

CASE REPORT

Pseudohyperkalemia associated with essential thrombocytosis; a hint for better clinical practice

Fatemeh Yaghoubi¹  | Davood Dalil²

¹Nephrology Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

²Student Research Committee, Faculty of Medicine, Shahed University, Tehran, Iran

Correspondence

Fatemeh Yaghoubi, Nephrology Research Center, 4th floor, Shariati Hospital, North Kargar Avenue, Tehran, Iran.

Email: yaghoobifatemeh@yahoo.com

Abstract

A 75-year-old man was admitted with a diagnosis of diabetic ketoacidosis and hyperkalemia. During the treatment, he developed refractory hyperkalemia. Following our review, diagnosis of pseudohyperkalaemia secondary to thrombocytosis was made. We report this case to remind the importance of clinical suspicion of this phenomenon to prevent its serious consequences.

KEYWORDS

hyperkalemia, potassium, pseudohyperkalemia, thrombocytosis

1 | INTRODUCTION

Routine blood tests are taken in clinical practice for almost all hospitalized patients, and serum electrolyte evaluation is always considered. The normal serum potassium (K^+) ranges from 3.5 to 5 meq/L in healthy individuals. K^+ value more than 5 meq/L is defined as hyperkalemia, and when exceeds 7 meq/L, it is called severe hyperkalemia.¹ Hyperkalemia is an emergency condition and calls for immediate intervention. The release of potassium from activated thrombocytes during blood clotting, which is necessary for the recovery of serum, always causes the serum potassium to be higher than its plasma values. However, this difference should not exceed 0.4 meq/L.²

Pseudohyperkalemia is defined as a raised serum potassium with concurrent normal plasma potassium levels. In this situation, the in vitro potassium concentration raises without any actual increase in the in vivo values (which is called true hyperkalemia).³ Hyperkalemia without any related clinical symptoms or obvious risk factors strongly raised the suspicion of pseudohyperkalemia. Substantially, pseudohyperkalemia must be noted, because the wrong administration of hyperkalemia treatment in this condition can lead the patient to severe hypokalemia and cause

serious complications such as tachycardia, ventricular fibrillation, and hypoventilation.⁴ Even in some cases, pseudohyperkalemia may cause patients to undergo unnecessary hemodialysis.⁵ Therefore, it is significant to be familiar with this situation and perform the proper cause-related intervention to prevent inappropriate diagnosis and treatment. This report documented a case of spurious severe hyperkalemia (pseudohyperkalemia) associated with essential thrombocytosis, in a 75-year-old man.

2 | CASE PRESENTATION

A 75-year-old Iranian man admitted to the emergency ward of Shariati Hospital, Tehran, Iran, with symptoms of weakness, lethargy, nausea, and vomiting. His past medical history was remarkable for diabetes mellitus, hypertension, and hyperlipidemia. The patient was on metformin 500 mg daily and losartan 25 daily but admitted to not always being compliant.

On examination, the patient was alert and oriented. Her temperature, O_2 saturation, respiratory rate, and pulse rate were normal. But his systolic blood pressure was 147 over 73 mmHg. Initial blood tests revealed a

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blood sugar (BS) of 472 mg/dL (normal range less than 140 mg/dL), blood urea nitrogen 52 mg/dL (normal range 6–24 mg/dL), and serum creatinine 1.3 mg/dL (normal range 0.6–1.3 mg/dL for men). The serum potassium (K^+) was high (8 meq/L, normal range 3.5–5 meq/L) which indicated the severe hyperkalemia. The serum sodium (Na^+) was within a normal range (140 meq/L, normal range 135–145 meq/L). The ECG showed no changes associated with hyperkalemia.

The arterial blood gas (ABG) test showed pH 7.27 (normal range 7.35–7.45), pCO_2 33 mmHg (normal range 41–51 mmHg), and bicarbonate (HCO_3^-) 15.2 mmol/L (normal range 23–29 mmol/L), which confirmed the condition of metabolic acidosis. Also, the urine analysis reported 1+ protein and 1+ ketone. Based on findings, including BS > 250 mg/dL, pH < 7.30, bicarbonate < 18 mmol/L, positive urine ketones, and $K^+ > 7$ meq/L, the patient was admitted to the endocrinology service due to diabetic ketoacidosis (DKA) and severe hyperkalemia.

3 | TREATMENT AND OUTCOME

He was initially treated for severe hyperkalemia of 8 meq/L by administration of 10% intravenous calcium gluconate and regular insulin. Also, infusion of half-saline serum and fast-acting insulin were prescribed to manage the DKA at the endocrinology ward. The patient's potassium was monitored daily during hospitalization. On day 2, the serum potassium level was checked every 4 h to evaluate the response to hyperkalemia treatment, which showed treatment-resistance hyperkalemia with a mean potassium level of 6.98 mEq/L (Figure 1). Therefore, the

patient was referred to the nephrology department for consultation.

