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Case Report

Benefit of point of care testing in patient with major hyperleukocytosis

Guillaume Grzych[a,b,*], Estelle Roland[a], David Beauvais[c], Patrice Maboudou[a], Thierry Brousseau[a]

[a] CHU Lille, Service de Biochimie automatisée Protéines, F-59000 Lille, France
[b] INSERM, UMR-1011-European Genomic Institute for Diabetes, Institut Pasteur de Lille, Lille, France
[c] CHU Lille, Service des Maladies du Sang, Hospital Huriez, F-59000 Lille, France

ABSTRACT

We report a case of a child with major leukocytosis (800 × 10^9/L) leading to a false increase in plasma potassium and an unexpected spurious decrease in sodium. To suppress interferences due to hyperleukocytosis, our laboratory protocol consists of collecting blood on Clotting Activator/Serum tubes (CAS) and/or carrying samples by human courier. CAS tube analysis showed a decreased level of hyperkalemia and sodium within the reference range (consistent with point of care measurements). Pseudo-hyperkalemia caused by extreme hyperleukocytosis has been well documented and is caused by lysis of leukocytes and cell contents release (including potassium) into the plasma, especially regarding blast cells, which are at even higher risk of lysis. Pseudo-hyponatremia mechanism has not yet been described. This interference could be multifactorial; blast lysis could cause intracellular ionic content release, therefore, modifying extracellular fluid ionic ratios. To correct this interference, the hypothesis is that collecting samples on CAS tubes or monitoring patient using point of care analysis are the most efficient solutions, as transport mode did not resolve interference issues. We speculate that cell lysis related to interference is multifactorial but mainly caused by centrifugation. To confirm this, we would have liked to compare ion levels before and after centrifugation.

1. Introduction

Many interferences on biochemistry analysis are in relation with hyperleukocytosis. The most widely documented interferences are due to *in vitro* release of intracellular contents in the medium, causing a significant rise of, at least, potassium (K), lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) [1,2]. These interferences are frequently associated to the use of a pneumatic transport system (PTS) [3–5]. We report a case of a child with a major leukocytosis leading to an unexpected spurious hyponatremia in addition to a false hyperkalemia.

2. Case report

A 4-years-old female child with fever, splenomegaly and cervical adenopathy was admitted to a pediatric emergency care unit. Complete blood counts were: hemoglobin 4.8 g/dL, platelet count 22 × 10^9/L, white blood cells (WBC) 812 × 10^9/L. Blood analysis showed a 94% immature blasts rate. Bone marrow aspiration revealed a high cellularity with 98% blast cells. Immunophenotyping confirmed the diagnosis of B-cell acute lymphoblastic leukemia.

Plasma obtained from lithium-heparin microtubes without gel separator (LiH, Lithium Heparin Polypropylene 1.3 mL, Sarstedt, Nümbrecht, Germany) were used for biochemistry analysis. They were transported to the laboratory by pneumatic tube system (PTS) (Swisslog, Switzerland) and centrifuged for 10 min at 2500 *g*. Analyses were performed on Cobas 8000 (Roche Diagnostics, Mannheim, Germany). Data showed a severe hyperkalemia (27.2 mmol/L) and high LDH (2612 U/L) but also a severe and unexpected hyponatremia (117 mmol/L). Specific hyperkalemic electrocardiogram abnormalities were not reported.

Due to the severe hyperleukocytosis, spurious hyperkalemia and hyponatremia were suspected and interferences were investigated. True ionic disorders and blood collection errors were excluded since further blood sample controls sent to the laboratory showed similar results [6]. Hemolysis was non-significant (hemolysis index did not exceed 100).

From day 0 to day 5 (sample 1 to sample 12), sodium and potassium varied in opposite way: the more potassium increased, the more sodium decreased. Interestingly, systematic reanalysis of these consecutive samples using a point of care materiel (i-STAT Handheld Blood analyzer, Abbott) showed that potassium and sodium were within the reference range (Fig. 1).

Leukocyte count remained over 500 × 10^9/L from day 1 to day 5 (sample 1 to sample 21). During this period of time, we still found discordances between laboratory and point of care (POC) measurements of sodium and potassium.

