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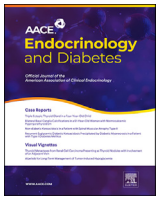

Case Report

Artifactual Hypoglycemia Masquerading as a Medical Emergency: A Diagnostic Pitfall of High-Dose Vitamin C

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ABSTRACT

Introduction: Severe hypoglycemia prompts emergent intervention, yet not all low glucose readings reflect true hypoglycemia. We present a striking case of extreme artifactual hypoglycemia due to high-dose vitamin C therapy, highlighting the diagnostic challenges and management implications.
Case Report: A 76-year-old man with metastatic prostate cancer, receiving high-dose vitamin C as part of alternative therapy, presented with worsening malaise, oliguria, and edema. On presentation, despite critically low blood glucose (BG) reading (<20 mg/dL) on both point-of-care glucometer and laboratory testing, the patient remained asymptomatic. Repeated dextrose infusions failed to increase the recorded BG levels, contradicting the expected response in true hypoglycemia. Dialysis, rather than dextrose, ultimately corrected his BG readings. Additionally, his liver enzymes, initially undetectable on presentation, became measurable as dialysis progressed. Further investigation identified markedly elevated vitamin C levels as the interfering substance, affecting both standard glucose and liver enzyme assays, leading to pseudo-hypoglycemia.
Discussion: This case highlights the impact of high-dose vitamin C on glucose oxidase-based assays, causing pseudohypoglycemia and potentially triggering inappropriate clinical interventions. Also, over-reliance on laboratory values without clinical correlation can be costly and problematic particularly in critically ill patients, emphasizing the need for contextual interpretation of biochemical data. Alternative glucose measurement methods, such as hexokinase assays, may be required in suspected cases.
Conclusion: Clinicians should suspect pseudohypoglycemia when glucose readings are critically low but the patient lacks corresponding symptoms, especially in patients pursuing alternative medicine. Whipple's Triad remains vital in differentiating true hypoglycemia from laboratory artifact, preventing unnecessary escalation of care.

Introduction

Hypoglycemia is classically defined by Whipple's Triad: (1) low blood glucose (BG), (2) corresponding symptoms of hypoglycemia, and (3) symptom resolution upon glucose correction.[1,2] Severe hypoglycemia, often characterized by altered mental or physical status requiring external assistance, demands prompt recognition and treatment. In individuals without diabetes, etiologies such as insulinoma, hepatic or renal dysfunction, and critical illness are commonly implicated.[2,3] However, spurious laboratory values resulting from assay interference can mimic hypoglycemia, leading to inappropriate interventions.

Here, we present a case of extreme pseudohypoglycemia in a patient receiving high-dose vitamin C as part of alternative therapy for metastatic prostate cancer, exploring the diagnostic process and highlighting the importance of critical thinking in cases of discordant clinical and laboratory findings.

Abbreviations: BG, blood glucose; POC, point of care.

Patient consent: Written informed consent was obtained from the patient to document this case and submit it for publication.

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Case Report

This case describes a 76-year-old male with atrial fibrillation, on apixaban and metoprolol, and metastatic prostate cancer diagnosed roughly 10 months before his presentation. He had no history of diabetes. He had declined chemotherapy, choosing instead to pursue alternative therapies. He would receive 75 g of vitamin C infusion twice weekly, with his last infusion administered on the morning of his hospital presentation. He would also continuously sip a vitamin C solution throughout the day. His alternative therapy regimen also included ivermectin 21 mg daily, metformin 500 mg twice daily, ibuprofen 400 mg daily, desiccated thyroid 105 mg, fish oil, Iodoral 12.5 mg, magnesium glycinate, losartan 50 mg, and furosemide 20 mg daily. All his medications and supplements, except for metoprolol and apixaban, were permanently discontinued on admission.

Two weeks prior, patient had begun experiencing reduced oral intake that had worsened 4 days before his emergency department visit. This was associated with anuria, leg swelling, shortness of breath, flu-like symptoms, and malaise. He also reported a weight loss of about 35-45 pounds since his prostate cancer diagnosis. He denied symptoms suggestive of hypoglycemia such as changes in mental status, confusion, sweating, headaches, tremors, or palpitations. He had no history of kidney failure and he believed his kidney function was normal before starting the alternative treatment. He consumed alcohol moderately on a daily basis, with his last drink 3 days before admission. He was a nonsmoker.

