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Case Report

Nephrogenic Diabetes Insipidus or Bartter Syndrome? A Dilemma of Refractory Hypokalemia in Pregnancy: A Case Report from Soedono Regional Public Hospital in Madiun

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ABSTRACT

Hypokalemia is a rare condition in pregnant women. Muscle weakness and life-threatening heart damage can occur if the baseline condition is not treated, especially if it recurs and persists. The differential diagnosis in recurrent hypokalemia includes nephrogenic diabetes insipidus, characterized by the kidneys' inability to respond to vasopressin to concentrate urine, or Bartter syndrome, a tubulopathy resulting from a rare genetic mutation affecting the loop of Henle, leading to potassium wasting. A 24-year-old primigravida at 35/36 weeks gestation presented with refractory hypokalemia, indicative of diabetes insipidus or a differential diagnosis of Bartter syndrome. The patient complained of limb weakness combined with polydipsia, polyuria, and a history of periodic paralysis due to severe hypokalemia since 2016. She consistently took potassium supplements and monitored her potassium levels. Since becoming pregnant in November 2021, the patient has been hospitalized three times due to limb weakness, with the lowest serum potassium level recorded at 1.6. Throughout her pregnancy, fetal growth and development remained within normal limits, and her blood pressure ranged from 100-120/60-80. In patients with limb weakness, evaluating serum potassium levels is crucial. In this case, the suspicion of nephrogenic diabetes insipidus could not be confirmed due to the unavailability of antidiuretic hormone (ADH) tests. Bartter syndrome, although rarely encountered, should be considered in patients with recurrent hypokalemia. The challenge in Indonesia lies in the lack of specific gene examinations for diagnosis, making diagnostics relatively difficult. Our recommendation for cases like this is to conduct ADH examinations and thoroughly investigate refractory hypokalemia.

Keywords: Hypokalemia, ADH, Bartter Syndrome, Diabetes insipidus, Pregnancy.

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INTRODUCTION

Diabetes insipidus (DI) is a rare endocrine disorder reported to occur in one in 30,000 people.[1] This syndrome is particularly prevalent during pregnancy, leading to only a small number of reported cases of DI in pregnant individuals. DI during pregnancy is infrequent but can give rise to severe complications, such as preeclampsia and abnormalities in liver function. DI may either persist from a pre-existing syndrome discovered before pregnancy or manifest for the first time during pregnancy and subsequently resolve.[2]

Common signs of DI include polydipsia and polyuria. Diagnosing DI during pregnancy is challenging due to alterations in water metabolism. The initial step involves confirming diuresis to rule out diabetes mellitus. In pregnant patients with polydipsia and polyuria, a diagnosis of diabetes insipidus can be established when serum osmolality exceeds 285mOsm/L and there is an absence of glycosuria, hypokalemia, or hypercalcemia. The exclusion of organic diseases is crucial for a DI diagnosis.[3]

In our case, the patient also presented with refractory hypokalemia, prompting an investigation for other conditions or syndromes similar to DI, which may indicate an underlying organic disease.

Bartter syndrome encompasses a group of rare genetic disorders specifically affecting kidney function.[4] This disorder impairs the kidney's ability to reabsorb salt, leading to an imbalance in electrolytes and fluid concentration in the body. Symptoms include hypokalemia, polyuria, and normal arterial blood pressure. Bartter syndrome results from various genetic defects affecting ion transporters or channels along the ascending loop of Henle, crucial for regulating blood volume and NaCl reabsorption.[5] Potassium wasting is a condition characterized by the loss of salt in the proximal tubule segment, leading to the secretion of potassium from the distal nephron and subsequent excessive potassium excretion. Consequently, Bartter syndrome disrupts the normal concentration and dilution of urine, which, under normal conditions, involves salt absorption in the loop of Henle, with antidiuretic hormone (ADH) playing a central role in maintaining the concentration gradient in the medulla for urine concentration.[6]

CASE DESCRIPTION

A 24-year-old woman, a primigravida at 35/36 weeks of gestation, presented with complaints of weakness. Upon reviewing the patient's anamnesis, it was disclosed that she had a pattern of consuming a significant amount of water, approximately 5-6 liters per day, accompanied by an equal volume of urine production. The patient did not report nausea, vomiting, or loose stools. Since 2016, the patient has been experiencing weakness in the limbs, and her serum potassium test results consistently indicated values ≤ 2 mmol/l. Treatment involved

