

Case Report

Pseudohyperkalemia in Patients with Chronic Lymphocytic Leukemia

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Pseudohyperkalemia occurs occasionally in patients with extreme leukocytosis. Increased white blood cell fragility coupled with mechanical stress is felt to be causal. Serum and plasma potassium levels have been both associated with pseudohyperkalemia. Whole blood potassium determination will usually verify the correct diagnosis. It is important to diagnose this condition early so that patients are not inappropriately treated. Two patients with chronic lymphocytic leukemia and extreme leukocytosis are presented, one with pseudohyperkalemia and one with probable pseudohyperkalemia, and diagnostic considerations are discussed

1. Pseudohyperkalemia

Artificial hyperkalemia or pseudohyperkalemia is most commonly seen secondary to red cell hemolysis. It is also seen in patients with thrombocytosis and in the rare patient with familial pseudohyperkalemia [1]. Not well appreciated is its occasional occurrence in patients with extremely elevated white blood cell counts, particularly in patients with chronic lymphocytic leukemia (CLL). Here, two patients with CLL and hyperkalemia are presented, and diagnostic issues are discussed.

2. Case Reports

Case 1. The patient is a 51-year-old male who recently was diagnosed with CLL and had not yet received any chemotherapy. He was admitted with fatigue. He was on no medications. His initial lab showed a plasma potassium of 6.8 meq/L (repeated at 6.6 meq/L), creatinine of 1.1 mg/dL, hemoglobin of 7.3 g/dL, platelet count of 147 K/UL, and WBC of 273.9 K/UL. No conduction abnormalities were seen on EKG. He was treated in the emergency room for his presumed hyperkalemia with calcium gluconate, sodium bicarbonate, albuterol aerosol, glucose and insulin, and kayexalate. Over the next two days his potassium generally remained in the low 6's, and nephrology was consulted. A tentative diagnosis of pseudohyperkalemia was made, and

whole blood potassium was ordered using the blood gas machine. The result was 2.7 meq/L, confirming the diagnosis of pseudohyperkalemia. The next, day plasma potassium was elevated at 9.0 meq/L, but whole blood potassium was 3.6 meq/L.

Case 2. The patient is a 90-year-old female with an eight-year history of chronic lymphocytic leukemia. She had recently refused further chemotherapy and had been on hospice care. She also had a history of diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and blindness. She had been on potassium chloride, furosemide, and an angiotensin-converting enzyme inhibitor at home. She was admitted to Tampa General Hospital for evaluation of a fractured hip. She was virtually unresponsive. Plasma potassium values over the initial 24 hours of her admission ranged from 7.8 meq/L to 10.2 meq/L (Beckman Unicel DxC800 using an ion selective electrode). Her creatinine level ranged from 1.9 mg/dL to 2.3 mg/dL. Urinalysis showed 300 mg% protein. Her white blood cell count was 986 K/UL. Her hemoglobin was 6.6 g/dL and her platelet count was 79 K/UL. She was initially given intravenous calcium and placed on telemetry, but received no other treatment for hyperkalemia. Her EKG showed only a left anterior fascicular block. A whole blood potassium level utilizing the blood gas machine (Nova Biomedical Critical Care Express) was 10.6 meq/L. At that point, her family decided to reconsult

hospice, and no further studies were performed. She experienced no cardiac events during the six days of her hospitalization.

3. Discussion

The cause of pseudohyperkalemia associated with extreme leukocytosis is presumably cell lysis with release of intracellular potassium. The etiology of this cell lysis can be multifactorial. It was originally felt to be secondary to clotting, but recent reports suggest mechanical issues may also play a major part. The use of vacuum tubes [2], pneumatic tube transportation [3–5], prolonged incubation, and tourniquet use [6] have all been implicated as causing cell lysis and pseudohyperkalemia. Recentrifugation after storage in gel separator tubes has also been reported to cause pseudohyperkalemia, and the degree of hyperkalemia was noted to increase as storage times increased [7]. Increased fragility of leukemic white cells is thought to contribute to their tendency to lyse and liberate potassium. Depletion of metabolites may contribute to the hyperkalemia associated with prolonged storage [8].

