Unexpected Hyperkalemia During Kawasaki Disease

Kawasaki Hastalığının Seyri Sırasında Beklenmedik Şekilde Gelişen Hiperkalemi

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ABSTRACT

Pseudohyperkalemia is defined as a markedly elevated serum potassium level with a normal plasma potassium concentration. It is mainly caused by leucocytosis and thrombocytosis. Here we report an infant treated with aspirin for Kawasaki disease who developed hyperkalemia during follow-up. He was finally diagnosed with pseudohyperkalemia based on a normal whole blood potassium level measured with a blood gas analyser.

Key Words: Hyperkalemia, Kawasaki disease, Pseudohyperkalemia

ÖZ

Psödohiperkalemi, plazma potasyum konsantrasyonu normal iken serum potasyum seviyesinin belirgin şekilde yüksek bulunması olarak tanımlanır. Esas olarak lökositoz ve trombositozdan kaynaklanır. Burada, Kawasaki hastalığı için aspirin tedavisi alan ve takip sırasında hiperkalemisi gelişen bir bebek bildirilmektedir. Kan gazı cihazı ile ölçülen tam kan potasyum seviyesinin normal bulunması ile psödohiperkalemi tanısı konulmuştur.

Anahtar Kelimeler: Hiperkalemi, Kawasaki hastalığı, Psödohiperkalemi

INTRODUCTION

Hyperkalemia is defined as a potassium level greater than 5.5 mmol/L (mEq/L) (1). Haemolysis should be investigated first when the potassium level is unexpectedly high and inconsistent with the patient's clinical status and treatments received. Fist clench during venipuncture, prolonged use of tourniquets, squeezing the extremity during blood collection and holding the sample for more than 30 minutes before testing all lead to haemolysis. Several drugs can cause hyperkalemia (1,3). Hyperkalemia associated with non-steroidal anti-inflammatory drug (NSAID) has rarely been reported (4,5).

Another cause is pseudohyperkalemia. Pseudohyperkalemia is defined as a markedly elevated serum potassium level with a normal plasma potassium concentration. It is mainly caused by leucocytosis and thrombocytosis (2). Here, we report an infant who was treated with aspirin for Kawasaki disease and developed hyperkalaemia during follow-up.

CASE

A 7-month-old male patient was admitted with a 5-day history of fever and generalized maculopapular rash. The patient was born

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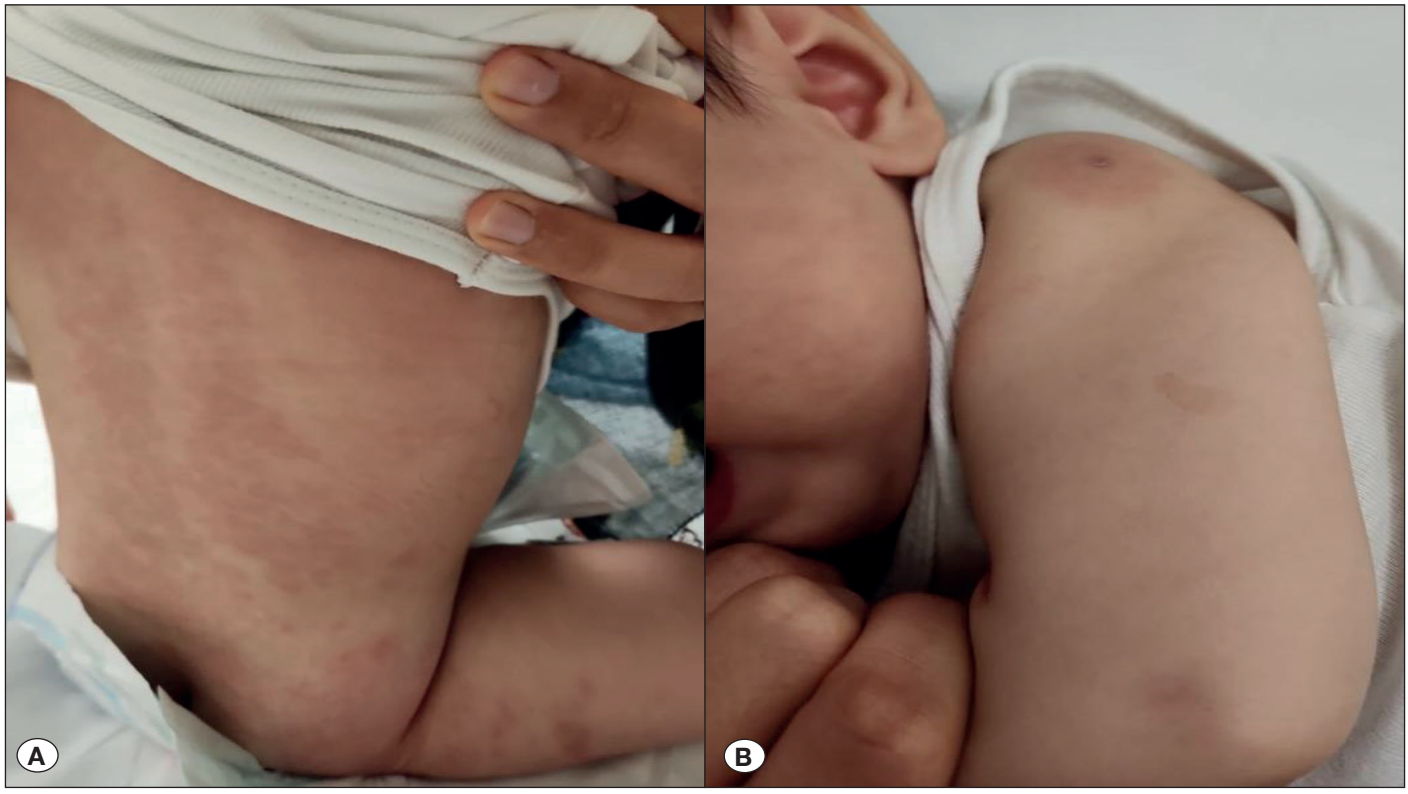