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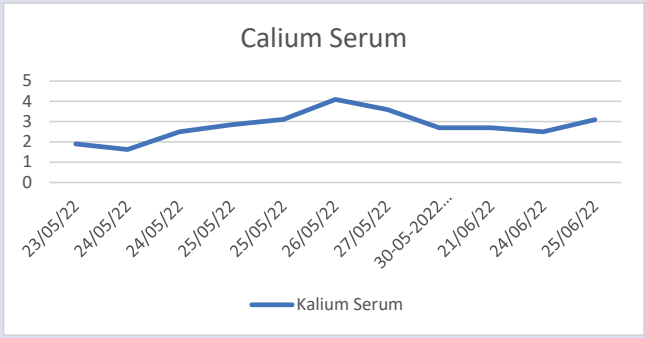

Figure 1: Patient Serum Potassium Levels Over Time.

the administration of potassium supplementation, and the patient had undergone multiple treatments for the same complaint during her medical history. During her current pregnancy, the patient had been hospitalized twice before—at 6/7 weeks and 16/17 weeks of gestation with the same complaints. Routine potassium supplementation was provided as part of the standard care during pregnancy. Throughout the pregnancy, the patient underwent regular check-ups, with blood pressure consistently ranging from 100-120/60-80. Ultrasound evaluations indicated normal fetal development according to gestational age, with an appropriate amount of amniotic fluid. Despite routine controls and supplementation, the patient continued to experience periodic weakness.

At the 35/36-week gestational age check-up, the patient complained of weakness, and the ultrasound evaluation revealed fetal development in line with the gestational age. The interpretation indicated a fetal weight of 2,563 g, with a normal amount of amniotic fluid. Doppler velocimetry evaluation showed results within normal limits. However, the serum potassium examination revealed a level of 1.9 mmol/l, prompting the patient to take additional oral potassium supplementation. As the evening progressed, her condition worsened, leading her to seek re-evaluation at the Comprehensive Emergency Obstetric and Neonatal Care (CEmONC), where the serum potassium results were found to be 1.6 mmol/l. The patient was diagnosed as G1P0000, with a single live intrauterine fetus at 35/36 weeks of gestation, along with periodic paralysis due to Refractory Hypokalemia due to Diabetes Insipidus, alongside a differential diagnosis of Bartter syndrome. Additional intravenous potassium supplementation was administered. Fluid balance calculations were conducted to assess complaints of polyuria and polydipsia, revealing a fluid intake of 3 liters to 5.8 liters per 24 hours and urine production of 4.1 liters to 6.8 liters per 24 hours. A urine potassium examination yielded results of 85 mmol/l. Throughout the treatment, the patient underwent periodic evaluations for serum potassium, with results documented in the following graph (Figure 1).

Following the latest treatment, the patient underwent a contrast-free head MRI, specifically focusing on the pituitary gland, to assess for abnormalities. The MRI revealed normal findings. At 39/40 weeks of gestation, the serum potassium evaluation indicated a level of 2.5 mmol/l. Corrective measures were taken for the patient's serum potassium, and it was decided to proceed with termination. A baby girl weighing 3300 g and measuring 49 cm, with an Apgar score of 8-9, was delivered at 39 weeks without complications. The amniotic fluid at birth was clear, and the baby exhibited spontaneous breathing. Follow-up monitoring of the mother can involve assessing sodium osmolality, serum, and urine volume, as well as addressing any complaints related to polyuria, polydipsia, or nocturia.[7]

