Case Report

An unusual case of pseudohyperkalaemia

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Introduction

Pseudohyperkalaemia is a clinical condition in which there is an artifactual elevation of the serum potassium level due to in vitro release of potassium from blood cells [1–3]. Pseudohyperkalaemia has been reported in clinical settings such as in vitro haemolysis due to mechanical trauma during venipuncture, severe thrombocytosis and leukocytosis, and familial pseudohyperkalaemia [4–13]. We report the first case of a patient with normal white blood cell (WBC) and platelet counts who presented with pseudohyperkalaemia due to excessive potassium release from blood cells during coagulation. This case has important therapeutic implications in that pseudohyperkalaemia needs to be excluded in any patient with unexplained hyperkalaemia to avoid unnecessary and potentially detrimental therapy.

Case

The patient is a 42-year-old female who was referred to the renal clinic for evaluation of unexplained hyperkalaemia. She was seen by her primary care physician for a routine check up. Routine laboratory studies revealed a serum potassium level of 6.0 meq/l. A repeat serum potassium level was 5.4 meq/l. The patient denied any past medical problems. She denied taking any medications except for her oral contraceptive pill Levora. She was asymptomatic. Physical examination revealed a well-developed white female in no distress. Her blood pressure was 98/64 mmHg, pulse 68, temperature 36°C, respiratory rate 16. Her jugular venous pressure was estimated to be 7 cm. Her lungs were clear to auscultation and percussion. Her cardiovascular examination revealed a regular rate and rhythm, and no murmurs, rubs or gallops. Her abdomen was non-tender, non-distended and without hepatosplenomegaly. She did not have any peripheral oedema. Neurological examination revealed no focal deficits. Laboratory test results were: haemoglobin 14 g/dl; mean red blood cell (RBC) volume 95.3 fl; WBC 6.04 × 10^3/μl; platelet count 256 × 10^3/μl; platelet volume 12.1 fl; serum sodium 145 meq/l; serum potassium 6.0 meq/l; chloride 106 meq/l; total CO₂ 29 meq/l; blood urea nitrogen (BUN) 6 mg/dl; creatinine 0.8 mg/dl; glucose 96 mg/dl. Lactate dehydrogenase (LDH), haptoglobin, peripheral blood smear and erythrocyte osmotic fragility were normal. Simultaneous serum and plasma potassium levels were obtained which were 5.4 and 4.1 meq/l, respectively. To confirm the discrepancy between serum and plasma potassium concentrations, a repeat set of blood tests revealed a serum potassium level of 5.6 meq/l and plasma potassium level of 4.3 meq/l. Blood was also drawn into heparinized tubes, allowed to stand at room temperature, and was centrifuged and separated at 0 and 6 h for plasma potassium measurements. The plasma potassium levels at 0 and 6 h were 4.3 and 4.4 meq/l, respectively.

Discussion

This is an interesting case in which an asymptomatic patient was incidentally found to have an elevated serum potassium level on routine laboratory testing. The patient was not taking any drugs that may have contributed to the elevated serum potassium level at the time of the blood draw. The patient had no apparent cause for the hyperkalaemia based on her history, physical examination and initial laboratory findings. The possibility of pseudohyperkalaemia was, therefore, entertained in this otherwise asymptomatic patient.
A common cause of pseudohyperkalaemia is mechanical trauma during venipuncture, resulting in the release of potassium from RBCs. In this setting, the serum typically has a characteristic reddish tint since there is concomitant release of haemoglobin from RBCs. Pseudohyperkalaemia may also be seen with prolonged use of a tourniquet or an excessively tight tourniquet by inducing release of potassium from skeletal muscles into venous blood [14]. Similarly, repeated clenching and unclenching of the fist (in an attempt to make the veins more apparent for blood draw) may artificially increase the potassium concentration by as much as 1–2 mmol/l [15]. The above conditions were excluded in this particular patient.

Spuriously elevated plasma potassium levels have also been reported in patients with familial pseudohyperkalaemia [10–13]. Familial pseudohyperkalaemia is an autosomal dominant disorder which maps to the same locus, 16q23–ter, as hereditary xerocytosis [13]. The product of this gene is not known. This rare familial condition is characterized by a temperature-dependent loss of potassium from RBCs when stored at room temperature. The pseudohyperkalaemia in affected individuals is attributable to an abnormally increased potassium permeability of the red cell membrane [10–13]. It has been shown that there are three components to the net potassium flux across the red cell membrane: the Na\(^+\), K\(^+\)-ATPase pump, the Na\(^+\)K\(^+\)2Cl\(^-\) co-transport system and the passive diffusion of potassium across the membrane by yet uncharacterized transport processes [12]. These three components can be assessed experimentally by the use of appropriate inhibitors. Potassium flux through the Na\(^+\), K\(^+\)-ATPase pump is measured as the ouabain-sensitive component, whereas flux via Na\(^+\)K\(^+\)2Cl\(^-\) co-transport is measured as the decrease in the rate of potassium flux in the presence of furosemide. The residual passive permeability of the RBC plasma membrane to potassium is defined as that flux which is unaffected by either inhibitor. In familial pseudohyperkalaemia, affected individuals exhibited a greater passive permeability to potassium at low temperatures. Plasma potassium in these individuals progressively rises when the collected blood is allowed to stand at room temperature for several hours. However, the plasma potassium measurement is normal in fresh blood which is centrifuged and separated immediately. Therefore, the in vitro plasma potassium concentration is normal in these affected individuals. In our patient, blood was drawn into heparinized tubes, allowed to stand at room temperature, and was centrifuged and separated at 0 and 6 h. There was no significant in vitro change in the plasma potassium concentrations in our patient. The plasma potassium levels at 0 and 6 h were 4.3 and 4.4 meq/l, respectively.