On day 4 (sample 16), a hypokalemic treatment was introduced, leading to hypokalemia on POC. Moreover, hyponatremia was treated with hypertonic saline infusion although signs of hyponatremia were not present. In response to this, investigations were carried out in the

* Corresponding author at: Pôle de Biologie Pathologie Génétique, CHU Lille, Pr J. Leclercq Boulevard, 59037 Lille Cedex, France.
E-mail addresses: guillaume.grzych@inserm.fr (G. Grzych), patrice.maboudou@chru-lille.fr (P. Maboudou).

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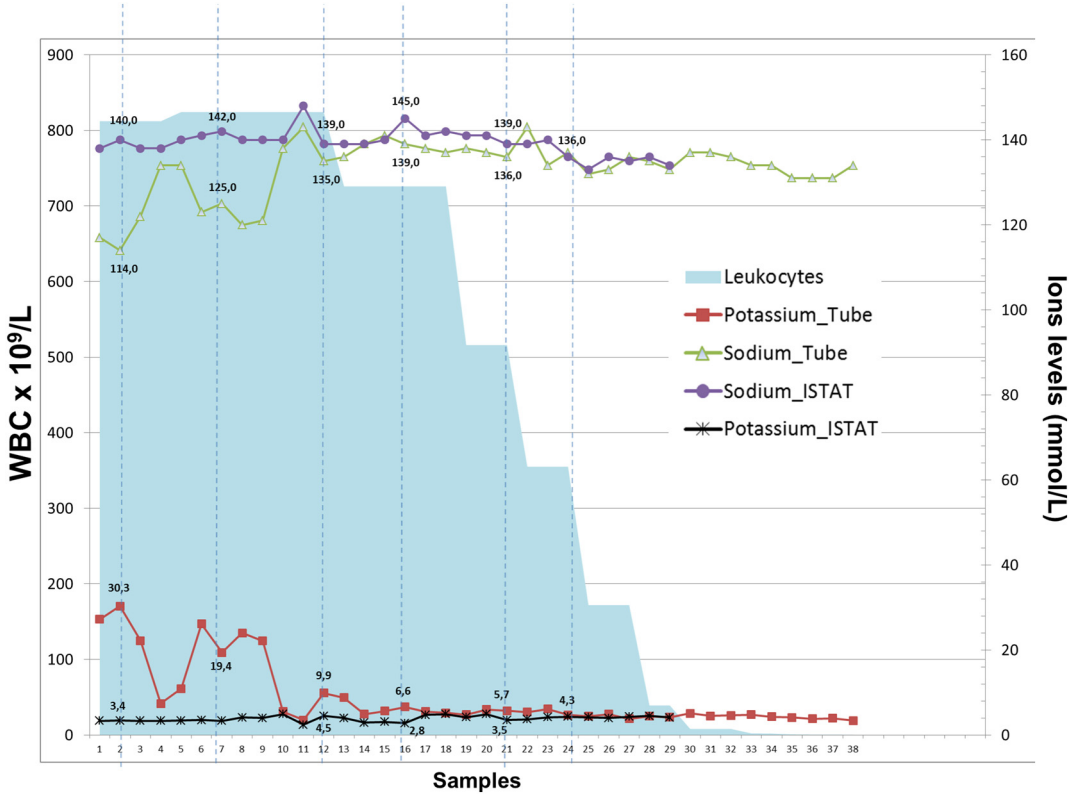

Fig. 1. Evolution of potassium and sodium on both Cobas 8000 analyzer and Istat point of care analysis (mmol/L), and WBC: white blood cells (x10^9/L) until interference resolution. Selected values of Cobas/Istat discordance and concordance are highlighted. Point of care analysis (IStat) remained stable and within reference range, whereas tubes analyses showed unpredictable variations of ions levels.

laboratory.