Upon presentation to the emergency department, he was fully alert and oriented. His vital signs were largely unremarkable: blood pressure 145/88 mmHg, heart rate 71 beats per minute, respiratory rate 18 breaths/minute, oxygen saturation 90% on room air, and temperature 36.3°C. His body mass index was 27.1 kg/m^2. Physical examination revealed bilateral pedal edema and an irregularly irregular pulse. A standard urine 11-drug screen and respiratory 4-plex swab were both negative. However, point of care (POC) ACCU-CHEK glucose was unrecordably low (error code: LO).

The initial laboratory findings (Table 1) revealed a critically low BG level <20 mg/dL, an anion gap metabolic acidosis (pH 7.14), acute kidney injury (creatinine 10.74 mg/dL, blood urea nitrogen 128 mg/dL, eGFR 8.4 mL/min/1.73 m^2), and hemoglobin A1c of 4.5%.

Table 1
Summary of Laboratory Tests and Their Results

Day collected	Normal ranges	Day 1	Day 4	Day 8
WBC	4.3-10.0 k/uL	7.6	8.1	8.1
Hemoglobin	13.6-16.5 g/dL	8.3	7.2	7.3
MCV	82-99fl	103.2	99.5	99.5
Platelet count	140-350 k/uL	209	176	186
Sodium	137-145 mmol/l	134	131	131
Potassium	3.4-5.1 mmol/l	5.1	4.4	4.0
Blood urea nitrogen	9-20 mg/dL	128	59	46
Creatinine	0.7-1.30 mg/dL	10.74	7.45	6.51
Glucose	74-106 mg/dL	<20	74	80
Albumin	3.5-5.0 g/dL	3.7	3.2	-
Alkaline phosphatase	38-126 U/l	81	83	-
Total bilirubin	0.2-1.3 mg/dL	<0.1	<0.1	-
AST	14-54 U/l	<3	17	-
ALT	=<50 U/l	<4	16	-
TSH	0.47-4.68 uIU/mL	2.43	-	-
pH	7.32-7.43	7.14	-	-
Anion Gap	7-16 mmol/L	33	16	9

Day 1 was the day the patient presented to the emergency department. (−) means test was not done.
Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; MCV = mean corpuscular volume; TSH = thyroid stimulating hormone; WBC = white blood cell.

Highlights

- An adult presenting with biochemical level 2 hypoglycemia but without symptoms
- A need to critically analyze laboratory results, especially in atypical presentations
- Applying Whipple's Triad can minimize unnecessary investigations and treatments

Clinical Relevance

The case highlights the importance of recognizing artifactual hypoglycemia, particularly in asymptomatic patients, to prevent unnecessary interventions and diagnostic procedures that can strain healthcare resources. It also underscores the relevance of Whipple's Triad in clinical practice when evaluating hypoglycemia to improve diagnostic accuracy, reducing resource utilization and enhancing patient care.

Additional findings included hyperphosphatemia (8.4 mg/dL), high normal potassium level (5.1 mmol/L), and normal thyroid-stimulating hormone level of 2.43 μIU/mL. Alanine transaminase, aspartate transaminase, and bilirubin levels were unmeasurably low on the hepatic panel. Glucose, alanine transaminase, aspartate transaminase, and bilirubin levels were measured using the Vitros XT 7600 analyzer, which uses oxidase-dependent enzymatic assays.

Due to the low BG levels, a hypoglycemia protocol was activated. Despite multiple dextrose boluses and continuous infusion, his recorded BG levels remained persistently low, peaking at only 37 mg/dL. A 10% dextrose infusion was continued, and additional endocrine testing was performed (Table 2). A chest X-ray and noncontrast abdominal computed tomography scan revealed extensive bone metastases but no acute pathology. An electrocardiogram confirmed atrial fibrillation, and an echocardiogram demonstrated mildly reduced left ventricular systolic function (ejection fraction 50%).

The patient was admitted to the medical intensive care unit (ICU) and dialysis was initiated for the severe kidney failure. As dialysis sessions continued, his BG levels gradually normalized (Fig.), and previously undetectable liver enzymes became measurable (Table 1). Vitamin C levels, obtained on day 3, after multiple dialysis sessions, were marked elevated at 74.0 mg/dL (reference range 0.4–2.0 mg/dL). Given that vitamin C is dialyzable, we believe the patient's levels were even higher at the time of presentation.

