Pseudohyperkalemia in a Patient with T-Cell Acute Lymphoblastic Leukemia and Hyperleukocytosis

Madison Merritt[1] Hannah Kline[2] Sudha Garimella[1,3] Robert Seigler[1,4]

[1] Department of Pediatrics, University of South Carolina School of Medicine Columbia, Columbia, South Carolina, United States
[2] MS4 USC School of Medicine Greenville, Greenville, South Carolina, United States
[3] Department of Pediatrics, Division of Pediatric Nephrology, University of South Carolina School of Medicine Greenville, Greenville, South Carolina, United States
[4] Department of Pediatrics, Division of Pediatric Critical Care, University of South Carolina School of Medicine Greenville, Greenville, South Carolina, United States

Address for correspondence Sudha Garimella, MBBS, Pediatric Nephrology, Greenville Health System, Greenville, SC 29615, United States (e-mail: sgarimella@ghs.org).

J Pediatr Intensive Care 2018;7:166–168.

Abstract

A 7-year-old girl presented with lymphadenopathy and bruising suggestive of leukemia. Complete blood count was significant for white blood cell count of 479,000/mm^3. Basic metabolic panel sent via pneumatic tube system was significant for potassium $>$ 10 mEq/L. The stat venous blood gas potassium level was 4.6 mEq/L. A 12-lead-ECG showed sinus tachycardia without peaked T-waves. It was determined that this was pseudohyperkalemia associated with significant hyperleukocytosis. This brief report discusses rare causes of pseudohyperkalemia that can be overlooked, and details the postulated mechanisms for pseudohyperkalemia in the setting of hyperleukocytosis.

Keywords
- hyperkalemia
- pseudohyperkalemia
- hyperleukocytosis

Case Presentation

A 7-year-old female patient presented with a 2-week history of reduced appetite, generalized pain, and nausea. She was alert and interactive, with exam significant for pale conjunctivae, mild gingival hyperplasia, 3+ tonsils, firm, nontender submandibular and anterior cervical lymph nodes, and abdominal tenderness with hepatosplenomegaly and scattered lower extremity bruising. Complete blood count (CBC) from the outside hospital was significant for white blood cell count (WBC) of 479,000/mm^3 and potassium of 4.8mEq/L. Capillary blood gas (Abbott i-STAT 1) performed during transport had a potassium of 3.9 mEq/L. Complete metabolic panel (CMP) was done on arrival and sent to the laboratory via pneumatic tube system. Potassium was 6.9 mEq/L (Abbott Architect Plus c8000.) No electrocardiogram (EKG) changes were seen on continuous monitoring. Testing confirmed T cell acute lymphoblastic leukemia and the patient underwent leukopheresis. Repeat basic metabolic panel (BMP) sent via pneumatic tube system noted that the potassium was $>$ 10 mEq/L and WBC count 386,000/mm^3, however, was read as erroneous by the laboratory. A blood gas was run in the pediatric intensive care unit (PICU), and the resulting potassium level was 4.6 mEq/L (Radiometer ABL90 FLEX). So, treatment and further hyperkalemia evaluation were not performed at that time. Repeat BMP (Abbott Architect Plus c8000) and CBC 6 hours later had a potassium of 8.9 mEq/L and WBC of 594,800/mm^3 without an erroneous value report from the laboratory. Stat 12-lead-EKG showed sinus tachycardia without peaked T-waves. Due to concern for hyperkalemia, 1 mEq/kg of sodium bicarbonate was administered with 5 cc/kg 10% dextrose. Stat venous blood gas, run in the PICU, was ordered and potassium was 4.4 mEq/L (Radiometer ABL90 FLEX.) The discrepancy between potassium results on BMP and blood gases was noted, treatment for hyperkalemia was halted, and nephrology was consulted. It was determined that, with her normal EKG findings and normal potassium on venous blood gases, this was pseudohyperkalemia associated with significant hyperleukocytosis. This discrepancy continued until WBC count reduced

received
September 27, 2017
accepted after revision
December 20, 2017
published online
February 1, 2018

DOI https://doi.org/10.1055/s-0038-1624569.
ISSN 2146-4618.

to 198,000/mm^3 and BMP potassium values returned to a normal value of 4.1 mEq/L with a correlating blood gas value of 3.5 mEq/L.