Following the review of the patient's file and the treatments taken for him by the nephrology service, we found out that the patient has severe thrombocytosis. At the time of our examination, the patient's serum potassium was 7 meq/L and the platelet count was 2,071,000/ μ L (normal range 150,000–400,000/ μ L). According to these findings, we suspected pseudohyperkalemia associated with thrombocytosis. Thus, the plasma potassium level was requested, which was 3.8 meq/L. Consequently, after confirming the diagnosis of pseudohyperkalemia, hydroxyurea was administered for the treatment of thrombocytosis. During hospitalization, the complete blood tests were taken every day and the serum potassium level and platelet counts were monitored daily. Following the treatment of pseudohyperkalemia secondary to thrombocytosis, his serum potassium level decreased and remained within normal range. Figure 2 shows the decreasing trends of the serum potassium, creatinine, and platelets of the patient following thrombocytosis management.

4 | DISCUSSION

Hyperkalemia is a potentially life-threatening clinical condition. It is often diagnosed in hospitalized patients due to regular and sequential serum electrolyte tests. The hyperkalemic patient may complain of nausea, vomiting, paresthesia, and heart palpitation.⁶ It may cause ECG changes, including wide QRS, ST-segment depression, and peaked T-waves. However, there are multiple case reports of highly elevated potassium levels with no

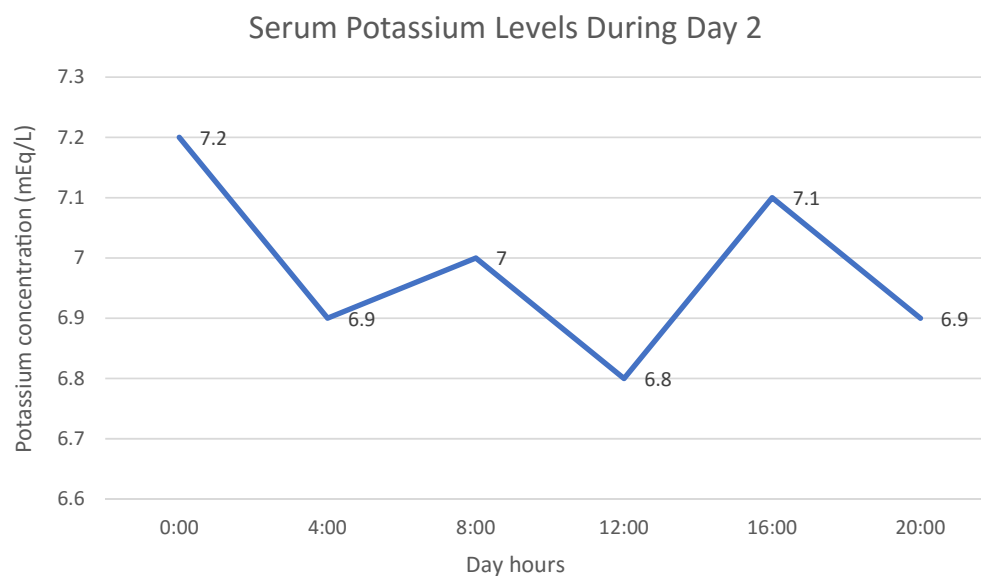


FIGURE 1 The changes of the serum potassium concentration during hospitalization on day 2.