Table 2
Laboratory Tests Performed for Hypoglycemia Evaluation and Their Results

Laboratory test	Normal ranges/ units	Day of sample collection	Result
Insulin	2.6-24.9[b]	Day 1	6.1
Proinsulin	0.0-10.0[b]	Day 1	**11.3**
C-peptide	1.1-4.4[b]	Day 1	**9.1**
Sulfonylureas screen[a,b]	-	Day 1	Negative
Acetaminophen	ug/mL	Day 1	<10.0
Salicylate	<30.0 mg/dL	Day 1	<1.0
Vitamin C	0.4-2.0 mg/dL	Day 3	**74.0**
Nicotinamide	5.2-72.1 ng/mL	Day 3	58.3
Nicotinic acid	0.0-5.0 ng/mL	Day 3	<5.0
Oxalate	-	Day 5	Not detected

Day 1 was the day the patient presented to the emergency department. Abnormal results are shown in bold for emphasis.
[a] Acetohexamide, chlorpropamide, tolazamide, tolbutamide, glimepiride, glipizide, nateglinide, repaglinide.
[b] Blood sample taken about 2 h after dextrose injections.

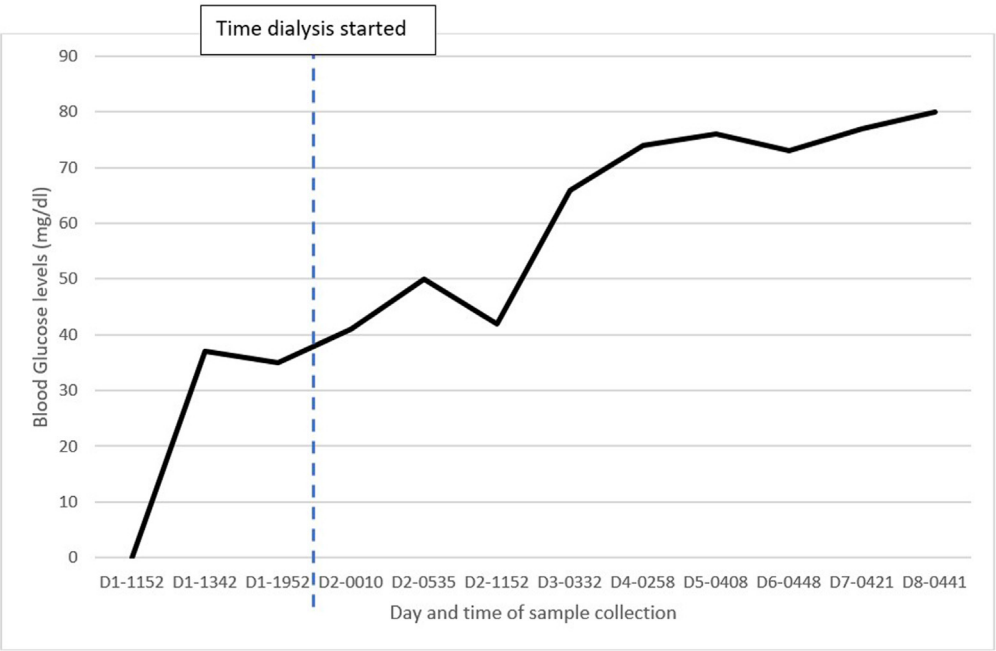

Fig. Trend of blood glucose levels throughout the patient's hospital stay, demonstrating improvement following the initiation of dialysis. The day of presentation to the emergency department is designated as day 1. The horizontal axis represents day and time, with notation such as D1-1152 indicating a sample collected at 11:52 AM on day 1.

Despite the persistently low BG readings, he remained asymptomatic for hypoglycemia throughout his hospital stay and no further dextrose injections were administered. He was discharged on day 9 with outpatient dialysis plans. At discharge, his POC ACCU-CHEK glucose reading was 115 mg/dL. His new medications included aspirin, sevelamer, and atorvastatin.

