Sudden Onset of Diabetic Ketoacidosis in a Patient with Discordant HbA1C: A Unique Case of Fulminant Type 1 Diabetes Mellitus (FT1DM) in a Middle-aged Man

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Abstract

Introduction: Diabetic Ketoacidosis (DKA) is an acute complication of diabetes mellitus (DM) which present as the first manifestation in fulminant type 1 diabetes mellitus (FT1DM) without significant elevation of HbA1C. We present a unique case of a 52-years-old male with DKA without previous history of DM and HbA1c of 6.6.

Case Illustration: A 52-years-old male was brought to hospital due to persistent vomiting. He experienced polyuria and unexplained weight loss but denied previous history of DM. He was diagnosed with DKA due to his blood glucose of 1107 mg/dL along with elevated blood ketone and metabolic acidosis. However, his HbA1c was a mere 6.6. His serum lipase was increased, consistent with pancreatic damage. He was then discharged with basal-bolus insulin.

Discussion: Although the symptoms of this patient was consistent with hyperglycemic crisis, the presentation of DKA is usually associated with elevated HbA1c, approximately 10.4 - 16.9%. This unusual HbA1c points to the diagnosis of FT1DM. It is caused by sudden beta-cell destruction triggered by viral infections, alongside genetic disposition, leading to sudden depletion of insulin occurred less than a week and presents with ketoacidosis. It is characterized by low HbA1c (< 8.7%) yet extremely high blood glucose (≥ 288 mg/dl) and elevated pancreatic enzymes (depicting pancreatic damage). A diagnosis of FT1DM can be ascertained in this patient as his presentations matches its characteristics.

Conclusion: FT1DM is a sub-type of T1DM which can suddenly occur in patients and associated with discordant HbA1c. It is important to recognize and treat it accordingly to avoid fatal outcomes.

Introduction

Diabetic Ketoacidosis (DKA) is an acute complication of diabetes which may occur in people with a known history of diabetes, or present as the first manifestation in people with Type 1 Diabetes, specifically in those with fulminant type 1 diabetes mellitus (FT1DM).[1,2] This sub-type of type 1 diabetes mellitus (T1DM) is characterized by rapid development of pancreatic b-cell destruction and dysfunction that can result in DKA within less than 7 days,

accompanied with an increase in pancreatic enzymes, low C-peptide levels, no pancreatic b-cell auto- antibodies, and near-normal HbA1c or glycosylated hemoglobin.[2] Until recently, HbA1c has been the gold-standard for assessment of glycemic control and complications of diabetes. However, it is important to know that the usage and reliability of HbA1c is dependent on multiple factors which may result in a falsely elevated or lowered result.[1,3]

Here, we discuss a unique case of a 52-years-old male presenting with DKA which occurred in a week, with no previous history of diabetes symptoms, and a HbA1c of less than 7%.

Case Illustration

A 52-years-old Indonesian male was brought to the emergency department due to nausea and vomiting which started four days prior to admission. The symptoms had started in the evening with an increase in thirst and mouth dryness, alongside an increase in micturition frequency and amount. He claimed that within 15 minutes after drinking water, he had to go back to the toilet to urinate. Due to intense thirst, he drank approximately more than 2 litres of water. The patient's vomit was described to be watery and without blood. The patient denied any projectile vomiting and any experience of intense headache. The day before, patient was also brought to the emergency department due to nausea and vomiting with similar characteristics. The patient claimed to have been described medicine which he drank once after being discharged. He claimed to have gone home feeling better than he had on his first admission.

The patient had a history of sore throat which was first documented by the patient on the day before admission with a VAS of 4/10. The pain was quite debilitating, as the patient had difficulties in eating and drinking due to it. The patient denied any coughing or phlegm. He also admitted to experiencing colicky pain on his upper left abdomen for 3 months ago. The pain was described as a feeling of tightness and fullness with nothing to exacerbate nor relieve it. The patient denied any radiation towards his back, jaw, or left arm.

The patient also denied ever experiencing these symptoms prior to onset. He had denied any tingling in his extremities, blurry vision, increase in hunger, or any complaints regarding towards micturition and defecation. He had also denied any history of diabetes mellitus, hypertension, heart disease, and others. The patient admitted to a history of surgery for a mass in his right armpit in 2019, which was then followed by a regimen of medicine for 9 months which he completed. He confessed of not remembering the name of the medicine but remembered that he experienced abdominal discomfort and tingling in his hands while completing that regimen. He also admitted to smoking 2 years ago but had stopped since then.

On presentation, the patient looked moderately sick, but conscious. His blood pressure was 93/60, with a heart rate of 73 bpm, respiratory rate of 17 breaths per minute, and temperature of 37^{o}C. On physical examination, the patient had an oral lesion near his left glossopharyngeal arc (*arcus glossopharyngeus sinistra*), dry oral mucosa, with normal skin turgor. The patient also had a single noticeable mass around his left supraclavicular area, approximately 4x5 cm in size, with a soft consistency and a smooth surface with no nodules. On abdominal examination, the

patient had tenderness around his epigastric and left hypochondriac area, and a single lump which was felt on deep palpation, approximately 3.5x5 cm in size, which felt hard but smooth with no nodules.

