

PSEUDOHYPERKALEMIA DUE TO PNEUMATIC TRANSPORT IN ACUTE LYMPHOCYTIC LEUKEMIA PATIENTS: REPORT OF TWO CASES

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Pseudohyperkalemia occurs occasionally in leukemic patients with excessively elevated white blood cells. Early diagnosis of pseudohyperkalemia is crucial for proper treatment. Increased white blood cell fragility coupled with mechanical trauma may be the causal mechanism. We describe two cases of pseudohyperkalemia caused by mechanical disruption of white blood cells due to pneumatic tube transport of the specimens. In case when the white blood cell is extraordinarily elevated, specimen should be delivered in person instead of using pneumatic tube transport and specimen should be analyzed as soon as possible. Whole blood potassium analysis by blood gas analyzer is more reliable to confirm or rule out pseudohyperkalemia.

Keywords: Pseudohyperkalemia, pneumatic transport, acute lymphocytic leukemia.

I. INTRODUCTION

Hyperkalemia is a potentially life-threatening condition that requires immediate medical intervention. However, artifactual hyperkalemia or pseudohyperkalemia can be misleading as clinical manifestations which might result in inappropriate patient management. Pseudohyperkalemia is defined as an elevation in measured serum or plasma potassium caused by the cellular release of potassium during phlebotomy or specimen processing.¹ Pseudohyperkalemia is most seen secondary to red blood hemolysis.² It is also seen in patients with thrombocytosis and leukocytosis.³⁻⁷ Immediate recognition and appropriate interpretation of pseudohyperkalemia prevent misdiagnosis and unnecessary intervention.

Although the phenomenon of pseudohyperkalemia has long been

recognized and understood, it continues to be misinterpreted and improperly managed in the clinic. Differentiation of pseudohyperkalemia from true hyperkalemia, particularly in clinical situations in which cells may release potassium *in vivo* such as tumor lysis syndrome, is critical to avoid iatrogenic hypokalemia from treatment for pseudohyperkalemia. We describe two cases of pediatric patients admitted to our hospital with leukemia diagnosed with pseudohyperkalemia caused by pneumatic tube transportation. These cases highlight the importance of differentiation between true hyperkalemia and pseudohyperkalemia when evaluating patients with leukemia and aberrant chemistry results.

II. CASE PRESENTATION

Case 1. A 26-month-old male patient who has been diagnosed with T cell acute lymphocytic leukemia L1, was admitted to the National Children's Hospital for introduction chemotherapy on 14th September 2019. His laboratory tests on the second day of

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admission showed elevated potassium level of 5.5 mmol/L (reference range 3.5 - 5 mmol/L) with normal renal function and no other electrolyte abnormality. His cell blood count had white blood cell (WBC) of 279,500/ mm³. Plasma lactate dehydrogenase (LDH) activity was 2928 U/L, nearly 6 times higher than the upper limit of reference range (150 - 500 U/L). His plasma uric acid and renal function tests were in normal range. The pediatric oncologist was concerned about the tumor lysis syndrome (TLS) and requested tumor lysis syndrome panel measurement every 6 hours and managed prevention TLS by hyperhydration. The plasma potassium level at that time was 8.9 mmol/L. The doctor asked the laboratory to check again for potassium level on this sample, the result was nearly the same, but no hemolysis was documented (Hemolysis index was normal). The electrocardiography (ECG)

was normal. Although the patient had no sign of hyperkalemia, he received treatment with nebulizing Ventolin, intravenous infusion (IV) of Insulin, Lasix, calcium gluconate, and oral Kayexalat. However, because there was not a correlation between the clinical presentation and plasma potassium level, whole blood potassium of this patient was checked right after the start of the treatment by using blood gas analysis. This provided a result of 3.7 mmol/L, totally within the normal range. Therefore, the plasma potassium was tested again by manually transporting whole blood in heparin collection tube to the laboratory rather than by pneumatic tube. Laboratory staff centrifuged the test tube immediately and the plasma potassium level dropped to 2.6 mmol/L, that was below the lower limit of potassium reference range. A tentative diagnosis of pseudohyperkalemia was made and the treatment was discontinued.

Table 1. Potassium result of specimens handled by different methods in patient number 1 on the second day of admission.

Sample No	Time Drawn	Potassium concentration (mmol/L)	Method of measurement*	Transportation
1	9:10	5.5	Venous plasma in heparin tube, indirect ISE on chemistry analyzer	Pneumatic tube
2	16:33	8.9	Venous plasma in heparin tube, indirect ISE on chemistry analyzer	Pneumatic tube
3	18:52	3.7	Arterial whole blood, blood gas analyzer	In person
4	21:55	2.6	Venous plasma in heparin tube, centrifugation and running right after sample reception, indirect ion selective electrode on chemistry analyzer	In person (after treatment)

**Internal quality control and external quality assurance are regularly performed following the good laboratory practices to ensure quality test results*

