CLINICAL VIGNETTE

Reverse Pseudohyperkalemia Complicating Management in a Patient with Chronic Kidney Disease

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Introduction

Aberrations of serum potassium are among the most common and dangerous manifestation of declining renal clearance in patients with chronic kidney disease (CKD). Hyperkalemia (serum K > 5.5meq/L) occurs more often in patients treated with renin-angiotensin-aldosterone (RAAS) blocking agents and more often in patients with CKD than those who do not have renal impairment.[1] Although the risk of death is higher with acute hyperkalemia, chronic hyperkalemia also poses a risk for increased cardiovascular arrhythmias with their attendant morbidity and mortality.[2] Restricting potassium in diet is one way for patients with CKD to avoid hyperkalemia as well as treatment with potassium binders. Other measures include: laxatives to avoid constipation and avoidance of medications such as beta blockers, RAAS blocking agents, and non-steroidal-anti-inflammatory agents (NSAIDs) in patients with chronic kidney disease.

Therapy with diuretics that enhance kaliuresis, or binders (sodium polystyrene or patiromer a newer option) are active therapeutic options for removing excess potassium from the body. In emergency situations methods to shifting potassium into cells (50% dextrose with intravenous insulin, sodium bicarbonate pushes, and beta 2 agonists) along with calcium gluconate to stabilize the myocardium form the mainstay of emergency therapy. Ultimately relief of post obstructive renal failure, reversal of prerenal azotemia, or resolution of acute tubular necrosis (ATN)/intra renal causes of renal failure will be necessary for potassium homeostasis to occur without need for emergent dialysis.

Given the danger of hyperkalemia and the potential need for urgent therapy, it is important that the results be accurate to ensure timely therapy and to avoid treating patients with falsely elevated readings with medications that may cause harm. There are many procedural hurdles in obtaining an accurate potassium level. First is the need to obtain a non hemolyzed sample by avoiding placing a tourniquet for more than one minute and to avoid fist pumping or clenching.[3] The needle size must not be too large and the tubing and needle need to be compatible to avoid excessive sheer stress on red cells. The transport of samples must be in padded containers to avoid cell lysis particularly when patients have fragile red blood cells in certain pathological disease states.[3] Ethanol must be allowed to dry off the skin before the blood draw, use of the proper tube to avoid potassium containing additives, and careful attention to temperature needs to be maintained throughout transporting and test-ing process. The samples must also be processed in a timely manner to avoid inadvertent cellular potassium release and a false positive result.[3,4]

When optimal care is utilized in drawing, handling, transporting, and processing the sample the clinician must also be aware of potential patient issues that could result in a hyperkalemic response. Respiratory variation (hyperventilation) may increase serum potassium,[3] but most often sustained and reproducible rise in serum potassium is due to an underlying disorder in which cells in serum release potassium excessively.[4] This phenomenon; known as reverse pseudo-hyperkalemia, is due to in vitro potassium release from cellular elements rather than in vivo hemolysis. The cells involved are white blood cells, platelets, and now it was recently discovered that red blood cells also make a contribution.[3,4] Conditions like essential thrombocytosis, polycythemia vera, and a variety of leukemic conditions have been associated with reverse pseudo-hyperkalemia.[5]

We present a case of a patient with chronic kidney disease and a steadily increasing serum potassium despite a lack of medications that could interfere with potassium hemostasis and relatively stable renal function. He was not found to have a significant post void residual and underwent workup that revealed reverse pseudohyperkalemia that was suspected in light of his diagnosis of essential thrombocytosis.

Case report

Our patient is a 77-year-old Caucasian male with a past medical history of benign prostatic hypertrophy (BPH), and CKD and essential thrombocytosis who presented to nephrological care with an elevated serum potassium of 5.8 meq/L. His renal function as estimated by serum creatinine was 1.16-1.32 mg/dL, and his estimated glomerular filtration rate (eGFR) for a Caucasian patient was 56-67 ml/min (stage II-IIIa). He had no significant proteinuria (0.1g/g creatinine urine protein to creatinine ratio), his cystatin C level was mildly elevated, comparable to his serum creatinine level at 1.2 mg/L. His post void

residual estimated by bladder ultrasound was not significantly elevated.

Repeated lab draws from UCLA and outside labs revealed a consistently elevated serum potassium of >5.5 meq/L. He also was noted to have an elevated trans tubular potassium gradient (TTKG) indicating normal to high levels of potassium excretion in urine. Renin to aldosterone ratio was about 4 and serum aldosterone and plasma renin activity was not elevated. He was not on RAAS blockade, did not take high doses of NSAIDs, except occasional two low dose aspirins (162mg) instead of his prescribed 81mg.

He was being evaluated for thrombocytosis with a mean platelet level of 853,000 platelets per microliter (uL). He was diagnosed during course of renal workup with essential thrombocytosis. Given findings that did not explain his hyperkalemia and the persistence of it despite stopping his aspirin and urological findings not consistent with post renal obstruction, pseudo-hyperkalemia was considered as the diagnosis. A plasma potassium was obtained and was found to be 4.2 meq/L for a comparable serum value of 5.2 meq/L. The diagnosis was thus established and his medical team was advised to use plasma potassium instead of serum potassium for estimation of his blood potassium level. Please see figure 1 for plot of serum potassium, serum creatinine, and platelet levels for patient.

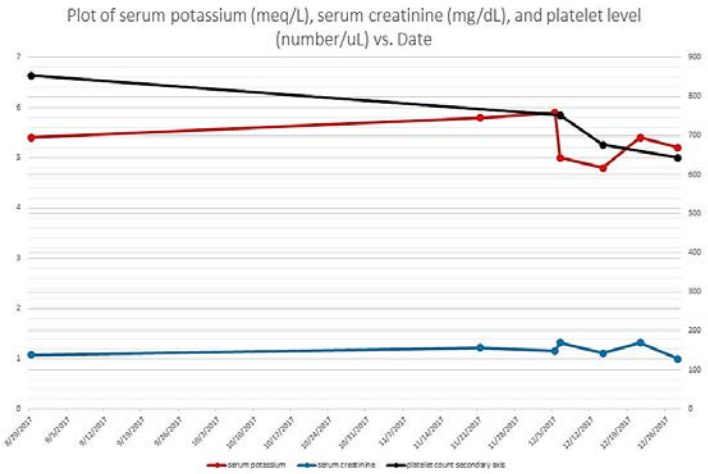

Figure 1: Graphs of lab parameters in reverse pseudo-hyperkalemia case

Discussion

The definition of reverse pseudohyperkalemia is a difference of 0.4meq/L between serum and plasma levels. The reported patient had several reasons for a clinical practitioner to be concerned for true hyperkalemia. These include BPH (post obstructive renal failure) and CKD stage 2-3a, the presence of a normal TTKG in face of hyperkalemia could indicate a high potassium diet but his serum potassium remained elevated despite appropriate dietary measures. The presence of elevated platelets is what increased diagnostic suspicion of reverse pseudohyperkalemia. It is important to consider this diagnosis to avoid treatment with medications that can cause harm like sodium polystyrene, diuretics, or more benign medications that may incur an undue cost to patient like patiromer.

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