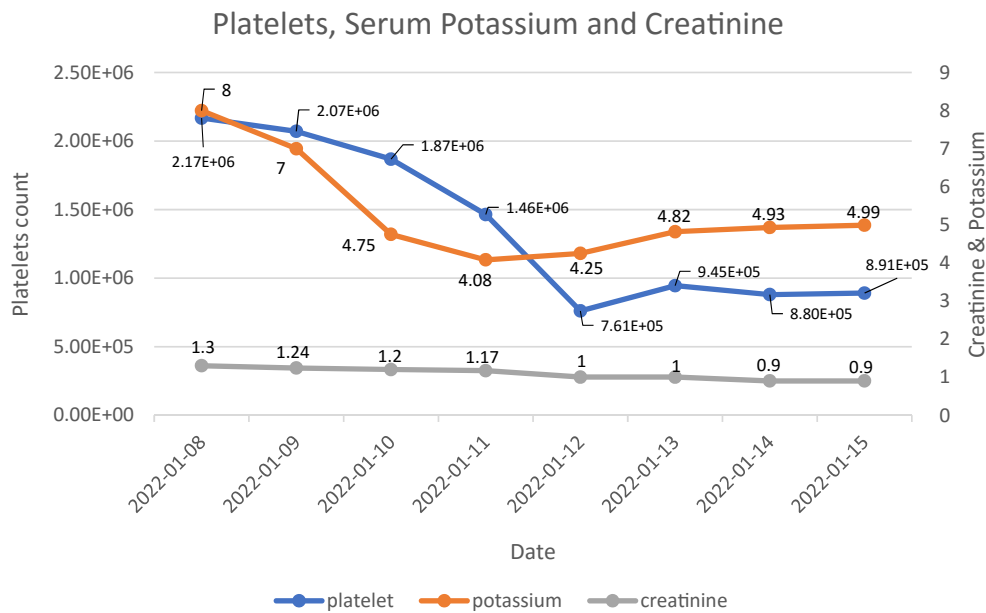


FIGURE 2 The changes of the serum potassium, creatinine, and platelets following the diagnosis of pseudohyperkalemia.

significant ECG changes.⁷ Hyperkalemia requires immediate medical interventions to shift extracellular K^+ intracellularly.

In DKA, the potassium levels decrease due to osmotic diuresis following both hyperglycemia and high concentration of ketone bodies. According to American Diabetes Association (ADA), the potassium deficit of a patient with ketoacidosis must be replaced by 20–30 mEq potassium per liter of infusion fluid when serum potassium is less than 5.2 mEq/L. Further, it must be noted that since insulin therapy shifts the potassium intracellularly, it is not recommended to start insulin for the potassium level <3 mEq/L to prevent the worsening of hypokalemia.⁸

Pseudohyperkalemia was first described by Hartmann and Melinkoff in 1955 as an *in vitro* phenomenon is characterized by the lack of signs and symptoms of true hyperkalemia, such as ECG changes, along with no response to common treatments of hyperkalemia.⁹ The difference between serum and plasma potassium is further increased in thrombocytosis.¹⁰

In the laboratory, a serum separating tube (SST) is used to collect a sample for measuring serum potassium. This tube contains silica particles and serum separating gel, such as acrylic gel polymer. The silica particles promote clotting, and the inert polymer gel forms a physical barrier between plasma and blood cells to stabilize the sample. Thus, due to the lack of anticoagulants, the platelets are degranulated, and the intracellular potassium is released.¹¹

In contrast, a tube containing an anticoagulant, such as heparin, is used to measure plasma electrolytes,

and the release of potassium from platelets is prevented.³ Therefore, numerous platelets in thrombocytosis cause more release of intracellular potassium from thrombocytes in the measurement of serum potassium while no elevation in plasma levels, leading to pseudohyperkalemia.

Furthermore, one of the common causes of pseudohyperkalemia is *in vitro* hemolysis, with a prevalence of up to 3.3%. This often occurs during or after blood collecting, particularly in the case of difficult venous accessibility.¹² In 1960, Nilsson et al. reported that the red blood cells could be assumed as a source of potassium releasing.¹³ The other cause is leukocytosis, in which the white blood cell's fragility increases and causes the release of intracellular potassium to blood circulation.¹⁴ Familial pseudohyperkalemia can also cause spurious hyperkalemia, which is characterized by a mutation in the ABCB6 transporter together with RBC defects, such as hereditary spherocytosis.¹⁵

In conclusion, pseudohyperkalemia must be served as a remarkable clinical condition that every clinical practitioner must be aware of this phenomenon to have better clinical management. The wrong treatment for pseudohyperkalemia, based on what is done for true hyperkalemia, can lead to life-threatening complications caused by severe hypokalemia. In this study, we presented a case of pseudohyperkalemia secondary to thrombocytosis to remind the importance of clinical suspicion of this phenomenon, especially in patients with thrombocytosis, to avoid erroneously therapeutic interventions, as well as complications of induced hypokalemia.

AUTHOR CONTRIBUTIONS

Fatemeh Yaghoubi: Conceptualization; supervision; writing – review and editing. **Davood Dalil:** Data curation; writing – original draft; writing – review and editing.

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None.

CONFLICT OF INTEREST STATEMENT

None of the authors have any conflicting interests to declare.

DATA AVAILABILITY STATEMENT

None.

ETHICAL APPROVAL

The Research Ethics Committee approved all procedures performed in the current study with the approval number: IR.TUMS.MEDICINE.REC.1400.1472. The patients expressed her informed consent through a written form.

CONSENT STATEMENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Fatemeh Yaghoubi  <https://orcid.org/0000-0003-3120-7111>

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