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Case report

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Pseudohyponatremia and falsely increased serum osmolal gap caused by paraprotein in a patient with severe metabolic acidosis – a case study

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Abstract

Introduction: *The aim of the study is to present a case study of a 63-year-old male with pseudohyponatremia, falsely increased serum osmolal gap and severe metabolic acidosis.* ***Material and Methods:*** *Venous whole blood (direct sodium selective electrode measurement) and serum (indirect sodium selective electrode measurement) were used to measure sodium concentration. Serum cholesterol, triacylglycerides and total protein were measured to confirm pseudohyponatremia. Base excess in extracellular fluid and serum bicarbonate concentrations were employed as markers of metabolic acidosis. Serum protein electrophoresis and free light chain analysis were used for the detection of paraproteins.* ***Results:*** *Venous whole blood acid base analysis showed a pH of 7.171, negative base excess in extracellular fluid of – 18.6 mmol/L and sodium concentration of 140 mmol/L. Serum test measurement revealed serum sodium concentration of 130 mmol/L, osmolal gap of 24 mmol/kg, creatinine concentration of 702 µmol/L, HCO3- concentration of 6.1 mmol/L and total protein concentration of 134.9 g/L. Serum paraprotein IgG kappa with a concentration of 86 g/L and a serum free light chains kappa/lambda ratio of 223.5, along with the final diagnosis of multiple myeloma were detected. Toxic alcohol ingestion was considered, both methanol and ethylene glycol tests were negative.* ***Conclusions:*** *High paraprotein concentrations in serum may lead to pseudohyponatremia when measured by indirect ion selective electrodes. Multiple myeloma frequently leads to renal failure with metabolic acidosis.*

Keywords: *pseudohyponatremia, hyponatremia, acidosis, paraproteins, multiple myeloma*
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Introduction

The differential diagnosis of severe metabolic acidosis in the emergency department is broad and heterogeneous, it includes mainly hypoxia states, renal failure, sepsis, drug induced metabolic acidosis and, rarely, toxic alcohol poisoning (1). The serum osmolal gap (OG) is a useful parameter for the detection of toxic alcohol poisoning. The OG is calculated according to the following equation:

OG = measured serum osmolality – calculated serum osmolality

Serum calculated osmolality (OSMcalc) is derived from serum sodium, glucose and urea concentrations using the following equation:
OSMcalc = 2*sodium (mmol/L) + glucose (mmol/L) + urea (mmol/L) (2).
If serum OG is higher than 10 mmol/kg the presence of an alcohol is possible (3).
The aim of this case study is to present a patient with severe metabolic acidosis and a falsely increased serum OG.
The local hospital Ethic committee approved the publication (approval number 2021–20).
The patient signed an informed consent regarding the publication of his case study.

Case report

A 63-year old male was presented to the Emergency department with lower back pain lasting for two weeks. He received non-steroid anti-inflammatory drugs from his general practitioner without effect. The medical history included hypertension and benign prostate hyperplasia. He had an inguinal hernia surgery in 2012. The medication included 10 mg perindopril and 10 mg amlodipine daily. He was without allergies.
The venous whole blood acid base analysis measured by direct ion selective electrodes in the Emergency department showed severe metabolic acidosis, respiratory alkalosis, low hemoglobin level, and increased potassium, chloride and ionized calcium concentrations (Table1).
The serum biochemical tests revealed a newly diagnosed renal failure, decreased sodium concentration (measured by indirect sodium selective electrode), low serum bicarbonate concentration, serum OG of 24 mmol/kg, ethanol concentration below the limit for quantification and hypoalbuminemia. The lower serum concentrations of both potassium (pseudonormokalemia) and chloride compared to whole blood are also visible (Table 2).
Different sodium concentrations were found in serum and whole venous blood. New sample collections were obtained and the results con-

Table 1. Venous whole blood acid base analysis tests

Whole blood test	Result	Unit	Reference range
Glucose	4.5	mmol/L	3.9 – 5.5
Sodium	140	mmol/L	136 – 144
Potassium	5.6	mmol/L	3.5 – 4.8
Chloride	123	mmol/L	95 – 107
Calcium (ionized)	1.49	mmol/L	1.15 – 1.29
pH (37°C)	7.171	pH units	7.36 – 7.44
pCO_2 (37°C)	3.17	kPa	4.8 – 5.8
Base excess in extracellular fluid	- 18.6	mmol/L	-2.5 – +2.5
Hemoglobin	70	g/L	135 – 175
Lactate	0.7	mmol/L	0.2 – 2.0

firmed decreased serum sodium concentration and normal whole blood sodium concentration.

Increased serum total protein concentration of 133.4 g/L was detected in the next serum sample while paraprotein IgG kappa with the concentration of 86 g/L was detected later. Serum free light chain analysis showed a markedly increased kappa/lambda ratio. The results of serum proteins are shown in Table 3.