Figure 1: A) There was a maculopapular rash predominantly on the arms and legs and in the lumbar region, **B)** Hyperemia around the BCG vaccination scar

at 40 weeks with a weight of 3800 g and has been completely healthy until now. On physical examination, his temperature was 38.6°C, a 1.5x1 cm cervical lymphadenopathy was palpated in the right cervical region. The patient had bilateral hyperemic conjunctiva, hyperemic lips, non-pitting edema of the hands and feet; the scrotum was edematous. There was a maculopapular rash predominantly on the arms and legs and in the lumbar region and hyperemia around the BCG vaccination scar (Figure 1). Laboratory tests showed hemoglobin 7.9 g/dL (10.2–13.4 g/dL), white blood cell count (WBC) 19.460x10^6/L (6.600-15.600x10^6/L), platelets 574.000x10^6/L (240.000-520.000x10^6/L), C-reactive protein (CRP) 301 mg/L (normal range 0-5). An echocardiogram performed with the diagnosis of Kawasaki's disease showed small pericardial effusion of surrounding the heart. IVIG at a dose of 2 g/kg was infused over 12 hours and acetylsalicylic acid (ASA) at a dose of 50 mg/kg/day and ceftriaxone was started. On day 5 of ASA treatment, the dose was reduced to 5 mg/kg because the patient remained afebrile. Serologic tests for common viral infections associated with maculopapular rash were negative. Ceftriaxone was stopped because there was no growth in blood and urine cultures. On the same day, laboratory tests revealed a potassium level of 5.9 mEq/L (Table I). The patient had not received any intravenous fluids for last days. The patient's nurse was interviewed and asked if there were any difficulties in taking the blood. It was noted that the patient's blood was easily drawn without any external pressure and after the blood sample was taken, it was immediately sent to the laboratory. There was no hyperpotassemic changes were seen on the ECG. A pneumatic tube system was used to transport the sample to laboratory. While this system allows the sample to reach the laboratory faster, it also increases the risk of haemolysis. However, visual inspection of the serum sample that reached the laboratory showed no haemolysis. The venous blood sample collected in a lithium heparin-containing syringe and analyzed on a blood gas analyser immediately after collection was normokalemic and potassium levels were found to be 4.9 mEq/L. On the following day, the serum potassium level was found to be 6.1 mEq/L. Potassium level measured on blood gas analyser was 3.7 mEq/L. The diagnosis of NSAII-associated hyperkalemia was ruled out as the potassium level was normal on blood gas analyser. As hyperkalemia developed simultaneously with thrombocytosis, the patient was considered to have pseudohyperkalemia secondary to thrombocytosis (Table I). The patient's echocardiographic findings were normal at follow-up and the patient discharged at the 11th day of hospitalisation.

DISCUSSION

The most common cause of hyperkalemia in children is mechanical haemolysis during difficult blood draws from small veins. Once the possibility of mechanical haemolysis has been ruled out, the first step in investigating the etiology of

Table I: The laboratory findings of the patient during hospitalisation

Hospitalisation day	1	6	7	9	10	11	12	13
K (mEq/L)	4.2	5.9/5.8	6.1	5.8	5.5	4.5	4.6	4.9
K (mEq/L) (measured by blood gas analyser)		4.9 /4.2	3.7	4.2	-	-	-	-
PLT (x 10^6/L)	574.000	631.000		1.232.000		837.000	752.000	360.000
Hgb (g/dL)	7.9	10.5		10		9.0	9.3	10.9
WBC (x 10^6/L)	19.460	13.490		12.970		6.750	6.090	9.450
Na (mEq/L)	135	133	134	136		137	136	134
Glu (mg/dL)	115		80					90
Urea (mg/dL)	13	17	23	15				17
Krea (mg/dL)	0.09	0.27	0.22	0.27				0.24
CK (U/L)	26							
GFR (mL/min/1.73 m^2)	340	113	139	113				127
UA (mg/dL)	2.1	2.6	2.4	2.5				
ALB (g/L)	31	38	41					
AST (U/L)	24	25	24	22				24
ALT (U/L)	31	15	14	16				14
ALP (U/L)	85		104	121				
LDH (U/L)	404	357	302					
Ca (mg/dL)	9.1	10.6	9.9	10.5				
Mg(mg/dL)	2	2.2		2.3				
P (mg/dL)	3.2	6.2	4.7					
CRP (mg/L)	301	22						
Ph		7.53	7.44	7.43				
HCO3		24	24	24				
pCO_2		29	36	36				
BE		1.7	0.4	0.0				
Lactate		1.98	1.87	1.29				

