African Journal of Nephrology

Official publication of the African Association of Nephrology

Volume 23, No 1, 2020, 15-18

CASE REPORT

Pseudohypokalaemia and pseudohypoxaemia in a patient with acute myeloid leukaemia

Mogamat-Yazied Chothia, Mogamat Razeen Davids

Division of Nephrology, Department of Medicine, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa.

ABSTRACT

Spurious laboratory results are frequently encountered in patients with haematological disorders and lead to unnecessary additional laboratory investigations and inappropriate treatment. An 80-year-old woman, known with acute myeloid leukaemia, was admitted with suspected sepsis. Laboratory tests revealed a leukocyte count of 358 x 10^9/L, serum potassium concentration of 2.6 mmol/L and partial pressure of arterial oxygen of 5.3 kPa. The patient did not display any clinical or electrocardiographic features of hypokalaemia and there were no signs of respiratory distress. A diagnosis of pseudohypokalaemia and pseudohypoxaemia was made and inappropriate therapeutic interventions were avoided. Pseudohypokalaemia and pseudohypoxaemia should always be a consideration in patients with hyperleukocytosis due to haematological malignancies, especially when there are no clinical features to support these findings. The inappropriate administration of potassium in such cases may cause serious cardiac arrythmias.

Keywords: spurious laboratory tests; pseudohypokalaemia; pseudohypoxaemia; leukaemia; hyperleukocytosis.

INTRODUCTION

Spurious laboratory results are frequently encountered in patients with haematological disorders and may lead to unnecessary additional laboratory investigations and inappropriate treatment [1]. Causes of spurious laboratory results may originate from pre-analytical (in vivo and in vitro), analytical or post-analytical factors [1]. In vivo factors include pre-existing comorbid diseases and drugs, whereas in vitro factors include phlebotomy technique, ambient temperature and turn-around time to sample analysis [1,2].

We present a case of an 80-year-old woman, known with acute myeloid leukaemia, who was found to have pseudohypokalaemia and pseudohypoxaemia, the identification of which resulted in the avoidance of inappropriate therapeutic interventions.

CASE PRESENTATION

An 80-year-old woman was admitted with the clinical picture of neutropaenic sepsis. She had been diagnosed with acute myeloid leukaemia not otherwise specified (AML-NOS) 4 months earlier and had not received any chemotherapy. She had hypertension, which was controlled with enalapril 5 mg twice daily and atenolol 50 mg daily. There was no history of vomiting or diarrhoea and she was not using any diuretics. On admission her blood pressure was 136/85 mmHg, pulse rate was 99 beats per minute, temperature was 36.5°C and oxygen saturation while breathing ambient air was 99% (pulse oximeter reading). Chest examination was unremarkable with no respiratory distress, abdominal examination revealed no hepatosplenomegaly and she had no muscle weakness.

A chest radiograph revealed upper lobe interstitial infiltrates suggestive of pulmonary tuberculosis. Routine blood tests revealed a serum potassium concentration of 2.6 mmol/L, leukocyte count of 358 x 10^9/L, haemoglobin concentration of 6.7 g/dL, platelet count of 62 x 10^9/L

Received 07 January 2020; accepted 24 February 2020; published 15 March 2020.

Correspondence: Yazied Chothia, yaziedc@sun.ac.za.

and an arterial blood sample revealed severe hypoxaemia (Table 1). Hypokalaemia had also been noted with previous admissions. An electrocardiogram showed a multifocal atrial rhythm without U-waves or QT prolongation. Blood cultures were negative.

A diagnosis of pseudohypoxaemia was made because of the absence of respiratory distress and normal oxygen saturation on pulse oximetry despite the severe hypoxaemia in arterial blood. Owing to the absence of muscle weakness or electrocardiographic features of hypokalaemia, pseudohypokalaemia was also considered. A repeat serum sample was taken and hand-delivered to the laboratory on ice. The potassium concentration of this sample was 4.2 mmol/L, confirming our suspicion of pseudohypokalaemia. As a result, potassium supplementation as well as the administration of supplemental oxygen was avoided.

Due to the overall poor prognosis, a decision was made to initiate palliative care. The patient died 3 days following admission.

DISCUSSION

Pseudohypokalaemia is a phenomenon of spuriously reduced serum potassium concentration in vitro and needs to be recognised by clinicians to avoid the inappropriate administration of potassium, which may result in hyperkalaemia and life-threatening cardiac arrhythmias.