On the other hand, to suppress interferences related to hyperleukocytosis, our laboratory protocol recommends collecting blood on Clotting Activator/Serum without gel separator ((CAS) Microtube 1.3 mL, Sarstedt, Nümbrecht, Germany) and/or carrying samples by human courier (HC). In the present case, analyses realized on CAS tubes showed a less pronounced but not normalized hyperkalemia; sodium was within reference range and consistent with POC measurements. The transport by dispatch rider did not avoid interferences (Fig. 2).

Finally, corticotherapy and chemotherapy were introduced at day 2 (vincristine, daunorubicin and PEG aspargase), WBC and blast levels decreased, electrolyte interferences disappeared at day 8 (sample 25, Fig. 1).

3. Discussion

Pseudo-hyperkalemia caused by extreme hyperleukocytosis has been well documented and is caused by lysis of leukocytes and cell contents release, including potassium, into the plasma, especially regarding blast cells, which are at even higher risk of lysis [1,7,8]. Pseudo-hyponatremia mechanism has not yet been described.

The interference between major hyperleukocytosis and natremia could be multifactorial. Blast lysis causes intracellular ionic content release that could modify extracellular fluid ionic ratios. This interference could be exacerbated by alteration of ionic gradients between intracellular and extracellular fluids. In a previously major hyperleukocytosis case, alteration of Na/K concentration gradients and ionic channel and pump dysfunctions led to *in vitro* hypokalemia [2]. In our case, partial lysis of blast cells could have caused massive potassium release into the extracellular fluid. However, the remaining living cells added to the already existent sodium gradient modifications could impact Na and K active and passive fluxes, leading to massive sodium intracellular uptake.

Our protocol to correct leukocytosis interferences is based on

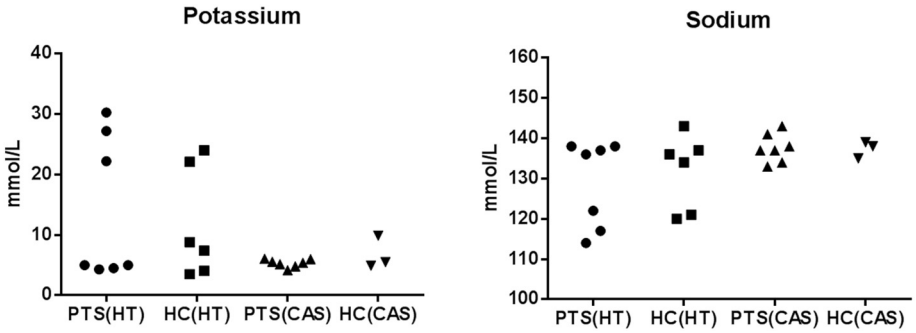

Fig. 2. Electrolyte levels (potassium and sodium) during hyperleukocytosis phase (WBC $>$ 500 $\times$ 10^9/L) with different types of tube: CAS (Clotting Activator Serum tube) and HT (Heparinized Tube) or different types of sample transports: HC (Human Courier) PTS (Pneumatic Tube System).

literature involving the pneumatic system as the major cause of lysis, serum from clotting activator tube without gel seems to reduce this interference as described [1,9]. Therefore, to reduce the impact of blast lysis, tubes were brought to the laboratory by human courier. In our case, we did not see a difference between human courier and PTS; but only with different types of tube.

We hypothesized that the clot could prevent the release of cell contents by mechanical protection forming a physical barrier between cells and serum. But it should be noted that the use of CAS with patients with hematologic malignancies could lead to other interferences such as spurious hyperkalemia induced by clotting. However pseudo hyperkalemia induced by heparin tube is more important than spurious hyperkalemia related to clot CAS tube, indeed lower kalemia with CAS than heparin tube in this case was reported. So there is a benefit of use of CAS tube in case of hyperleukocytosis instead of heparin tube if use of POC device is not possible.

We cannot exclude that this interference was exacerbated by microtube use and/or by centrifugation. To confirm that, we would have liked to compare ion levels before and after centrifugation but whole blood ion analysis using direct potentiometry on CAS tubes could not be performed due to clotting. Interestingly, the use of POC, which does not require transport nor centrifugation steps, gave electrolyte measurements fully compatible with the clinical state of the patient, independently of WBC and blast count.

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