Factitious acidosis and severe hypoalbuminemia caused by unsuspected assay interference

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ABSTRACT
It is relatively common to have some discord between laboratory biomarkers and clinical status. The current practice of medicine relies on imaging and biochemical testing in order to guide decision-making. In the clinical setting, an unsuspected laboratory artifact can have harmful impacts on patients. These circumstances can invariably lead to misdiagnoses, unnecessary testing and inappropriate treatments. We present a case of very low serum bicarbonate (4 mmol/L) in concert with a very low albumin level (0.3 g/dL). It turned out that the lab measurements were erroneous and a lot of harmful interventions could have ensued when dealing with this peculiar case.

Keywords: assay interference, falsely/spuriously low, hypoalbuminemia, hypobicarbonatemia, paraproteinemia

BACKGROUND
It is relatively common to have some discord between laboratory biomarkers and clinical status. An unsuspected laboratory artifact can have harmful impacts on patients, as providers tend to respond to numbers, especially when these are excessively low, triggering panic buttons that are often fueled by electronic systems. These circumstances may lead to misdiagnoses, unnecessary tests and, in the worst cases, inappropriate treatments. Erroneously low serum bicarbonate levels have been reported in the medical literature. We present a case of very low serum bicarbonate in concert with a very low serum albumin level. It eventually turned out that those lab measurements were completely false due to unsuspected interference.

CASE REPORT
A patient was referred to our specialty clinic for severe metabolic acidosis. His measured serum bicarbonate was 4 mmol/L. His kidney function and electrolytes were normal. His serum albumin was 0.3 g/dL. He had no physical edemas. He was admitted to the hospital with a pH of 7.46 on arterial blood gas (ABG) and a calculated bicarbonate level of 22 mmol/L. Following an extensive workup, he was found to have 4.09 g/dL of immunoglobulin A (IgA) kappa monoclonal protein, which was also found in his urine electrophoresis. Interestingly, albumin measured by serum protein electrophoresis was 3.7 g/dL. He was started on chemotherapy with a measured serum bicarbonate of 3 mmol/L and a serum albumin of 0.7 g/dL. Three weeks into therapy, the monoclonal IgA was significantly suppressed and his measured serum bicarbonate increased to 23 mmol/L while his serum albumin improved to 3.3 g/dL, confirming the fact that the paraprotein was interfering with both assays.

DISCUSSION
At our institution, serum bicarbonate is measured indirectly by detecting the decrease in absorbance that ensues from the enzymatic consumption of nicotinamide adenine dinucleotide...
phosphate (NADPH) analog, which is proportional to the concentration of bicarbonate in the sample being assayed. Hyperlipidemia has been the most commonly described cause of falsely low serum bicarbonate levels in case series [1]. Our patients lipid panel was not overtly impaired. Conversely, Goldwasser et al. [2] reported a case of severe metabolic acidosis where the serum bicarbonate level was spuriously low in the setting of IgM paraproteinemia, and this was confirmed by reanalysis using the electrode-based method, which yielded a result that was higher by 7 mEq/L. The concept around this phenomenon is that mixing the paraproteinemic serum with the total carbon dioxide assay reagents causes gross turbidity that can be seen visually, where absorbance is initially increased (for a couple of minutes) before it starts to decrease gradually and steadily to low levels, yielding a falsely low measured serum bicarbonate. Why absorbance decreases remains unclear [3].

Nonetheless, simultaneously spuriously low serum bicarbonate and albumin levels in the setting of paraproteinemia have never been reported in the published literature. Furthermore, IgA paraproteins have not been reported to interfere with serum bicarbonate or albumin assays.

In our patient, we had to fend off intravenous bicarbonate therapy among other aggressive interventions by fellow physicians, who were distraught at seeing the excessively low measured serum bicarbonate, while not trusting the calculated bicarbonate on ABG, which is unfortunately a prevalent reaction among physicians due to an established bias from older publications [4]. The patient finally did very well. In the overall scheme of things, when numbers do not make sense, it is always best to remember that first impressions oftentimes turn out to be quite accurate.

**PATIENT CONSENT**

Informed consent was obtained to publish this case.

**CONFLICT OF INTEREST STATEMENT**

None declared.

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