, A., et al. (2021). SARS-CoV-2-related MIS-C: A key to the viral and genetic causes of Kawasaki disease? *J Exp Med,* 218(6), e20210446.
14. Schweiger, B., Moriarty, M.W., Cadnapaphornchai, M.A. Case report: severe neonatal hyperkalemia due to pseudohypoaldosteronism type 1. *Curr Opin Pediatr*, 21(2), 269-271.
15. Egloff, C., Vauloup-Fellous, C., Picone, O., Mandelbrot, L., Roques, P. (2020). Evidence and possible mechanisms of rare maternal-fetal transmission of SARS-CoV-2. *J Clin Virol,* 128, 104447.
16. Zeng, H., Xu, C., Fan, J., et al. (2020). Antibodies in Infants Born to Mothers With COVID-19 Pneumonia. *JAMA*, 323(18), 1848-1849.
17. Dong, L., Tian, J., He, S., et al. (2020). Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. *JAMA*, 323(18), 1846-1848.
18. Vivanti, A.J., Vauloup-Fellous, C., Prevot, S., et al. (2020). Transplacental transmission of SARS-CoV-2 infection. *Nat Commun,* 11(1), 3572.
19. Shah, P.S., Diambomba, Y., Acharya, G., Morris, S.K., Bitnun, A. (2020). Classification system and case definition for SARS-CoV-2 infection in pregnant women, fetuses, and neonates. *Acta Obstet Gynecol Scand,* 99, 565–568.
20. Zhao, Y., Huang, B., Ma, H., Shang, Y., Nie, X., Zou, L. (2020). Follow-up Study on the Outcomes of Recovered Pregnant Women with a History of COVID-19 in the First and Second Trimesters: A Case Series from China. *Matern Fetal Med*, 3(1), 24-32.
21. Flannery, D.D., Gouma, S., Dhudasia, M.B., et al. (2021). Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios. *JAMA Pediatr,* e210038.
22. Feld, L., Belfer, J., Kabra, R., et al. (2020). A Case Series of the 2019 Novel Coronavirus (SARS-CoV-2) in 3 Febrile Infants in New York. *Pediatrics,* 146(1), e20201056.
23. Naicker, S., Yang, C-W., Hwang, S-J. (2020). The novel coronavirus 2019 epidemic and kidneys. *Kidney Int,* 97, 824–828.
24. Prabhu, V., Hsu, E., Lestin, S., Soltanianzadeh, Y., Hadi, S. (2020). Bradycardia, Renal Failure, Atrioventricular Nodal Blockade, Shock, and Hyperkalemia (BRASH) Syndrome as a

Presentation of Coronavirus Disease 2019. *Cureus,* 12(4), e7816.
25. Daly K, Farrington E. Hypokalemia and hyperkalemia in infants and children: pathophysiology and treatment. *J Pediatr Health Care.* 2013; 27(6):486-496; quiz 497-8.
26. Bonilla-Félix M. Potassium regulation in the neonate. *Pediatr Nephrol.* 2017; 32(11):2037-2049.

Table 1. Patient serum electrolyte levels and blood platelet counts levels during and following hospitalization

Parameter	K (potassium), mmol/L	Na (sodium), mmol/L	Platelets, cells/ml
Reference range	3.6-6.1	132-147	150-450
Hospitalization (day after admission to the hospital)			
3rd	7.53	131.9	621
4th	6.64		
7th	6.16	138.5	617
10th	7.08		569
13th	7.09		559
20th	3.87		548
After hospitalization (period after discharge from the hospital)			
2 weeks	5.62	139	535
6 weeks	5.30	136	614
3 months	5.95	142	575
6 months	5.20	138.5	375

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