Urine immunofixation electrophoresis showed the monoclonal kappa chains (Bence Jones protein) concentration of 0.106 g/L and monoclonal the IgG kappa concentration of 0.026 g/L. Tests for the detection of methanol and ethylene glycol

Table 2. Serum test results (sampling at the same time as acid base analysis tests)

Serum test	Result	Unit	Reference range
Glucose	6.2	mmol/L	3.9 – 5.5
Sodium	130	mmol/L	136 – 144
Potassium	5.1	mmol/L	3.8 – 5.1
Chloride	116	mmol/L	95 – 107
Ethanol	< 0.1	promille	< 0.1
Osmolality measured	331	mmol/kg	275 – 295
Osmolality calculated	307	mmol/kg	–
Calculated osmolal gap	24	mmol/kg	0 – 10
Urea	41	mmol/L	3.0 – 8.0
Creatinine	702	µmol/L	64 – 104
Uric acid	731	mmol/L	140 – 360
HCO_3^-	6.1	mmol/L	22 – 29
Total bilirubin	3	µmol/L	< 20
Alanine aminotransferase	10.2	U/L 37 °C	< 43.8
Aspartate aminotransferase	11.4	U/L 37 °C	< 40.2
Gamma-glutamyl transferase	45.6	U/L 37 °C	< 106.2
Alkaline phosphatase	109.9	U/L 37 °C	< 150
Cholesterol total	2.53	mmol/L	< 5.0
Triacylglycerides	1.81	mmol/L	< 1.7
Albumin	32.3	g/L	36.0 – 45.0
C-reactive protein	8.0	mg/L	< 2.0

Table 3 Serum proteins and calcium test results

Serum test	Result	Unit	Reference range
Total protein	134.9	g/L	64.0 – 79.0
Albumin	29.4	g/L	36.0 – 45.0
Free kappa	1788	mg/L	3.3 – 19.4
Free lambda	8	mg/L	5.7 – 26.3
Free kappa/free lambda ratio	223.5	–	0.26 – 1.65
Paraprotein concentration by serum protein electrophoresis	86	g/L	0 – 0
Type of paraprotein by Immunofixation electrophoresis	IgG kappa	–	–
Beta-2-micriglobulin	22.28	mg/L	< 2.64
Calcium	2.20	mmol/L	2.15 – 2.55
Calcium corrected for 40 g of albumin	2.41	mmol/L	2.15 – 2.55

concentrations were negative. A complete blood count revealed a white blood cell count of 8.9 x 10^9/L and a thrombocyte count of 165 x 10^9/L.
The final diagnosis was multiple myeloma. High concentrations of paraprotein have likely interfered with the serum sodium concentration measurement and affected the serum OG calculation.

Discussion

We presented the case study of pseudohyponatremia and false positive serum osmolal gap due to the presence of a large quantity of paraprotein. Liamis et al reported that pseudohyponatremia can be caused by hyperproteinemia or hyperlipidemia when serum sodium concentration is measured by indirect sodium selective electrodes. Direct ion selective electrodes are not prone to indicating pseudohyponatremia (4). Our patient had marked serum hyperproteinemia and indirect ion selective electrode serum sodium measurement in the hospital's central laboratory led to pseudohyponatremia. Lower serum concentrations of both potassium and chloride compared to whole blood are also visible.
Yu et al found pseudohyponatremia and falsely increased osmolal gap in a patient with multiple myeloma (5). We found similar results in our case study.
Nikolac reported that accumulation of lipoprotein particles in the blood sample affects measurement of serum electrolytes by the volume displacement effect. Flame photometry and indirect potentiometry measure electrolyte concentrations in the total plasma volume, including the lipid phase (6). Serum lipids were not markedly increased in this case study.
Ghersin et al showed that the lysis of high number of fragile white blood cells in patients with T-cell acute lymphoblastic leukemia causes pseudohyponatremia (7). Our patient had normal white blood cell count.
Quiñones-Torrelo evaluated serum of 18 278 patients and diagnosed eight cases of monoclonal gammopathies in patients with suspected interferences of serum conjugated bilirubin and uric acid measurement (8). It shows that paraprotein interferences are relatively frequent.
Raphael reported that chronic kidney disease is commonly accompanied by metabolic acidosis (9). Our patient presented to the Emergency department with renal failure but it was not clear if metabolic acidosis could be completely attributed to renal failure. Neither methanol nor ethylene glycol were detected.
Šálek demonstrated a case study of a patient with pseudohyperkalemia and concluded that pseudohyperkalemia should be always excluded before implementing treatment (10). Similar approach should also be chosen in patients with pseudohyponatremia.
The limitation of this study is the fact that we did not perform arterial blood gas analysis that is the test of choice for blood gas analysis. But venous whole blood gas testing is also acceptable (11).

Conclusion

The presence of paraprotein in blood can cause analytical interferences in laboratory testing. Both laboratory experts and clinical professionals should be aware of it. This case study demonstrated serum pseudohyponatremia and falsely increased osmolal gap due to the presence of a large quantity of paraprotein.

Abbreviations

OG – osmolal gap
OSMcalc – serum calculated osmolality

Authors´ contributions

TŠ; writing the article, data collection, interpretation of results, final approval, accountable of all aspects of work

Conflict of interest

Author declare no conflict of interest

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