ISE: ion selective electrode

Case 2. An 8-year-old male patient has been diagnosed with T cell acute lymphocytic leukemia L2. He had been admitted at the surgical intensive care unit on 29th April 2022 with dyspnea, an anterior mediastinal tumor, superior vena cava syndrome, lesions of leukemia in kidneys, pleural, and a lot of lymph nodes in the abdomen. TLS panel was measured every 6 hours and prevention of TLS was managed by hyperhydration. On the second day, he had plasma potassium concentration of 6.1 mmol/L, but calcium, urea and creatinine concentrations were in the normal range. He did not have any symptoms of hyperkalemia. TLS was suspected and he was giving IV Calcium gluconate, and aerosol Ventolin. After treatment, blood gas analysis revealed that his potassium level was 3.9 mmol/L. He had completed remission, but he dropped out after that. He had a check-up again on 30th November 2022 after abandonment. He

had been diagnosed with relapsed T cell acute lymphocytic leukemia with WBC of 472,200/mm³. His plasma potassium level was 9.7 mmol/L at the outpatient clinic although he had no sign of hyperkalemia. His plasma calcium was 2.1 mmol/L, below the lower limit of the reference range (2.31 - 2.64 mmol/L); and his plasma phosphorus was elevated (2.12 mmol/L compared with the normal range 1.06 - 1.96 mmol/l). His plasma uric acid and renal function tests were in normal range. Although the patient did not present any symptoms of hyperkalemia, TLS was suspected, and the patient was immediately referred to the emergency department; ECG and blood gas analysis were ordered. His whole blood potassium level was 3.6 mmol/L and ECG was normal. Doctor did not prescribed any drug for hyperkalemia. He experienced no cardiac event during the several days of his hospitalization. As such pseudohyperkalemia was confirmed and TLS was excluded.

Table 2. Potassium result of specimens handled by different methods in patient number 2 with relapsed T cell acute lymphocytic leukemia.

Sample No	Time Drawn	Potassium concentration (mmol/L)	Method of measurement*	Transportation
1	10:06	9.7	Venous plasma in heparin tube, indirect ISE on chemistry analyser	Pneumatic tube
2	11:19	3.6	Arterial whole blood, blood gas analyser	In person

*Internal quality control and external quality assurance are regularly performed following the good laboratory practices to ensure quality test results

ISE: ion selective electrode

III. DISCUSSION

Pseudohyperkalemia, the most common pre-analytical error, is defined as a rise in the plasma potassium concentration that occurs *in vitro* because of excessive leakage

of potassium from blood cells while blood is drawn, or afterward, in the absence of clinical evidence of electrolyte imbalance.¹ It can be misinterpreted as hyperkalemia and resulted in

inappropriate patient management.

Pseudohyperkalemia has been extensively reported and discussed in the literature.³⁻¹³ It is usually induced by excessive tourniquet time or fist clenching during phlebotomy, by hemolysis due to mechanical stress during venipuncture, or during specimen transportation.¹⁴ It has been increasingly seen in hematological disorders such as leukocytosis and thrombocytosis. The mechanism of pseudohyperkalemia in patients with severe leukocytosis is thought to be intracellular potassium release by cell lysis. The etiology of this white blood cell lysis may be multifactorial. Originally it was thought to be secondary to coagulation, but recent reports suggest mechanical stress may also play a major role. The use of vacuum sampling tubes, pneumatic tube transportation, and prolonged use of tourniquet may be contributing factors in leukocyte lysis.^{6,7,15,16} The weakness of leukemic white blood cells is also thought to be a mechanism that makes them more susceptible to lysis and release of potassium. Deficiency of metabolites can also cause hyperkalemia during long-term storage.¹⁷

TLS occurs because of the rapid lysis of proliferating tumor cells, leading to the release of intracellular contents into circulation.^{18,19} It is characterized by a classic tetrad of hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. Without prompt treatment, TLS can lead to acute kidney injury (AKI), cardiac arrhythmia, seizure, or sudden death. Hyperkalemia can be the most dangerous component of TLS.¹⁸ However, pseudohyperkalemia can lead to improper clinical treatment and expose patients to a high risk of hypokalemia.

The clinical course of our patient highlights the problem associated with the diagnosis of pseudohyperkalemia in patients with a greatly

elevated WBC. Patient number 1 with elevated potassium was initially not recognized as spurious despite a normal electrocardiography and lack of clinical manifestation for his hyperkalemia and he was thus briefly inappropriately treated. Patient number 2 had markedly elevated plasma potassium, slightly decreased calcium and sodium, and elevated phosphorus. He had a dramatically elevated WBC. Although no clinical signs of hyperkalemia were seen, tumor lysis syndrome was suspected in this patient based on laboratory data. This patient was sent to the emergency department for blood gas analysis and electrocardiography. His whole blood potassium level using blood gas analysis was in normal range and there was no abnormality in his ECG, that led to confirmation of pseudohyperkalemia and unnecessary treatment was avoided. In both patients, the measurement of potassium on arterial blood samples using blood gas analyzer has been a reliable method of diagnosis. This may be due to the rapid way blood is drawn and analyzed.²⁰

Our case also illustrates that often ordering a specimen redraw is not sufficient when pseudohyperkalemia is suspected. Close communication between clinical and lab staff is necessary in case of unexplained hyperkalemia condition. Leukocytosis is the cause of pseudohyperkalemia but is relatively rare and therefore less familiar to physicians in clinical practice. In the presence of severe leukocytosis, clinicians need to be alert to the possibility of pseudohyperkalemia. In this situation, we suggest that potassium level should be obtained by blood gas analysis, as this is an extremely quick and reliable test. Moreover, when the WBC is extraordinarily elevated, minimization of mechanical trauma to the blood sample should be implemented even if whole blood is used, such as in person

delivery of blood specimen instead of pneumatic tube transport and handling of the specimen as soon as possible.

IV. CONCLUSION

Early diagnosis of pseudohyperkalemia is important in all severe leukocytosis patients presenting with hyperkalemia, in the absence of clinical or ECG-based evidence of hyperkalemia, to avoid any harmful consequences resulting from improper management. Clinicians should be aware of pseudohyperkalemia in plasma samples from a patient with hematological malignancy. In such cases, whole blood potassium analysis using blood gas analyser is more accurate and can support confirmation or rule out pseudohyperkalemia.

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