DISCUSSION

In the aforementioned case, refractory hypokalemia is observed, a condition characterized by a persistent and resistant decrease in serum potassium levels. Hypokalemia, a prevalent clinical issue, can arise from oral or parenteral potassium intake, with the majority stored in the intestines and excreted in urine.[8] The reduction in serum potassium concentration can be attributed to factors such as diminished consumption, increased translocation into cells, or augmented losses via urine, gastrointestinal tract, or sweat. Over 98% of total body potassium is intracellular, primarily residing in muscle tissue. The equilibrium between cellular and extracellular fluid potassium distribution is chiefly regulated by the Na-K-ATPase pump in the cell membrane.[9] Hypokalemia can result from heightened Na-K-ATPase pump activity and/or alterations in other potassium transport pathways, leading to increased potassium influx into cells.[1,8,10,11] Patients may also exhibit periodic hypokalemic paralysis, a neuromuscular disorder characterized by episodes of muscle weakness, occasionally severe or even resulting in paralysis affecting respiratory muscles. Acute attacks, marked by a sudden shift of potassium into cells, can reduce serum potassium levels to as low as 1.5-2.5 mEq/L. Notably, serum potassium levels return to normal during intervals between recurring paralysis episodes, a distinctive feature aiding in the differentiation of periodic paralysis from other forms of hypokalemic paralysis. Patients experiencing hypokalemic periodic paralysis typically display low urinary potassium excretion, a contrast to the normal urine potassium results observed in the present case. This discrepancy serves as a valuable diagnostic indicator, distinguishing these patients from those with hypokalemic paralysis due to renal potassium loss.[8]

Interestingly, in this case, where a pattern of polyuria and polydipsia was evident in the patient, the fluid balance during treatment revealed a range of 3,000-5,850 cc/24 hours with a fluid output of 4,100-6,800 cc/24 hours, aligning with signs indicative of diabetes insipidus (DI), which is linked to the loss of renal concentration and aquaresis. In the absence of vasopressin, either due to central causes or resistance from nephrogenic causes, the permeability of renal collecting ducts diminishes, resulting in decreased water resorption. This may lead to an increase in urine flow and a decrease in urine osmolality to less than 100 mOsm/kg, with a specific gravity ≥ 1.010.[7] In most cases, pregnant women can augment central vasopressin release to ensure sufficient water reabsorption, preventing polyuria.[12] However, in cases where there is impaired reserve vasopressin secretion, as seen in pre-existing or subclinical DI, polyuria and polydipsia become apparent during pregnancy. DI itself comprises three subtypes, each exhibiting distinct characteristics: Transient DI, Central DI, and Nephrogenic DI.[13] Transient DI is typically associated with conditions like preeclampsia (PE) or liver function abnormalities, often manifesting in the third trimester.[1,14,15] Central DI can be identified through an MRI examination of the head without contrast, focusing on the normal pituitary. In this case, the absence of central DI is established through the MRI findings, suggesting a potential inclination towards nephrogenic DI. Unfortunately, the unavailability of an antidiuretic hormone (ADH) examination and osmolality poses a challenge in definitively diagnosing DI in this patient.

In addition to DI, cases of hypokalemia, as mentioned earlier, can also be associated with Bartter Syndrome,[5,16] characterized by electrolyte and acid-base abnormalities, predominantly hypokalemia and metabolic alkalosis in nearly all instances.[17,18] Other deviations include elevated serum renin and aldosterone levels, alongside reduced magnesium and phosphate levels observed in some patients.[19] Urine electrolyte analyses reveal heightened excretion of sodium, potassium, and PGE2. Typically, Bartter Syndrome is accompanied by fetal growth disturbances and polyhydramnios[20]; however, these manifestations were not evident in the current case based on the results. It is worth noting that diagnosing Bartter Syndrome involves examining specific genes, a procedure that is, unfortunately, not feasible in this particular case.[6]

CONCLUSION

Hypokalemia, though a common clinical issue, plays a crucial role in life, given its potential to be perilous and fatal, particularly when manifested

in pregnant women. This case report underscores the significance of examining the condition of pregnant women presenting with refractory hypokalemia. It emphasizes the need for a specialized approach in both treatment and management to avert potential complications that may arise for both the mother and the baby.

CONFLICTS OF INTEREST

The author reports no conflicts of interest in this work.

ETHICAL CONSIDERATION

The study was ethjically approved by the Research and Community Service of Dr. Soedono Madiun Regional Public Hospital, Indonesia, reff letter No : 070/20.150/313/2022.

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AUTHOR'S CONTRIBUTION

All the authors contributed to the study from the conceptual framework, data gathering, and analysis until the study's results were interpreted upon publication.

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