Discussion

We report a case of profound artifactual hypoglycemia in a patient with metastatic prostate cancer and renal failure, attributed to high-dose vitamin C therapy. Despite persistently low BG levels—confirmed by both POC glucometers and laboratory assays—the patient remained entirely asymptomatic, fulfilling only one component of Whipple's Triad. This discordance between laboratory findings and clinical presentation prompted reconsideration of the initial differential and ultimately led to a diagnosis of assay interference. The suspicion was further supported by the progressive normalization of BG levels following dialysis. Additionally, liver enzymes, initially undetectable at admission, became measurable with ongoing dialysis, suggesting that a circulating substance was broadly interfering with enzymatic assays. Moreover, pseudo-hypoglycemia on POC glucose testing has been previously reported.[4,5]

Endocrine Evaluation

Given the patient's extensive supplement use, including desiccated thyroid, and the unexplained hypoglycemia, an endocrinologist was consulted. Initial laboratory tests included insulin, C-peptide, proinsulin, thyroid-stimulating hormone level, and a sulfonylurea screen. Only modest elevations in C-peptide and proinsulin were noted, which were attributed to a physiological response to administered dextrose rather than autonomous insulin production. These markers were not repeated, as clinical suspicion for artifactual hypoglycemia increased.

Other possible causes of low BG levels were systematically explored. Previous reports have linked artifactual hypoglycemia to discrepancies between fingerstick and plasma glucose readings, particularly in the setting of peripheral hypoperfusion and acidosis[6] or severe leukocytosis with delayed sample processing.[7] In such cases, POC values are low while laboratory values remain normal. However, this explanation was unlikely in our patient, who had a normal white cell count and demonstrated consistently low glucose levels on both platforms. Samples were processed promptly, and although the patient had severe acidosis, in-vitro studies suggest that pH has minimal impact on glucose measurement.[8]

Mechanism of Interference

Vitamin C is a potent reducing agent and interferes with glucose measurement through redox chemistry.[9-11] Most POC devices use glucose oxidase-peroxidase reactions, generating hydrogen peroxide that reacts with a chromogen or electrode. Ascorbic acid can scavenge peroxide or alter chromogen oxidation, leading to falsely low readings.[9,12] Laboratory platforms, including the Vitros XT 7600 used in this case, rely on similar enzymatic reactions and are also vulnerable at high vitamin C levels. The normalization of liver enzymes with dialysis suggests that assay interference extended beyond glucose.

Dose-Response and Risk Factors

Interference correlates with serum vitamin C levels. Effects typically appear at serum concentrations above 10–20 mg/dL, usually achieved by intravenous doses greater than 10 g/d.[11,13,14] Our patient's postdialysis level was 74 mg/dL, suggesting even higher predialysis levels. He had been receiving a total of 150 g intravenously every week, in addition to daily oral supplementation. With renal impairment, accumulation likely occurred over time, pushing levels high enough to interfere with multiple assays.[15]

Could Vitamin C Cause True Hypoglycemia?

While some studies suggest ascorbic acid may enhance insulin sensitivity or glucose uptake,[16] clinical evidence for true hypoglycemia is limited.[17] Other contributors—metformin use, critical illness, and poor intake—were present, but the lack of neuroglycopenic symptoms and poor response to dextrose made true hypoglycemia unlikely. The pattern was consistent with an assay artifact.

Some reports have speculated that niacin and vitamin C might cause hypoglycemia, but data suggest that they synergistically induce hyperglycemia.[18] Niacin levels were also normal in our patient, ruling this out.

Interestingly, vitamin C can also cause artifactual hyperglycemia in POC meters that use amperometric sensors.[11,19] Thus, ascorbic acid has the potential to produce both falsely low and high glucose readings, depending on the assay platform. This underlines the importance of understanding the analytic platform when interpreting results.

Diagnostic Strategy

In cases of suspected interference, oxidase-based platforms should be avoided. Laboratory assays utilizing the hexokinase method are preferred, although they too may still be prone to interference.[10] When results remain unclear, confirmatory testing with high-performance liquid chromatography or mass spectrometry may be helpful.[20] Simultaneous testing using different analytic methods can also aid interpretation. Awareness of the methodologies used by one's institution is also essential to recognizing and avoiding diagnostic pitfalls.

Conclusion

Artifactual hypoglycemia should be considered in patients with critically low glucose values but no symptoms, especially in those receiving high-dose vitamin C. This case emphasizes the continued relevance of Whipple's Triad and the importance of correlating clinical presentation with laboratory data. Misinterpreting artifactual results may lead to unnecessary interventions and delays in appropriate care. As alternative therapies gain popularity, clinicians must remain vigilant for their potential to interfere with diagnostic assays. An understanding of laboratory methods and thoughtful clinical reasoning are key to avoiding misdiagnosis.

Disclosure

The authors have no conflicts of interest to disclose.

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