Pseudohyperkalemia: in vitro phenomenon or misdiagnosis. A case report

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ABSTRACT

Introduction: Hyperkalemia is a common electrolyte disturbance that occurs within many patients. The more often prevalence of cardiovascular or renal diseases is, the more frequent medical issue hyperkalemia will be. An increasing quantity of entities requires taking medications that affect electrolyte hemostasis. Therefore, reasons for hyperkalemia should be deeply reflected. One of them is pseudohyperkalemia.
Purpose: In this study diagnostics and treatment of hypokalemia were presented based on the case report of a 56-year-old man.
Case presentation: A 56-year-old man was admitted to the Department of Invasive Cardiology of Medical Hospital of Białystok for complaints of strong chest pain associated with palpitations, cold sweats, feelings of general weakness and anxiety. The patient had no medical history of chronic diseases and neglected to take any medications at length. The laboratory tests performed at admission showed an increased serum concentration of potassium. Through the whole hospitalization, many medications were implicated to overcome hyperkalemia (diuretics, calcium resonium, inhalation with beta2-adrenergic agonists, intravenous infusion of glucose with insulin) with no effect. Hormone test was performed, the results excluded Addison's or pituitary disease. Differential diagnosis with arterial blood draw showed normal potassium serum concentration.
Conclusions: Hyperkalemia is encountered in a broad spectrum of patients. The severely elevated level of potassium could lead to life-threating conditions. Therefore, proper diagnosis making process is a matter of great importance. As clinicians, we need to base not only on laboratory but also examine the whole picture of the patient. Misdiagnosing pseudohyperkalemia might result in unnecessary medical management.
Keywords: Hyperkalemia, pseudohyperkalemia, electrolyte disorders

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INTRODUCTION

Hyperkalemia is an electrolyte disturbance that often causes a serious clinical problem. It occurs often within patients suffering from cardiovascular or renal diseases, especially using certain medications (e.g., renin-angiotensin-aldosterone-axis related). Hyperkalemia is divided into 3 stadiums based on serum potassium concentration: mild (5.5-5.9 mmol/L), moderate (6.0 - 6.4 mmol/L) and severe (>6.5 mmol/L) [1]. It is highly recommended not to disregard this most common electrolyte abnormality [1], whereas hyperkalemia can lead to serious, life-threatening arrhythmias and sudden cardiac death [2]. Hyperkalemia occurs in up to 10% hospitalized patients [3,4] and has various etiology (most common reasons - Table 1).

Table 1. Causes of hyperkalemia in adults

Excessive load of potassium
Decreased renal potassium excretion:
1. Organic: Acute or chronic kidney disease
2. Functional:
A. Insufficiency of aldosterone or glucocorticoids - congenital or acquired
B. Hyporeninemic hypoaldosteronism
C. Drugs • ACE - inhibitor • Angiotensin receptor blocker • Aldosterone antagonist (spironolactone, eplerenone) • Nonsteroidal anti-inflammatory disease • Renin inhibitors • Calcineurin inhibitors (cyclosporine, tacrolimus) • Heparine • Cardiac glycoside • Amiloride • Trimethoprim
Insufficiency of intracellular potassium transport: • Blockage of beta2-adrenergic receptor • Stimulation of alfa-adrenergic receptor • Vegetative neuropaty • Insulin insufficiency • Metabolic acidosis
Excessive potassium release from cells: • Rhabdomyolysis • Malignant hyperthermia • Tumor lysis syndrome • Hypothermia - rewarming shock • Insulin resistance hiperglicemia • Hyperkalemic periodic paralysis • Sepsis

Pathophysiologically maintenance of potassium homeostasis depends on dietary potassium intake, shifting potassium cations between intracellular and extracellular compartment, and renal function [5]. Mild hyperkalemia is generally asymptomatic. Greater serum concentration of potassium is often associated with muscle weakness, paraesthesia, malignant arrhythmias (ventricular fibrillation or asystole), and specific findings in ECG (tall and narrow T waves, prolonged PR interval, QRS complexes widening) [6]. There is no single threshold above which hyperkalemia is considered imminently dangerous [7].

However, the risk of adverse effects increases along with elevation of potassium level. The diagnostic algorithm should be widely conducted in order to reduce eventual, unfavorable outcome.

We report a case of spurious hyperkalemia caused by pseudohyperkalemia phenomenon (Table 2)

Table 2. Causes of pseudohyperkalemia

Prolonged tourniquet application
Excessive fist clenching
Pneumatic tube transportation of blood samples
Traumatic venipuncture
Mechanical blood cells damage during specimen processing (e.g. re-centrifugation)
Ethanol-antiseptics contamination
Hemolysis

CASE PRESENTATION

A 56-year-old man was admitted to the Department of Invasive Cardiology of Medical Hospital of Białystok for complaints of strong chest pain associated with palpitations, cold sweats, feelings of general weakness and anxiety. The patient had no medical history of chronic diseases and neglected taking any medications at length. However, he had undergone surgical treatment of gastro-esophageal disease in 1989 (no medical documents containing detailed information available). In the referring hospital increased level of troponin I was observed, what suggested acute coronary syndrome.. The patient reported for the past 2 months having experienced fatigue and weakness. Periodically, suffered from momentaneous palpitation. 3 days before admission similar symptoms occurred – he felt relieved after taking non-steroidal anti-inflammatory drugs. About 30-years history of smoking (10 cigarettes per day) was his only risk factor for cardiovascular diseases. Subjective examination apart from regular tachycardia did not reveal any significant abnormalities. ECG reading showed atrial flutter with atrioventricular block 2:1, the frequency of QRS complexes was about 130 beats per minute. No signs of myocardial ischemia or hyperkalemia were observed.

