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Case Report

Artifactual Hypoglycemia in Scleroderma: A Case Report and Review of Literature

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Abstract

Background: Artifactual hypoglycemia denotes discrepancy between fingerstick and plasma glucose measurements.

Objective: To report a case of artifactual hypoglycemia in a patient with scleroderma and review similar cases reported in the literature.

Methods: Pubmed search of English literature up to December 17, 2021. Search terms include scleroderma, artifactual hypoglycemia, pseudo-hypoglycemia, earlobe, fingerstick. Pertinent case reports, reviews, and guidelines of professional organizations are included.

Results: Review of literature revealed 7 patients hospitalized with scleroderma who presented with artifactual hypoglycemia. All patients had no hypoglycemic symptoms, and only one patient had type 2 diabetes. In most cases, diagnosis of artifactual hypoglycemia was delayed several days, which led to unnecessary treatment with intravenous dextrose and glucagon. Furthermore, patients were exposed to extensive investigations to rule out other causes of hypoglycemia. The diagnosis of artifactual hypoglycemia was established after demonstration of normal glucose levels obtained from the earlobe and plasma, whereas simultaneous glucose from fingertip showed low values in the hypoglycemic range. Glucose levels measured by earlobe prick correlate strongly with those sampled from plasma glucose. In addition, earlobe prick is less painful than fingerstick, and not affected in scleroderma.

Conclusion: Fingerstick measurement of blood glucose may be misleading in scleroderma. Measurement of glucose from earlobe should be performed in all cases of scleroderma while waiting results of plasma glucose. Physicians and nurses should be aware of this phenomenon to avoid potentially harmful treatment and unnecessary investigations.

Keywords: *Artifactual Hypoglycemia; Scleroderma; Pseudo-Hypoglycemia; Fingerstick; Ear Lobe*

Introduction

Artifactual hypoglycemia is defined as discrepancy between different laboratory measurements and actual blood glucose levels [1]. Some authors used the terminology pseudo-hypoglycemia to denote artifactual hypoglycemia [2]. However, in 2003, a workgroup representing The American Diabetes Association and Endocrine Society defined pseudo-hypoglycemia as event during which the person with diabetes reports any of the typical symptoms of hypoglycemia with a measured plasma glucose concentration > 70 mg/dl but approaching that level" [3]. Thus, artifactual hypoglycemia and pseudo-hypoglycemia should not be used interchangeably. Artifactual hypoglycemia

has been described in several conditions that impair capillary blood flow in extremities such as circulatory shock, hypothermia, and peripheral vascular disease [4]. Scleroderma (also called systemic sclerosis) is a complex connective tissue disease characterized by microvascular damage and fibrosis [5]. Point-of-Care (POC) or blood glucose checking in fingertips by a glucometer at bedside is an easy method for evaluation of glycemic status in hospitalized patients with or without diabetes. Meanwhile, such method may be inaccurate in scleroderma and result in serious consequences. The main purpose of this article is to alert physicians and nurses about the existence of artifactual hypoglycemia in scleroderma and outline a practical way for its diagnosis.

Case Report

A 60-year-old female presented to our hospital with acute heart failure, pneumonia and severe hypotension. She had history of mixed connective tissue disease including diffuse scleroderma, systemic lupus erythematosus and myositis. In addition, she has Raynaud's phenomenon involving fingertips and toes without digital ulcerations. She did not have personal or family history of diabetes. She was admitted to the intensive care unit and was treated with norepinephrine drip, amiodarone drip, furosemide, vancomycin, cefepime and heparin drip. She also had acute kidney injury but did not require dialysis. Her home medications were prednisone, aspirin, atorvastatin, colchicine, cyclobenzaprine, albuterol via nebulizer, calcium carbonate, famotidine, folic acid, furosemide, magnesium oxide, mycophenolate, metoclopramide, pantoprazole, and ursodiol. Patient had poor oral intake and her blood glucose on basic metabolic panel testing ranged from 70 to 110 mg/dl. On hospital day 6, patient was noted to have a fingerstick glucose of 49 mg/dl and was started on intravenous 10% dextrose for a few hours. The following day, she had fingerstick blood glucose levels close to 20 mg/dl despite using a different glucometer. At all times, patient did not exhibit any hypoglycemic symptoms. She received 4 doses of 50 ml 50% Dextrose in water and 1 mg glucagon injection intravenously. Yet, all fingerstick glucose levels remained very low below 20 mg/dl. Given the fact that there was complete absence of hypoglycemic symptoms, no further treatment was given. In the meantime, rapid literature search revealed few similar events recorded in scleroderma patients. Thus, a simultaneous plasma glucose was checked which returned as 371 mg/dl while the concomitant finger stick value was less than 10 mg/dl. In addition, checking glucose levels from the earlobe using the same glucometer yielded normal levels that were very close to plasma glucose values. A diagnosis of artifactual hypoglycemia was therefore established.

