Abnormally Low A1c Levels due to Hb I-Texas Hemoglobinopathy in a Geriatric Patient

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INTRODUCTION

Hemoglobin A1c is commonly used in the primary care setting for screening, diagnosis and management of diabetes mellitus. Multiple clinical scenarios may impact the accuracy of this valuable laboratory test. Here we report a case of abnormally low hemoglobin A1c that was the result of an asymptomatic hemoglobinopathy in the alpha 2-globin gene (Hb I-Texas) that had gone previously undiagnosed in a geriatric patient. Physicians should be aware of such drawbacks in the utilization of this valuable test and be equipped to utilize other values to monitor for and evaluate disorders of glucose metabolism such as diabetes mellitus.

CASE DESCRIPTION

This 75-year-old female with history of HLD, OA of bilateral hip and osteopenia presents to a geriatric clinic to establish care. Vitals & Physical Exam: were WNL. Meds: Atorvastatin, Vitamin D3 supplement, Calcium supplement, and diclofenac sodium gel. Labs: all WNL except a very low A1c. Given her abnormal A1c level, the patient was called back for additional lab testing. A repeat A1c was done to rule out lab error as well as a fasting glucose, a complete blood count with indices, iron studies and vitamin E levels. The repeat A1c value, again showed a very low A1c (<3.5%) with fasting glucose of 85 mg/dL, The complete blood count was essentially normal (hemoglobin, 14.4 g/dL; hematocrit, 44.6%) with normal mean corpuscular volume of 88.8 fL. Iron studies, Fructosamine and vitamin E levels all were WNL. Later patient underwent hemoglobinopathy evaluation testing which showed an alpha hemoglobin variant (28.5%) suggestive of Hb I-Texas. Further Alpha globin gene sequencing confirmed the foregoing diagnosis of Hb-I Texas variant (Heterozygous for the c. 49A>G (p. Lys17Glu) in the Alpha 2-globin gene).

DISCUSSION

Hemoglobin A1c was first introduced to physicians in 1978 and was first utilized for clinical use by the American Diabetes Association a decade later in 1988. Numerous studies over the years have validated the utility of hemoglobin A1c in managing, monitoring and predicting diabetes-related outcomes and complications. Since 2010, hemoglobin A1c has been recommended as one of the main criteria for the diagnosis of diabetes, further expanding its clinical value. The significance of Hemoglobin A1c (HbA1c) as the central parameter for assessing the quality of glycemic control over time is undisputable. Despite these benefits, several clinical syndromes may impact accurate results of this useful lab test. Potential clinal scenarios with false A1c results is noted in exhibit 1-1. Since hemoglobin A1c is a product of the glycosylation of hemoglobin A, its utilization in patients with hemoglobinopathies may not be accurate for predicting disorders of glucose metabolism. This is particularly true on those hemoglobinopathies that reveal an abnormal quantity of hemoglobin A. In the case of our patient, her hemoglobinopathy evaluation testing showed an alpha hemoglobin variant (28.5%) suggestive of Hb I-Texas which explains her A1c value of <3.5%. Since hemoglobin A1c cannot be utilized in the foregoing patients to screen for or monitor diabetes mellitus, physicians may utilize other American Diabetes Association's recommended screening methods; fasting plasma glucose ≥ 126 mg/dL, random plasma glucose ≥ 200 mg/dL with classic symptoms of hyperglycemia, or plasma glucose ≥ 200 mg/dL 2 hours after a 75-g glucose load. In terms of monitoring glycemic control, physicians may elect either following a glucose log of both fasting and postprandial values or utilizing other markers such as Fructosamine.

False Increase	False Decrease
Anemia (in particular those associated with increased red cell turnover)	Anemia (from acute or chronic blood loss)
Asplenia	Splenomegaly
Uremia	Pregnancy
Severe hypertriglyceridemia	Vitamin E ingestion
Severe hyperbilirubinemia	Medications (ribavirin, interferon-alpha)
Chronic ETOH consumption	Red blood cell transfusion
Chronic salicylate ingestion	Hemoglobin variants (most often with homozygous hemoglobinopathies)
Chronic opioid use	Vitamin C ingestion

Exhibit 1-1: Clinical scenarios causing false A1c results.

LESSONS

- Although Hemoglobin A1c (HbA1c) measurement has emerged to be the cornerstone in novel diabetes therapy, some clinical scenarios may gravely impact its accuracy.
- Clinician should be aware of various clinical syndromes that could falsely impact A1c values such as hemoglobinopathies and utilize alternative tests such as fasting blood glucose or Fructosamine for diagnosis and management of diabetes mellitus.

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