The laboratory tests performed at admission showed increased serum concentration of potassium (6.29 mmol/L), elevated level of high sensitive troponin I (340.5 ng/l – which was top level during hospitalization) and B-type natriuretic peptide (BNP – 904.9 pg/ml), dyslipidemia (total cholesterol 219 mg/dl, LDL 157 mg/dl, HDL 54 mg/dl). No significant signs of thyroid or renal insufficiency (TSH 1.45 μIU/ml, creatinine 0.98 mg/dl, GFR 84 ml/min, slightly increased uric acid – 8,78 mg/dl) were found. Echocardiography showed enlargement of left atrium (42mm) and ventricle (63mm – diastolic dimension), severe impairment of left ventricular contractility (ejection fraction 25%) with generalized hypokinesia. No significant valvular defect was observed.

According to the fact that duration of atrial arrhythmia was unknown, proper anticoagulant therapy (firstly low molecular weight heparine, then rivaroxaban) and remittent ventricular function strategy (beta-blockers, digoxin) were introduced. As it was accomplished, ECG readings have changed – showing negative T waves in V3-V6 leads. Therefore, coronary angiography has been performed. Surprisingly, no significant atherosclerotic lesions were found in the coronary vessels. On the second and third day of hospitalization patient reported loose bowels, that finally turned into 3-days lasting watery diarrhea. The growth of Salmonella group in stool culture was reported. Therefore, the patient was isolated and completed antibiotic course (trimethoprim/sulfamethoxazole). The patient admitted to the consumption of non-hospital food before the symptoms occurred what was the most possible source of infection, as other patients remained asymptomatic.

Hyperkalemia was noticed through the whole hospitalization, not only during diarrhea. Barely each venous blood draw showed exceeded potassium serum concentration (top 6.66 mmol/L). Surprisingly, patient's creatinine and sodium level remain stable throughout. He had properly maintained diuresis. The patient's complex treatment consisted among others of angiotensin-converting-enzyme inhibitors, mineral-ocorticoid receptor antagonist (rapidly withdrawn according to hypotension), beta-blockers, digoxin has bed continually adjusted to the potassium serum level, blood pressure and heart rate. Many medications were implicated to overcome hyperkalemia (diuretics, calcium resonium, inhalation with beta2-adrenergic agonists, intravenous infusion of glucose with insulin). Unfortunately, the effect was average. Despite normal serum concentration of sodium, a test with adrenocorticotrophic hormone was performed. Unsurprisingly, the result excluded Addison's or pituitary disease. Interestingly, arterial blood draws showed normal potassium serum concentration. Considering possibility of inappropriate phlebotomy technique, torniquetless venous blood draws were taken. It resulted in maintaining potassium serum concentration within normal range. Thus, the aim of the current case review

is to emphasized pseudohyperkalemia in every diagnostic algorithm associated with this electrolyte disturbance.

After two months follow-up was performed, as patient was readmitted in order to treat atrial arrhythmia with electrocardioversion. In the venous blood draw collected without using tourniquet, the potassium serum concentration was within normal limits (4.93mmol/L). Therefore, we were assured in belief that pseudohyperkalemia was a proper final diagnosis.

DISCUSSION

Hyperkalemia is a common electrolyte disturbance that occurs within many patients. The more often prevalence of cardiovascular or renal diseases is, the more frequent medical issue hyperkalemia will be. The increasing quantity of entities requires taking medications that affect electrolyte hemostasis. Therefore, reasons for hyperkalemia should be deeply reflected. One of them is pseudohyperkalaemia. As clinicians, we must undertake decisions based not only on the laboratory but also take into consideration the patient's physical condition. Unless specific symptoms resulting from elevated potassium level are observed, establishing diagnosis ought to be reconsidered. Especially that an artifact of measurement can be followed by inappropriate patient management. Neupane et al. described an interesting case of 91-year-old-woman with pseudohyperkalemia [8]. As a result of erroneous interpretation of laboratory results, the patient underwent unnecessary pharmacological treatment. Moreover, in order to restore potassium hemostasis hemodialysis was performed. Luckily, the procedure did not end up with any significant adverse effects.

The term pseudohyperkalemia could be defined by in vitro increased level of potassium that does not correspond with in vivo concentration. Although there may be various reasons responsible for this phenomenon, particular attention should be paid to the collection technique. Therefore, such factors as prolonged tourniquet application, excessive fist clenching, traumatic venipuncture, pneumatic tube transportation, mechanical blood cells damage while specimen processing (e.g., re-centrifugation), ethanol-antiseptics contamination may result in artifactually exceeded potassium concentration [9]. Moreover, clinical conditions such as leukocytosis and thrombocytosis are often associated with a mean elevation of potassium level [10].

In the matter of differentiation pseudohyperkalemia from the actual electrolyte disorder helpful seems to be arterial blood gas. Not only the majority of possible mechanical factors are eliminated, but also it is a quicker processing procedure. In our case, arterial blood draw allowed us to make the final diagnosis and spare patient unnecessary further interventions.

Moreover, in this case, there were no physical symptoms reported from patient or ECG findings crucial for hyperkalemia what also should be pointing towards another explanation for the potassium level imbalance.

CONCLUSIONS

Hyperkalemia is encountered in a broad spectrum of patients. The severely elevated level of potassium could lead to life-threating conditions. Therefore, proper diagnosis making process is a matter of great importance. As clinicians, we need to base not only on laboratory but also examine the whole picture of the patient. Misdiagnosing pseudohyperkalemia might result in unnecessary medical management. Thus, we want to emphasize this common entity as a potential reason for hyperkalemia. Finally, it is worth to mention that is an in vitro phenomenon pseudohyperkalemia does not require any specific medications.

Conflicts of interest

The authors declare no conflicts of interest.

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