Discussion

Reported cases and mechanisms of artifactual hypoglycemia in scleroderma

Our review of literature unraveled 7 patients with scleroderma presenting with artifactual hypoglycemia [2,4,6-10] (Table 1). Seven of the 8 patients were woman, and only one subject had type 2 diabetes [2] (Table 1). Two patients had history of peripheral vascular disease [7,8] (Table 1). The mechanisms of artifactual hypoglycemia in scleroderma are believed to be related to obliteration of capillary microcirculation leading to compromise of blood flow in distal fingers and increased extraction of glucose by surrounding tissues [8]. Artifactual hypoglycemia was also described in patients with Raynaud's phenomenon characterized by vasoconstriction in finger capillaries upon cold exposure. Raynaud's syndrome commonly coexists with scleroderma as seen in our patient and others [7,8] (Table 1). The mechanism of artifactual hypoglycemia in Raynaud's disease is unclear but could be attributed to the prevalent vasoconstriction and decreased availability of glucose in capillary beds.

Diagnosis of artifactual hypoglycemia

Artifactual hypoglycemia should be suspected if the following findings are present. First, absence of symptoms of hypoglycemia, Second, any intake of any medications that may cause hypoglycemia (e.g. diabetes medications) is ruled out. Third, if the patient has a condition that may compromise the capillary circulation in the extremities and fingers such as scleroderma, Raynaud's phenomenon, peripheral vascular disease, and hypovolemic shock [4]. In such conditions, and before the administration of any dextrose or glucagon, it may be wise to check blood glucose levels in the ear lobe simultaneously with fingerstick. In one study of 50 patients with type 2 diabetes, Toledo

and Taylor [11] showed that capillary blood glucose levels from ear lobe correlated strongly with those from fingertips, correlation coefficient being 0.97 ($P < 0.01$) [11]. Moreover, they found that earlobe pricking may be associated with less pain compared with finger sticks [11]. In another study of 50 patients (86% had type 2 diabetes), Anzalone [12] showed that the mean fingertip glucose concentrations were 5.8 mg/dl higher than the corresponding values from earlobe. This small difference is unlikely to be of major clinical significance. The author concluded that utilization of the earlobe as a site for blood glucose sampling may be safe and effective alternative to exclusive use of fingertips. It should be emphasized that scleroderma does not affect the ear lobe because the latter lacks connective tissue [9]. This explains why ear lobe glucose measurement was successful in the rapid demonstration of artifactual hypoglycemia in our case and other cases (Table 1). For instance, in our patient, blood glucose concentration from earlobe was 80 mg/dl whereas the simultaneous corresponding value from finger stick was 40 mg/dl. Likewise, in the patient reported by Drenthen., *et al*. [9], glucose levels were 54 mg/dl higher in earlobe capillary blood compared with finger-stick measurements. In fact, in the case reported by Drenthen., *et al*. [9] and Dubourdieu., *et al*. [10], glucose measured from earlobe was the only proof of artifactual hypoglycemia since these 2 patients had stiffened veins making drawing plasma glucose impossible.

Another strategy that should be done to establish the diagnosis of artifactual hypoglycemia is to draw venous blood for laboratory plasma glucose measurement simultaneously with blood glucose measured by the glucometer in fingertips. In our patient, plasma glucose was very high as result of intravenous dextrose administration, whereas simultaneous POC glucose value was < 10 mg/dl. However, glucose results from plasma take at least 1 hour to be available. In addition, it is difficult in some patients with vascular disease to find a vein suitable for blood withdrawal. Fortunately, these limitations do not apply to earlobe sampling which remains an accurate, fast, easy, and relatively non-painful way to measure capillary glucose.