Glu: *glucose,* ***US:*** *uric acid,* ***ALB:*** *albumin,* ***AST:*** *aspartate aminotransferase,* ***ALT:*** *alanine aminotransferase,* ***ALP:*** *alkaline phosphatase,* ***LDH:*** *lactate dehydrogenase,* ***Ca:*** *calcium,* ***P:*** *phosphorus,* ***Na:*** *sodium,* ***K:*** *potassium,* ***GFR:*** *glomerular filtration rate,* ***Hgb:*** *haemoglobin,* ***WBC:*** *white blood cell count,* ***PLT:*** *platelets,* ***CRP:*** *C-reactive protein,* ***ASA:*** *aspirin,* ***CLO:*** *clopidogrel*

hyperkalemia should be to check for oral or parenteral potassium intake (6). Secondly, it is important to check whether the patient is taking medication that may increase serum potassium levels. The commonly used drugs that may increase potassium levels are potassium-sparing diuretics, angiotensin-converting enzyme inhibitors, cyclosporine, tacrolimus, trimethoprim, mannitol and NSAIDs (3). Hyperkalemia associated with NSAIDs has been reported in elderly patients with diabetes and signs of diabetic nephropathy or type IV renal tubular acidosis and underlying renal insufficiency as well as in young and nondiabetic patients (5).

Since 98% of body potassium is intracellular, a small release of potassium from the inside to the outside of the cell can significantly affect the serum potassium concentration (7). Potassium is the major cation in the intracellular fluid of platelets, leukocytes, and erythrocytes. Therefore, when these cells are lysed during clotting, potassium is released, and the serum potassium concentration rises. The increase in serum potassium levels is not significant when platelet or leukocyte counts are normal but can be significant when platelet or leukocyte counts are markedly elevated (8).

Although it is more prominent in thrombocytosis, serum potassium levels can be higher than plasma potassium levels even when platelet counts are normal (9). This is probably due to the fact that serum contains activated platelets and plasma contains non-activated platelets. The platelet activation, which occurs during clotting, is associated with potassium release from platelets (10). The mean difference between serum and plasma is 0.36 ± 0.18 mmol/L (2). It has been reported that there is a significant positive correlation between serum potassium level and platelet count, and that serum potassium increases by 0.11 mmol/L for every 100x10^9/L increase in platelet count (10). Another study found a significant correlation between serum potassium and platelet count, with serum potassium increasing by 0.27 mEq/L per 100 x 10^9/L platelets ($r = 0.640$; $p<0.001$) (11). Serum potassium levels and platelet counts are not entirely directly proportional. While the potassium level

initially increased linearly with the platelet count, it decreased at higher platelet counts. This decrease has probably been interpreted as a decrease due to the re-entry of potassium into the erythrocytes to maintain homeostasis (7). As there is a positive but poor correlation between platelet count and serum potassium, correction of serum potassium by formulating according to platelet count has not been recommended (12).

In a study conducted in 16 patients with Kawasaki disease, both serum and plasma potassium levels were measured in the same blood sample. Serum potassium levels were higher than plasma potassium levels in all patients. There was a strong positive correlation between platelet count and the difference between serum and plasma potassium levels (8). Our patient had thrombocytosis as expected during Kawasaki disease. Pseudohyperkalemia associated with thrombocytosis was the most likely diagnosis in our patient because the whole blood potassium was normal.

It was reported that when serum, plasma and whole blood potassium levels were analysed in the same patient, serum potassium level was found higher than plasma and plasma was higher than whole blood. For whole blood potassium, blood was drawn with a lithium heparin injector and was analysed in the blood gas analyser. When potassium was measured in plasma, it was thought that the centrifugation performed to separate plasma from cells could lead to cell destruction and consequently an increase in plasma potassium. Therefore, plasma potassium is higher than whole blood (13). In our patient, we analysed whole blood potassium with a blood gas analyser. Plasma potassium is not a test that is done very often in our hospital. However, it is the most appropriate method to accurately determine potassium levels in patients with pseudohyperkalemia.

With this case we would like to draw attention to pseudohyperkalemia. In a patient with inappropriately high serum potassium levels, the possibility of pseudohyperkalemia should be considered. This will avoid unnecessary laboratory evaluations and unnecessary changes in treatment. As plasma potassium measurement is not widely used, it may not be considered by clinicians, as in this case. Pseudohyperkalemia can be practically excluded by plasma potassium measurement.

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