Our patient was noted to have a significant difference between the serum and plasma potassium levels. It is well known that potassium is released from the leukocytes and platelets when a blood sample is allowed to clot in vitro [1]. Normally, the serum potassium concentration is typically 0.1–0.4 meq/l greater than that measured in a plasma sample in which clotting is prevented by drawing the blood into a heparinized tube. This phenomenon becomes exaggerated in patients with leukaemia or myeloproliferative disease [4–9] where there is a marked elevation of the WBC count (>100 000/mm\(^3\)) or platelet count (>1 000 000/mm\(^3\)). Reverse pseudohyperkalaemia has also been reported to occur in leukaemic patients with significant leukocytosis in whom the plasma potassium levels are greater than the serum potassium levels [16,17]. The underlying mechanism in reverse pseudohyperkalaemia is postulated to be due to a heightened sensitivity to heparin-induced membrane damage in the setting of a haematological malignancy [17].

Although our patient did not have significant leukocytosis or thrombocytosis, her serum potassium concentration was 1.3 meq/l greater than the plasma potassium level. This difference between the serum and plasma potassium levels in this patient with normal WBC and platelet counts is about three times the maximum value previously reported [1]. The precise mechanisms underlying the excessive release of potassium from blood cells during clot formation in this patient are unclear at this time. Given the platelet count and mean platelet volume in this patient, assuming an intracellular potassium concentration of ~100 meq/l, were all the platelets to lyse or develop a significant change in permeability during clotting, the maximum expected serum vs plasma potassium difference is 0.7 meq/l. Therefore, it does not appear that platelet lysis per se can account for the findings in our patient. Since the LDH, haptoglobin, peripheral blood smear, erythrocyte osmotic fragility, and plasma potassium were normal in our patient, RBC lysis was not occurring prior to clot formation. It is possible that the potassium permeability of the RBCs increased specifically during the clotting process due to an alteration in membrane potential or channel/transporter function. Finally, given a WBC count of 6.04 \times 10^3/\mu l, abnormal WBC permeability during clot formation (assuming the release of all intracellular potassium) could also have accounted for the serum–plasma potassium difference of 1.3 meq/l in our patient. Further studies are needed to determine the cell (or cells) responsible for the clotting-induced excessive cellular potassium efflux.

Results of repeated plasma determinations were normal, indicating that potassium release occurred only if the coagulation process had taken place. The release of potassium from the cellular components of blood after collection can occur by either increased permeability of the cell membrane or lysis from the blood cells. In our patient, incubation of a heparinized specimen for 6 h at room temperature was not accompanied by a marked increase in the plasma potassium level. Therefore, the excessive release of potassium in our patient was unlikely to be due to an increased permeability of the cell membrane to potassium. Potassium levels in the plasma were normal by as much as 0.7 meq/l. Although our patient did not have significant leukocytosis or thrombocytosis, her serum potassium concentration was 1.3 meq/l greater than the plasma potassium level. This difference between the serum and plasma potassium levels in this patient with normal WBC and platelet counts is about three times the maximum value previously reported [1]. The precise mechanisms underlying the excessive release of potassium from blood cells during clot formation in this patient are unclear at this time. Given the platelet count and mean platelet volume in this patient, assuming an intracellular potassium concentration of ~100 meq/l, were all the platelets to lyse or develop a significant change in permeability during clotting, the maximum expected serum vs plasma potassium difference is 0.7 meq/l. Therefore, it does not appear that platelet lysis per se can account for the findings in our patient. Since the LDH, haptoglobin, peripheral blood smear, erythrocyte osmotic fragility, and plasma potassium were normal in our patient, RBC lysis was not occurring prior to clot formation. It is possible that the potassium permeability of the RBCs increased specifically during the clotting process due to an alteration in membrane potential or channel/transporter function. Finally, given a WBC count of 6.04 \times 10^3/\mu l, abnormal WBC permeability during clot formation (assuming the release of all intracellular potassium) could also have accounted for the serum–plasma potassium difference of 1.3 meq/l in our patient. Further studies are needed to determine the cell (or cells) responsible for the clotting-induced excessive cellular potassium efflux.

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membrane prior to clot formation. Our findings indicate that the increased cellular release of potassium was associated specifically with clot formation.

In summary, this is the first case report in the literature of a patient who presented with pseudo-hyperkalaemia due to excessive release of potassium during blood clotting occurring in the absence of significant leukocytosis or thrombocytosis and where a temperature-dependent loss of potassium from RBCs was ruled out. We postulate that the excessive potassium release from blood cells in this patient resulted from excessive cellular potassium efflux during the clotting process. This case has important clinical implications in that plasma and serum potassium levels should be obtained in any patient with unexplained elevated serum potassium level, irrespective of the presence or absence of leukocytosis or thrombocytosis. Failure to recognize pseudo-hyperkalaemia in such patients may result in further unnecessary diagnostic testing and potentially detrimental treatment.

References


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