Continuous glucose monitoring (CGM) may be potentially useful strategy in the diagnosis of artifactual hypoglycemia that is still under investigations. CGM measures glucose levels in the interstitial fluid and not capillary blood [8,13]. Hence, there is physiologic time delay of 6 - 10 minutes between the interstitial and capillary compartments [13]. CGM is not widely available in the hospital setting. Therefore, CGM should not be used to diagnose artifactual hypoglycemia until more data are available.

Clinical implications of failure to recognize artifactual hypoglycemia

In almost all reported scleroderma patients, including ours, the diagnosis of artifactual hypoglycemia was delayed several hours to days in large part due to unfamiliarity with this phenomenon. Failure to recognize artifactual hypoglycemia would lead to unnecessary investigations (Table 1), patient anxiety, and confusion among medical staff. Furthermore, it may result in harmful consequences by inappropriately giving glucose-rich fluids or glucagon leading to severe hyperglycemia. Furthermore, in patients with diabetes, inappropriate treatment of artifactual hypoglycemia may virtually lead to hyperglycemic crises (either hyperglycemic hyperosmolar state or diabetic ketoacidosis). However, in the 65-year-old woman with type 2 diabetes reported by Lee and Abadir [2], the authors did not report any hyperglycemic complications despite continuous dextrose intravenous administration. Indeed, due to the poor awareness of the concept of artifactual hypoglycemia in scleroderma, the nursing home patient reported by Meterns., *et al*. [8] was unnecessarily re-admitted to the hospital for recurrent artifactual hypoglycemia. Moreover, another patient had a prolonged 2-week hospital admission until the etiology of hypoglycemia was proved to be artifactual [4].

Reference	Patient	Methods of diagnosis of artifactual hypoglycemia*	Work-up before recognition of artifactual hypoglycemia
1. Current case	60-year-old woman with Raynaud's syndrome	Earlobe and plasma glucose	None.
2. Osman., *et al*. [6]	52-year-old woman	Plasma glucose	None.
3. Moreau., *et al*. [7]	59-year old woman with Raynaud's syndrome and **PVD	Plasma glucose and earlobe blood	Fasting 24 h test and ultrasound of pancreas to rule out insulinoma
4. Mertens., *et al*. [8]	87-year-old female at nursing home with Raynaud's syndrome and **PVD	Plasma and earlobe blood	Extensive testing for all causes of hypoglycemia. Patient was readmitted a few weeks later for "hypoglycemia'
5. Drenthen., *et al*. [9]	57-year-old man	Earlobe	Repeated testing to rule out insulinoma. Increase prednisolone dose from 5 to 10 mg/d causing 4 kg weight gain and anxiety.
6. Dubourdieu., *et al*. [10]	42-year-old woman	Earlobe blood	Ruling out adrenal insufficiency.
7. Bishay and Suryawanshi [4]	76-year woman	Plasma glucose	72-hour fasting test to rule out insulinoma, and ***MRI of pituitary to rule out apoplexy.
8. Lee and Abadir [2]	65-year-old woman with type 2 diabetes	Plasma glucose	Extensive examination for endocrine causes of hypoglycemia

Table 1: *Cases of scleroderma presenting with artifactual hypoglycemia.*
*Abbreviations: *Plasma and ear lobe sampling were performed almost simultaneously with fingerstick, **PVD: Peripheral Vascular Disease, ***MRI: Magnetic Resonant Imaging.*

Conclusion

Only a total of 8 cases of artifactual hypoglycemia (including our case) have been reported in patients with scleroderma. This number is likely to be underestimated. The diagnosis of artifactual hypoglycemia should be considered when POC testing shows low glucose values in absence of hypoglycemic symptoms. In this case, simultaneous glucose measurement from ear lobe is a rapid and relatively less painful method to provide a fast information about the actual blood glucose levels. Simultaneous withdrawal of venous blood to check plasma glucose in the laboratory will establish the diagnosis. Physicians and nurses should be mindful of the presence of artifactual hypoglycemia in scleroderma to avoid futile therapy and investigations that could result in patient harm and anxiety.

Conflict of Interest

The authors have no conflict of interest to declare.

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