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Factitious Anion Gap Metabolic Acidosis Caused by Hypertriglyceridemia: A Case Report

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Introduction: Severe hypertriglyceridemia can result in false metabolic derangements on biochemistry testing due to lipid interference with enzymatic and spectrophotometric chemistry analyzers. Elevated anion gap and low bicarbonate levels are commonly associated with an anion gap metabolic acidosis, which can indicate a broad differential diagnosis of threatening emergency conditions.

Case Report: We describe a 31-year-old man with moderate hyperglycemia whose laboratory results demonstrated metabolic derangements that did not correlate with blood gas analysis. Subsequent evaluation revealed severe triglycerides that interfered with the metabolic testing.

Conclusion: Emergency physicians should be aware of this interference from severe hypertriglyceridemia. False biochemical derangements mimicking an anion gap metabolic acidosis can lead to inappropriate diagnoses, testing, and management. [Clin Pract Cases Emerg Med. XXXX;X(X):X–X.]

Keywords: *hypertriglyceridemia; anion gap; metabolic acidosis; case report.*

INTRODUCTION

Anion gap metabolic acidosis is a common metabolic abnormality that emergency physicians look for in biochemistry testing because it can be a sign of serious pathology that requires emergent intervention. We discuss a patient whose biochemistry panel was consistent with an anion gap metabolic acidosis based on an elevated anion gap and low bicarbonate level. However, on further diagnostic testing the patient was not acidotic and ultimately was found to have severe hypertriglyceridemia as the etiology of their derangement in biochemical results. To our knowledge, this laboratory phenomenon from severe hypertriglyceridemia has not been reported in the emergency medicine literature.

CASE REPORT

A 31-year-old man presented with complaints of dizziness and vomiting. He had a history of noninsulin dependent diabetes mellitus and reported being out of his medication for two months. Biochemical evaluation demonstrated the following: glucose, 376 mg/dL (reference range, 74-106 mg/dL); sodium, 133 mmol/L (136-145 mmol/L); bicarbonate (HCO_3), <10 mmol/L (20-31 mmol/L), and anion gap, >25 (5-15). These results suggested an anion gap metabolic acidosis, with diabetic ketoacidosis considered as a potential etiology given the patient's hyperglycemia, history of diabetes, and medication nonadherence. Venous blood gas results demonstrated the following: pH, 7.37 (7.31-7.41), partial pressure of carbon dioxide, 46 mm Hg (41-55 mm Hg), and calculated bicarbonate (HCO_3), 27 mmol/L (22-26 mmol/L).

Additional biochemical evaluation demonstrated urinalysis negative for ketonuria, lactate level within normal limits, and negative salicylate level. A repeat blood sample was sent for testing given the discordance of the patient's biochemical testing; the sample continued to show signs of an anion gap metabolic acidosis, CO_2 of <10 mmol/L, and an anion gap > 27. The laboratory technicians were then contacted and staff reported a high level of lipids in the patient's blood samples. Triglyceride levels demonstrated severe hypertriglyceridemia, 2,753 mg/dL (reference range: 2-149 mg/dL).

The patient was admitted and started on an insulin

infusion to decrease his severe hypertriglyceridemia, and a dextrose infusion to prevent hypoglycemia. After 48 hours, his triglycerides down trended to <1,000 mg/dL. He was transitioned from an insulin infusion to oral therapy for hypertriglyceridemia using a fibrate and omega-3 fatty acids.

CPC-EM Capsule

What do we already know about this clinical entity?
Preanalytical laboratory errors are a type of endogenous interference where the measured value may not be accurate due to the quality of the blood sample.

What makes this presentation of disease reportable?
Hypertriglyceridemia resulted in lab derangements that mimicked an anion gap acidosis in a diabetic patient.

What is the major learning point?
Certain endogenous components of blood, when present in excess, can affect the ability of laboratory instruments to accurately measure certain values.

How might this improve emergency medicine practice?
Emergency clinicians should be aware of common causes of endogenous interference that can cause laboratory derangements and impact patient care.

DISCUSSION

Severe hypertriglyceridemia, resulting in a lipemic blood sample, is a known cause of interference with enzymatic and spectrophotometric chemistry analyzers. However, its effect on measured HCO_3 levels and its impact on emergency care is under-reported.[1] Patients with diabetes are clinically challenging because they can develop metabolic acidosis and may also have co-existing hypertriglyceridemia. Emergency physicians should maintain a high level of suspicion for alternative etiologies of pathophysiology when blood gas and ketone laboratory results are not consistent with reported HCO_3 and anion gap levels.

