Pseudohyperkalemia Caused by EDTA Contamination: a Not Uncommon Pre-analytical Error

To the Editor,

Pseudohyperkalemia from potassium ethylene-diaminetetraacetic acid (EDTA) contamination has been reported for decades. The mechanism of this anticoagulant is chelation of calcium, which is a divalent cation that is essential for the proper function of the clotting cascade. EDTA contamination is most often caused by inappropriate order of blood draw, and it can be recognized by the apparent presence of spurious coexisting hyperkalemia and hypocalcemia.[1]

We report the case of a 93-year-old cachexic Thai male who was diagnosed as having diabetes mellitus in a hyperosmolar hyperglycemic state. His laboratory test results showed markedly hyperkalemia and hypocalcemia. Electrocardiogram (ECG) showed sinus rhythm without tall peak T wave or widening of the QRS complex. The discordance between the ECG result and the reported hyperkalemia prompted a second blood draw to rule out pseudohyperkalemia in the first sample (Table 1). Thereafter, 20 ml of 10% calcium gluconate was pushed intravenously to treat the patient's hypocalcemia.

At our central laboratory and due to the abrupt change in potassium level, total calcium was performed in the second specimen which showed normocalcemia. No significant hemolysis was observed in either the first or second specimen. The patient had no known underlying medical conditions that could have been the cause of pseudohyperkalemia, such as thrombocytosis or marked leukocytosis. From these evidences together with the coexisting spurious hyperkalemia and hypocalcemia in the first sample, the most likely cause of pseudohyperkalemia was judged to be potassium EDTA contamination.

The mechanisms of EDTA contamination can be described, as follows: syringe needle contamination due to the filling of blood into the EDTA sample tube before other tubes, pouring the blood from EDTA sample tube into other tubes[1-3], and mistakenly switching the cap of EDTA sample tubes with others. The person who took the first blood specimen claimed that there was no transfer of blood or switching of tube caps from one tube to another, but could not confirm that the proper order of blood draw had been followed. According to European Federation of Clinical Chemistry and Laboratory Medicine guidelines, the order of blood draw should be, as follows: blood culture tubes, coagulation tubes, serum tubes, heparin tubes, EDTA tubes, glycolytic inhibitor tubes, and then other tubes.[4] In our case, the first blood draw included lithium heparin tube, K2EDTA tube, and sodium fluoride tube. There was, therefore, a high probability that blood was collected in the K2EDTA tube first, followed by the lithium heparin tube, which would have resulted in K2EDTA contamination in the lithium heparin tube.

TABLE 1. Patient blood glucose and electrolyte results.

Test	Unit	1st sample	2nd sample	Normal range
Blood glucose	mg/dl	1,031	869	74-99
Sodium	mmol/L	150	153	136-145
Potassium	mmol/L	9.9	4.2	3.4-4.5
Chloride	mmol/L	109	115	98-107
Bicarbonate	mmol/L	22.0	19.0	22-29
Total calcium	mg/dl	3.5	9.08	8.2-9.6

The failure of our laboratory staff to recognize coexisting distinct hyperkalemia and hypocalcemia in the first sample result caused misinterpretation and inappropriate calcium replacement in our patient. Fortunately, the patient showed no sign of hypercalcemia afterwards, and the follow-up calcium level was within normal range.

Recognition of coexisting hyperkalemia and hypocalcemia in the same sample strongly suggests an EDTA contaminated sample. A campaign designed to remind and reinforce appropriate blood collection procedures would help to decrease the frequency, but not totally eliminate EDTA contamination.[1,5] Furthermore, it only takes a very small amount of EDTA contamination to influence a pseudohyperkalemia and pseudohypocalcemia result, and the presence of EDTA can be difficult to identify.[1-3] Three previous studies reported that a lack of routine EDTA measurement as a screening protocol would result in 36-42% of pseudohyperkalemic samples going undetected and being reported as true hyperkalemia.[1,2,5] Thus, a cost-effective strategy would be to implement a routine EDTA analysis protocol.[1-3]

In conclusion, lack of awareness about EDTA contamination and clue for how to identify it can lead to misinterpretation and inappropriate treatment. We would like to highlight the need for ongoing reinforcement of the importance of blood draw protocols, and the need for implementation of EDTA assay for routine EDTA screening.

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