The diagnosis of pseudohyperkalemia can be made in a variety of ways. Comparison of serum and plasma can be made, with the typical expectation being that the serum potassium will be higher than the plasma potassium [9], but observed results have been conflicting. Dimeski and Bird [10] reported a patient with CLL in whom plasma potassium was higher than serum potassium and suggested that a likely reason was that the clotting process locks the WBCs in the clot, eliminating cell movement during mechanical stress processes and minimizing lysis. Guiheneuf et al. [5] found that the effect of pneumatic tube transport on potassium was almost completely eliminated when serum rather than plasma was used. Hembling et al. [11] reported a patient with CLL and an extraordinarily high WBC in whom hyperkalemia was observed only in plasma and not in serum. They speculated that there was an underlying abnormality in the lymphocytes of their patient that conferred sensitivity to lithium heparin anticoagulant. Abraham et al. [12] also reported a leukemic patient with what they called “reverse pseudohyperkalemia,” that is, pseudohyperkalemia in plasma but not serum or whole blood. On the other hand, Lee et al. [13] reported 4 patients with CLL in whom hyperkalemia was noted in serum, but not in plasma or on whole blood analysis using a blood gas analyzer. Sevastos et al. [14], in a study of 435 patients with either thrombocytosis, erythrocytoses, leukocytosis, or mixed-type disorders, observed an elevated index Dk (serum potassium minus plasma potassium) in patients with platelet, erythrocyte, or with a mixed disorders but did not observe this difference in a small subgroup of 20 patients with either CLL or AML. At the M.D. Anderson Cancer Center plasma was found to be the specimen of choice for potassium level determinations. In a study of 37 paired samples, serum potassium values were significantly greater than those obtained from plasma in average, and they found a significant relationship between serum potassium and platelet count, but not between plasma potassium and platelet count [15].

Recently, the measurement of potassium on arterial blood gas specimens has been reported to be a reliable method of diagnosis. This may be due to the way the blood is drawn and the rapid analysis of the specimen [16]. Smalley et al. [17] also observed the superiority of whole blood samples in the diagnoses of pseudohyperkalemia and, interestingly, noted no effect of pneumatic tube transport on the whole blood sample in contradistinction to the hyperkalemia noted when their patient’s serum was tubed.

Our patients’ presentations and courses highlight the issues involved in the diagnosis of pseudohyperkalemia in a patient with a greatly elevated WBC. Patient no. 1’s elevated potassium was initially not recognized as spurious in spite of a normal EKG and lack of any clinical reason for his hyperkalemia and he was thus briefly inappropriately treated. Patient no. 2’s clinical course is interesting in that her whole blood potassium was also markedly elevated. She had a dramatically elevated WBC, and the whole blood sample was sent to the lab via the pneumatic tube system. Unfortunately, because of her change in care status, no confirmatory tests were performed, but it is highly improbable, although not impossible, that her extreme hyperkalemia was real, as she had no typical EKG signs of hyperkalemia and had no cardiac complications over her hospital stay in spite of receiving no therapy for hyperkalemia. The probability of EKG changes increases with increasing potassium levels [18], and serum potassium levels higher than 8 mmol/L are almost invariably associated with EKG changes [19]. On the other hand, there have been reports of patients with extremely elevated potassium levels and unremarkable EKG findings, generally in patients with renal failure [19, 20]. It is speculated that her WBC of almost one million made her blood sample much more susceptible to stresses of the blood draw and the pneumatic tube system.

In the presence of substantial leukocytosis, clinicians need to be alert to the possibility of a spurious potassium result. The suggestion in this situation is to immediately obtain a potassium level by blood gas analysis, as this is an extremely quick and reliable test. If the WBC is extraordinarily elevated, then steps to minimize trauma to the blood sample should be implemented even if whole blood is used. It has also been suggested that the hospital information system flag potassium results in patients with WBC counts $>100 \times 10^3$ noting the relationship between extreme leukocytosis and pseudohyperkalemia [13].

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