The laboratory errors highlighted in this case are a result of preanalytical interference. Preanalytical interference is reported to contribute to 60% to 70% of all laboratory errors and refers to issues in blood sample quality prior to the sample being analyzed.[7] In this case, lipemia interfered with the signaling required to measure CO_2 values by laboratory equipment. To measure CO_2, chemistry analyzers use an enzyme to catalyze CO_2, and at the end of the reaction, perform a spectrophotometric analysis of the sample based on light absorbance. High levels of lipid particles increase the turbidity in blood, which interferes with the spectrophotometric portion of the analysis. This results in a falsely low reading, suggesting that there is less measured CO_2 in the sample. This in turn, gives the illusion that there are increased unmeasured anions resulting in an reported elevated anion gap.[1,2] The Atellica chemistry analyzer (Siemens Healthineers) used in this case utilizes a two-step analysis, enzymatic followed by spectrophotometric to measure CO_2.

Severe hypertriglyceridemia can also cause pseudohyponatremia due to preanalytical interference. Serum sodium is commonly measured using ion-specific electrodes, which use dilution and standardized ratios or serum water content to serum. Lipemic blood samples displace and dilute serum sodium, altering standardized ratios that are not accounted for by laboratory analyzers. In this case, the hyponatremia noted on biochemical testing represents pseudohyponatremia, from volume displacement by triglycerides in the serum sample.[2,3]

Emergency physicians rely on the assumption that reported laboratory values are accurate when determining the appropriate clinical care for a patient. It is important for emergency physicians to be aware of common causes of laboratory interference that can result in false positive or false negative results. Hemolysis, icterus, and lipidemia are common endogenous interferants that cause preanalytical errors. Paraproteins (monoclonal immunoglobulins) can also cause interference. The prevalence of paraproteins increases with age and is more common in elderly patients.[8,9] These common causes of preanalytical laboratory errors can result in incorrectly reported laboratory results.[4,5] The table describes these common endogenous interferants in further detail.

Clinical laboratories have methods to identify endogenous interference to mitigate the impact of interferences on clinical care.[5,6] When endogenous interference is confirmed or suspected, communication between laboratory technicians, nurses, and physicians is essential to ensure information is being openly shared to ensure laboratory results are appropriately interpreted. A lack of communication can lead to unnecessary testing and, in more serious situations, inappropriate treatment and patient harm.

CONCLUSION

There are numerous etiologies of anion gap metabolic acidosis, several of which require emergent intervention. When biochemistry testing shows evidence of an anion gap metabolic acidosis, emergency physicians must validate these results with a blood gas and other tests to identify the source of the anions. Emergency physicians should also be aware that severe

Table. Common endogenous interferants that can result in incorrectly reported laboratory values.

Endogenous Interferant	Mechanism of Interference	Laboratory Derangement
Hemolysis	Hemolysis occurs due to the in-vivo breakdown of RBCs. This results in release of RBC intracellular contents, spuriously increasing the concentration of intracellular analytes and dilution of extracellular components.[4,7] Cell-free hemoglobin can interfere with various light absorbance measurements in analyzers that rely on spectrophotometry.[4,7]	Release of intracellular contents results in falsely elevated potassium, phosphate, aspartate and alanine aminotransferase, and lactate dehydrogenase. Falsely low sodium can occur due to extracellular dilution.[7]
Icterus (Bilirubin)	An elevated bilirubin level causes spectrophotometric inference due to its strong light absorbance between 340-500 nm. High levels of bilirubin causing negative interference by decreasing absorbance of the sample at this wavelength.[4] Bilirubin has antioxidant properties that interfere with peroxidase-coupled enzymatic reactions.[7]	Spectrophotometric interference results in falsely low creatinine, albumin, and phosphate.[4] Interference with peroxidase-coupled reactions results in falsely low glucose, uric acid, and lipid studies.[4,7]
Lipidemia	Lipemic samples cause increased turbidity, causing derangements in spectrophotometric analysis due to nonspecific light scattering, light absorbance, or volume displacement.[1,2]	Interference from lipidemia can result in falsely low bicarbonate, sodium, chloride, and hypokalemia.[1,2,4]
Paraproteins	Paraproteins can cause interference through various mechanisms that are unique to the individual patient, based on the type and quantity of paraprotein presented and the specific type of the analytic testing performed.[8,9] Different types of analyzers inactivate test reagents by acting as antigens, and reduce the amount of water-soluble molecules through a relative decrease in a samples aqueous phase.[8]	Paraprotein interference is described as variable variability because it can cause both falsely low and falsely elevated levels. Interference is commonly reported with bilirubin, lipid studies, and iron assays.[9]

nm, nanometer; *RBC*, red blood cell.

hypertriglyceridemia is an under-reported cause of fictitious anion gap metabolic acidosis due to lipemia resulting in endogenous preanalytical interference. Open two-way communication should exist between nursing, physicians, and laboratory technicians to allow for early identification of endogenous interference in blood samples that can result in incorrect laboratory results.

The authors attest that their institution requires neither Institutional Review Board approval, nor patient consent for publication of this case report. Documentation on file.

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