Discussion

There are two major non-iatrogenic mechanisms of true hyperkalemia: (1) increased potassium secondary to lysis of cells and (2) reduced urinary potassium excretion, seen in patients who are severely hypovolemic with impaired renal function.[1] Complications seen in patients with serum potassium levels $>$ 7 mEq/L include muscle weakness, arrhythmias, and sudden cardiac arrest. It is important to correctly distinguish between true hyperkalemia versus pseudohyperkalemia. Pseudohyperkalemia has been defined as a difference between serum and plasma potassium concentrations of more than 0.4 mEq/L when samples remain at room temperature and are tested within an hour of collection.[2] Hartmann et al first noted elevated serum potassium without clinical evidence of electrolyte imbalance. Their initial conclusion was that the potassium elevation was secondary to leakage from platelets in vitro as clotting occurs.[3] Later, other sources were identified including both red and WBCs.[4] Causes of pseudohyperkalemia in pediatric patients are mechanical factors, hyperventilation alkalosis, delayed processing times, or hemolysis.[5]

Potassium is measured using an ion-selective electrode (ISE), which converts the activity of the ion dissolved in solution into an electric potential measured by a voltmeter.[5,6] Both plasma and serum can be used to measure potassium. Platelets release potassium during the clotting process, resulting in higher potassium concentrations in the serum as compared with plasma.[7] Since most body potassium is intracellular, a small release of potassium can significantly affect the concentration of measured potassium. The ratio of intracellular to extracellular potassium is approximately 40:1, and a change in the ratio as small as 2.5% will increase the potassium concentration by 0.1 mEq/L.[8]

The i-STAT System uses direct (undiluted) electrochemical methods on whole blood. Investigators have analyzed the interchangeability of electrolytes measured with point of care, blood gas, and central laboratory analyzers and generally found them to correlate well at concentrations above 3 mEq/L. However, Hawkins[9] demonstrated that over 33% of hypokalemic cases were missed when using whole blood to determine potassium concentration. Moreover, hand disinfectants have been shown to significantly elevate potassium concentration especially when direct ISEs were used in point of care testing of whole blood samples.[10] Thus, the method used to obtain potassium measurements can be critical.

Pseudohyperkalemia due to extreme hyperleukocytosis is uncommon in children.[11] Hyperleukocytosis is defined as a WBC count above 100,000/mm^3 and is typically seen in leukemias and myeloproliferative disorders. Pseudohyperkalemia has not been described with WBC counts under 100,000/mm^3, so many common causes of inflammation have not been seen to cause the degree of leukocytosis necessary to raise concern for pseudohyperkalemia. In patients with hyperleukocytosis, there are multiple hypotheses concerning the mechanism of pseudohyperkalemia. One case report postulated that mechanical stress secondary to blood collection along with the fragility of leukemic lymphocytes can cause lysis of the cells, increasing the potassium in the serum.[11] Another report theorized that pseudohyperkalemia was caused by trauma to the abnormal cells secondary to the blood sample being transported in a pneumatic transport system.[12] Delay in transport of a blood sample after collection from the patient could result in increased lysis of fragile leukocytes.[2] Dimeski and Bird proposed that serum samples provide a more accurate potassium concentration versus plasma samples in patients with hyperleukocytosis, likely secondary to the clotting process eliminating WBC movement, minimizing lysis if the sample undergoes mechanical stress. Also, other cellular components such as lactate dehydrogenase (LDH) and aspartate transaminase (AST) were elevated after minor mechanical stress.[13] In patients with leukemia, WBC membranes are also especially sensitive to disruption by heparin, the anticoagulant used for plasma estimations.[14]