Pseudohypokalaemia develops in cases of hyperleukocytosis when leukocyte counts are greater than 100 x 10^9/L, which occurs nearly exclusively in patients with haematological malignancies, particularly acute myeloid leukaemias (AML) [3]. A major mechanism for this phe-

Table 1. Laboratory test results in a patient with acute myeloid leukaemia.

Laboratory test	Ref. range	Initial analysis	Sample on ice
Serum			
Sodium	136–145 mmol/L	139	139
Potassium	3.5–5.1 mmol/L	2.6	4.2
Urea	2.1–7.1 mmol/L	4.1	–
Creatinine	49–90 µmol/L	72	–
Leukocyte count	3.9–12.6 x 10^9/L	358.8	–
Haemoglobin	12.0–15.0 g/dL	6.7	–
Mean cell volume	78.9–98.5 fL	109.2	–
Platelet count	186–454 x 10^9/L	62	–
C-reactive protein	<10 mg/L	345	–
Arterial blood sample*			
pH	7.35–7.45	7.52	–
P_aO_2	11–13 kPa	5.3	–
P_aCO_2	4–6 kPa	3.9	–
Bicarbonate	24–26 mmol/L	24.6	–
Oxygen saturation		81%**	–
Urine			
Potassium	mmol/L	39.2	–
Creatinine	mmol/L	18.5	–

*Patient breathing ambient air. **Oxygen saturation by pulse oximeter reading = 99%.

nomenon is the high sodium permeability of leukaemic cells with resultant increased activity of the sodium–potassium adenosine triphosphatase (Na^+/K^+-ATPase) pump, which causes the transcellular shift of potassium into leukaemic cells [4]. However, the monocytic subtype of AML may cause true hypokalaemia via renal potassium wasting [5]. Lysozymuria, that can affect renal tubular potassium reabsorption, is thought to be responsible [6]. In our patient, the absence of clinical and electrocardiographic features of hypokalaemia, as well as the hyperleukocytosis secondary to the non-monocytic subtype of AML, raised the suspicion of pseudohypokalaemia.

Other causes of pseudohypokalaemia include blood samples taken from patients that were recently administered insulin and seasonal pseudohypokalaemia, which occurs at times of high room temperatures [7]. The effect of temperature was confirmed by Sodi et al., who compared the serum potassium concentrations of blood samples collected from primary care patients to samples collected in hospitalised patients and found relatively lower serum potassium concentrations during the summer months in patients in primary care [2]. Because samples from the primary care setting were transported to a central laboratory, the additional time spent during transit at higher ambient temperatures during the summer months was identified as the cause for this phenomenon. Increased activity of the Na^+/K^+-ATPase pump was identified as the mechanism for the intracellular potassium shift in vitro. Neither of these mechanisms was applicable in our patient. When pseudohypokalaemia is a consideration, cellular components should be separated from the serum or plasma promptly or the blood sample should be stored at 4°C after collection to avoid the shifting of potassium [7].

Pseudohypoxaemia is less well recognised. It is a spurious reduction in partial pressure of oxygen in vitro. Red blood cells do not consume oxygen because of the absence of mitochondria and glucose metabolism occurs via anaerobic glycolysis. During physiological conditions, leukocyte and platelet concentrations are relatively low and therefore do not affect the partial pressure of oxygen in vitro [8]. However, haematological malignancies with hyperleukocytosis or conditions with extreme thrombocytosis (platelet count >1000 x 10^9/L), may affect the partial pressure of oxygen because these cells maintain their high metabolism following phlebotomy and consume oxygen dissolved in the plasma [9]. A direct relationship exists between the severity of the hyperleukocytosis and the reduction in the oxygen partial pressure [10]. As with pseudohypokalaemia, this phenomenon occurs frequently with AML of monocytic origin. The tendency for monocytes to produce hypoxaemia is due to their higher oxidative metabolism relative to other leukocytes [11].

Before considering pseudohypoxaemia in a patient with leukaemia, other causes of hypoxaemia should first be excluded including pulmonary leukostasis, pneumonia and pulmonary embolism [12]. Our patient did not display any clinical features of sepsis or respiratory distress, making these causes unlikely. Also, our patient's oxygen saturation, using the pulse oximeter, was 99% while breathing ambient air. The pulse oximeter is not affected by this in vitro phenomenon [13]. However, before fully relying on the pulse oximeter measurements, hypothermia and alkalosis should also be excluded as these two conditions shift the oxygen–haemoglobin dissociation curve to the left, which increases the oxygen saturation [12]. Neither of these conditions was present in our patient.