The patient received initial fluid resuscitation and was started on intravenous rapid-acting insulin infusion during the treatment in the emergency departemnt. The patient was also started on antibiotics, natrium bicarbonate, and kalium. He was then admitted to the hospital ward.

Due to the state of presentation, various laboratory examinations were done. One of them was random blood glucose (RBG). When admitted to the emergency department, his initial RBG was found to be 629. The overall hematology tests were normal. Blood chemistry tests showing results as follows, eGFR were decreased, blood ketone was positive, ureum were slightly increased, liver function test was slightly increased, HbA1c were 6.6% on the first day of admission and 6.9% on the last day. Urinalysis test was done, and the results are yellowish colored, cloudy, protein and nitrit were negative, occult blood positive (+2), ketone (+2) and glucose (+2).

On the second day of admission, the patient's ECG showed sinus tachycardia with tall T which was in accordance with the patient's serum K+. Meanwhile, there were no abnormalities shown in the patient's chest x-ray. Due to his LUQ tenderness, whole abdomen USG was done. It resulted in findings such as cholelithiasis with *adenomyomatosis* and fatty liver. Other intra-abdominal organs showed no abnormalities.

Throughout his stay, the patient's random blood glucose kept track of diligently. During the 5 days of hospital stay, random blood glucose was checked every 6 hours starting from 00.00AM until 10.00 PM showing fluctuations of the random blood glucose level in the patient's laboratorium results throughout his admission in the hospital. The lowest RBG level was on the last day of hospital stay, 74mg/dL and the highest level was on the first day of hospital admission, 486mg/dL.

Discussion

Glycosylated haemoglobin or HbA1c has been a validated diagnostic tool and a marker for glycaemic control in those with diabetes. It is based on the formation between haemoglobin and glucose. Haemoglobin is a metalloprotein in the erythrocytes which transports oxygen. It consists of two alpha-globin chains (HbA1 and HbA2) and two non-alpha globin chains (beta, gamma, delta). Normally, an adult haemoglobin consists of two alpha chains and two beta chains. However, in the condition of high glucose concentration, a process of chemical condensation of haemoglobin and glucose occurs slowly in accordance with the average erythrocyte's lifespan (120 days), resulting in a minor component called A1c. The formation of A1c is proportional to the concentration of glucose throughout an erythrocyte's lifespan. Therefore, chronic hyperglycaemia is associated with an increase in A1c formation.

In this case, a HbA1c amount of 6.6 and 6.9 was found. According to ADA (American Diabetes Association), a value of 5.7-6.4% is pre-diabetic, while a value above 6.5% signifies a person to suffer from diabetes.[4] This indicates that the patient in the case above to be diabetic. However, studies found that type 2 diabetes mellitus patients with DKA are usually associated with markedly elevated HbA1c, approximately a level of 10.4-

16.9%.[1] While the HbA1c found in this patient qualifies as diabetic and points to a possible diagnosis of type 2 diabetes mellitus, it is not elevated enough and does not match the usual presentation. This is because type 2 diabetes mellitus is a chronic insidious process, which results in chronic hyperglycaemia, represented by an extremely elevated HbA1c. The unusually low HbA1c which is in discordance with the patient's blood glucose levels insinuates another diagnosis, which is type 1 diabetes mellitus.[1,2]

In type 1 diabetes mellitus with DKA as its complication, low HbA1c is explained by the sudden onset of *insulinopenia*. This may be caused by abrupt destruction of complete beta-cell destruction in the pancreas. This results to a low HbA1c value which does not reflect the blood glucose level, as HbA1c values reflects glycaemic control in the time span of an erythrocyte (120 days).[1,3] A condition of sudden hyperglycaemia due to beta-cell destruction which leads to sudden depletion of insulin can be found in one the sub-types of diabetes mellitus – fulminant type 1 diabetes mellitus or FT1DM.[2]

FT1DM is a result of rapidly occurring pancreatic beta-cell destruction, usually in less than a week. Patients usually present with hyperglycaemic symptoms such as polydipsia, polyuria, and sudden weight loss in the same time frame. Studies has also found that the development of DKA in less than a week is one of its characteristics. Increased serum pancreatic enzyme levels and unusually low HbA1c levels with extremely elevated blood glucose levels can also be found in those suffering from FT1DM. Its aetiology is still unknown, but multiple factors have been suspected to be the cause of it, such as genetic factors e.g. human leukocyte antigens (HLA) and environmental factors like viral infections.[2]

Conclusion

FT1DM is a sub-type of T1DM which can suddenly occur in patients and associated with discordant HbA1c which caused by rapid pancreatic beta-cell destruction. The presence of DKA in T1DM with low HbA1c is explained by the sudden onset of insulinopenia. It is important to recognize and treat it accordingly to avoid fatal outcomes.

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