Multiple variables may have caused pseudohyperkalemia in our patient. First, three different techniques were used to measure potassium level. Second, two transportation methods were used to transport the blood samples: pneumatic tubing system and delivery by foot. Third, the sample analyzed in the PICU involved a significantly shorter amount of time in transit. Fourth, analysis on serum and whole blood samples can differ and attention needs to be paid to this. Lastly, this case demonstrates the possible treatment of pseudohyperkalemia as true hyperkalemia. Due to the significant risks associated with hyperkalemia in this critically ill patient, we chose to start treatment while awaiting confirmation despite her lack of EKG changes. Had we not stopped treatment quickly upon blood gas results, we could have easily caused iatrogenic hypokalemia. This illustrates the importance of serial electrolyte measurements as well as their interpretation in the clinical context, of recognizing the possibility of pseudohyperkalemia and taking appropriate steps to identify it.

Disclosure
The authors have no disclosures pertinent to the publication of this article

Funding
None.

References

1 Mount DB. Causes and Evaluation of Hyperkalemia in Adults. In Forman JP, ed. 2017. UpToDate. Available at: https://www.uptodate.com/contents/causes-and-evaluation-of-hyperkalemia-in-adults. Accessed January 12, 2018
2 Dickinson H, Webb NJ, Chaloner C, Wynn RF, Bonney DK. Pseudohyperkalaemia associated with leukaemic cell lysis during pneumatic tube transport of blood samples. Pediatr Nephrol 2012;27(06):1029–1031
3 Hartmann RC, Auditore JV, Jackson DP. Studies on thrombocytosis. I. Hyperkalemia due to release of potassium from platelets during coagulation. J Clin Invest 1958;37(05):699–707
4 Sevastos N, Theodossiades G, Archimandritis AJ. Pseudohyperkalemia in serum: a new insight into an old phenomenon. Clin Med Res 2008;6(01):30–32

5 Asirvatham JR, Moses V, Bjornson L. Errors in potassium measurement: a laboratory perspective for the clinician. N Am J Med Sci 2013;5(04):255–259
6 Bertini A, Milani GP, Simonetti GD, et al. Na(+), K(+), Cl(-), acid-base or H2O homeostasis in children with urinary tract infections: a narrative review. Pediatr Nephrol 2016;31(09): 1403–1409
7 Nijsten MW, de Smet BJ, Dofferhoff AS. Pseudohyperkalemia and platelet counts. N Engl J Med 1991;325(15):1107
8 Rastegar A. Serum potassium. In: Walker HK, Hall WD, Hurst JW, eds. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Chapter 195. Boston: Butterworths; 1990. Available at: https://www.ncbi.nlm.nih.gov/books/NBK307/
9 Hawkins R. Measurement of whole-blood potassium–is it clinically safe? Clin Chem 2003;49(12):2105–2106
10 Lam HS, Chan MH, Ng PC, et al. Are your hands clean enough for point-of-care electrolyte analysis? Pathology 2005;37(04): 299–304
11 Colussi G, Cipriani D. Pseudohyperkalemia in extreme leukocytosis. Am J Nephrol 1995;15(05):450–452
12 Chawla NR, Shapiro J, Sham RL. Pneumatic tube "pseudo tumor lysis syndrome" in chronic lymphocytic leukemia. Am J Hematol 2009;84(09):613–614
13 Dimeski G, Bird R. Hyperleukocytosis: pseudohyperkalaemia and other biochemical abnormalities in hyperleukocytosis. Clin Chem Lab Med 2009;47(07):880–881
14 Garwicz D, Karlman M. Early recognition of reverse pseudohyperkalemia in heparin plasma samples during leukemic hyperleukocytosis can prevent iatrogenic hypokalemia. Clin Biochem 2012;45(18):1700–1702

Erratum: The article has been corrected as per erratum published on March 28, 2018. DOI of the erratum is 10.1055/s-0038-1636924. Affiliation 4 was missing in the above article. The affiliation is now mentioned correctly in the affiliations section of the article.