Another potential mechanism for pseudohypoxaemia involves large numbers of leukaemic cells coating the electrode responsible for measuring the partial pressure of oxygen [14]. This may be avoided by simply measuring oxygen partial pressure using plasma rather than whole blood samples [14]. Other strategies for accurate measurement of oxygen partial pressure include continuous intra-arterial blood gas monitoring and adding sodium fluoride to the blood sample before blood gas analysis [15,16]. The latter reduces oxygen consumption by leukocytes.

CONCLUSIONS

Pseudohypokalaemia and pseudohypoxaemia should always be a consideration in patients with hyperleukocytosis due to haematological malignancies, especially when there are no clinical features to support these findings. Recognition of these conditions is important to avoid inappropriate therapy such as potassium supplementation, which may cause deadly cardiac arrhythmias. Pseudohypokalaemia can be excluded by sending the blood sample to the laboratory on ice and non-invasive pulse oximeter measurements will exclude pseudohypoxaemia.

Ethical considerations

Consent to publish this case report was granted by the Human Research Ethics Committee of Stellenbosch University (reference number C19/04/013, project identification number 10045).

REFERENCES

1. Dalal BI, Brigden ML. Factitious biochemical measurements resulting from hematologic conditions. Am J Clin Pathol. 2009; 131:195-204.
2. Sodi R, Davison AS, Holmes E, Hine TJ, Roberts NB. The phenomenon of seasonal pseudohypokalemia: Effects of ambient temperature, plasma glucose and role for sodium–potassium-exchanging-ATPase. Clin Biochem. 2009; 42:813-818.
3. Naparstek Y, Gutman A. Spurious hypokalemia in myeloproliferative disorders. Am J Med Sci. 1984; 288:175-177.
4. Depner TA, Magee JA. Severe hypokalemia associated with pseudohypoxemia in acute nonlymphocytic leukemia. West J Med. 1988; 149:332-334.
5. Muggia FM, Heinemann HO, Farhangi M, Osserman EF. Lysozymuria and renal tubular dysfunction in monocytic and myelomonocytic leukemia. Am J Med. 1969; 47:351-366.
6. Pickering T, Catovsky D. Hypokalaemia and raised lysozyme levels in acute myeloid leukaemia. QJM. 1973; 42:677-682.
7. Liamis G, Liberopoulos E, Barkas F, Elisaf M. Spurious electrolyte disorders: a diagnostic challenge for clinicians. Am J Nephrol. 2013; 38:50-57.
8. Cline M. Metabolism of the circulating leukocyte. Physiol Rev. 1965; 45:674-720.
9. Hess CE, Nichols AB, Hunt WB, Suratt PM. Pseudohypoxemia secondary to leukemia and thrombocytosis. N Engl J Med. 1979; 301:361-363.
10. Chillar RK, Belman MJ, Farbstein M. Explanation for apparent hypoxemia associated with extreme leukocytosis: leukocytic oxygen consumption. Blood. 1980; 55:922-924.
11. Roos D, Balm A. The oxidative metabolism of monocytes. In: Sbarra AJ, Strauss RR, editors. Biochemistry and Metabolism. Boston, MA: Springer; 1980. pp. 189-229.
12. Lele AV, Mirski MA, Stevens RD. Spurious hypoxemia. Crit Care Med. 2005; 33:1854-1856.
13. Sacchetti A, Grynn J, Pope A, Vasso S. Leukocyte larceny: spurious hypoxemia confirmed with pulse oximetry. J Emerg Med. 1990; 8:567-569.
14. Charan NB, Marks M, Carvalho P. Use of plasma for arterial blood gas analysis in leukemia. Chest. 1994; 105:954-955.
15. Mizock BA, Franklin C, Lindesmith P, Shah PC. Confirmation of spurious hypoxemia using continuous blood gas analysis in a patient with chronic myelogenous leukemia. Leuk Res. 1995; 19:1001-1004.
16. Roe BJH, Irish OJ, Boyd JI. The preservation of blood for chemical analysis by the use of sodium fluoride. J Bio Chem. 1927; 75:685-695.