Case Report

Pancreatogenic diabetes presenting with diabetic ketoacidosis: A rare manifestation of chronic pancreatitis

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Abstract

Diabetes mellitus (DM) is a clinical syndrome that is manifested by hyperglycemia. Out of the numerous causes of diabetes, an uncommon cause is chronic pancreatic disease due to destruction of islet cells. Diabetic ketoacidosis is a rare entity in such cases as alpha cells are destroyed along with beta cells, which causes lack of glucagon that is responsible for ketogenesis. We hereby report a case of a 55-year-old woman with history of gall stone disease and who presented to the emergency department with multiple episodes of non-bilious, non-blood mixed vomiting along with increased frequency of micturition on background of malaise and anorexia along with significant weight loss. Her capillary blood glucose was 501 mg/dl, arterial blood gas showed high anion gap metabolic acidosis, and urine ketone were largely positive. Thus, she was diagnosed with diabetic ketoacidosis. She was admitted to the high dependency unit and her condition was treated along the lines of diabetic ketoacidosis. Further evaluation showed high HbA1c values without previous history of diabetes and computed tomography of the abdomen revealed presence of chronic pancreatitis. Though being a rare entity, this case outlines that DM3c can present with diabetic ketoacidosis (DKA); thus, early diagnosis and management are crucial to prevent mortality.

Keywords: Chronic pancreatitis, diabetic ketoacidosis, diabetes mellitus type 3c, pancreatogenic diabetes

Introduction

Type 3c diabetes mellitus (DM3c) is a type of diabetes that occurs mainly due to chronic pancreatic dysfunction. Around 75% of chronic pancreatitis cases go on to develop this form of diabetes. It has a prevalence of about 5%–10% in western countries; however, its prevalence in the South Asian population remains underreported.[1]

The pathogenesis of DM3c has been mainly attributed to cytokine production and endocrine islet cell destruction, though less likely causes include pancreatic manipulation such as pancreatic surgery.[2] The management of DM3c remains more difficult than type 1 and 2 diabetes because in chronic pancreatic insufficiency, there is destruction of both alpha and beta cells secreting insulin and glucagon, respectively. Deficiency of glucagon, the hormone largely responsible for ketogenesis, makes the development of diabetic ketoacidosis (DKA) an unusual manifestation in such patients.[3] Because only a handful of such cases have been reported in literature,[4] we report a case of newly diagnosed DM3c presenting with DKA.

Case

A 55-year-old post-menopausal lady, with no history of substance abuse and who had been diagnosed with gallstones, presented with multiple (4–5 times/day) episodes of non-bilious, non-bloody vomiting for one week on a background history of progressive, painless increase in frequency of micturition associated with burning sensation, increased thirst, anorexia, and malaise for the last 15 days. She also had a history of

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episodic, intermittent, mild-to-moderate, periumbilical pain in the last one year, for which she was taking over-the-counter analgesics. The patient denied any significant history of loss of consciousness, abnormal body movement, fever, chest pain, shortness of breath, diarrhea, or any other complaints. On examination in the emergency department, she was agitated, pale and hypotensive, requiring vasopressor support. Her capillary blood glucose at presentation was 501 mg/dl with arterial blood gas analysis showing the presence of high anion gap metabolic acidosis (serum bicarbonate of 14 mmol/L, corrected anion gap of 22). Urine analysis for ketone was largely positive. In view of the above findings, her condition was managed along the lines of diabetic ketoacidosis (DKA). The patient was admitted to the high dependency unit, and insulin infusion was started after correction of hypokalemia along with adequate resuscitation with intravenous fluids. A total of eight liters of Ringer's lactate was infused, after which the vasopressors were gradually tapered off. Insulin infusion was continued unit the anion gap closed, after which the patient was shifted to basal bolus regimen after she started accepting oral feeds.

On routine evaluation, ultrasonography of abdomen revealed findings of chronic pancreatitis. A contrast-enhanced CT of the abdomen [Figure 1] was obtained, which showed atrophic pancreas with dilated pancreatic ducts along with calcifications. Her HbA1c level was 16.4%. Autoimmune work-up for diabetes was negative. Thus, she was diagnosed to have DM3c unusually presenting with DKA. The patient was subsequently discharged with insulin aspart 6 units TDS before meals and insulin glargine 10 units at night along with pancreatic enzyme replacement therapy.

Discussion

Diabetes mellitus (DM) is a complex clinical syndrome that is manifested by hyperglycemia. Hyperglycemia that occurs secondary to pancreatic dysfunction has been termed as DM3c and that occurs in context of disease of exocrine pancreas has been termed pancreoprivic diabetes.[5] Pancreatogenic diabetes, though like more prevalent type 1 and type 2 DM, has some unique pattern of metabolic and hormonal characteristics with increased risk of the patient developing pancreatic cancer.[2] DM3c is diagnosed by proposed criteria which consist of presence of exocrine pancreatic insufficiency, pathological pancreatic imaging, and absence of type 1 DM–associated autoimmune markers. Further evidence of incretin, pancreatic polypeptide (PP), or insulin secretory defects would also support the diagnosis. Confirmation can be made by absent PP response to mixed-nutrient ingestion, which best discriminates the pathological process of type 3c versus type 2 DM.[6] In DM3c due to repeated inflammation, there is early destruction of beta cells of pancreas leading to decreased insulin production and, hence, the development of diabetes in these patients. In due course of time, with progression of the disease, there is destruction of glucagon-secreting alpha cells which is one of the counter-regulatory hormones.

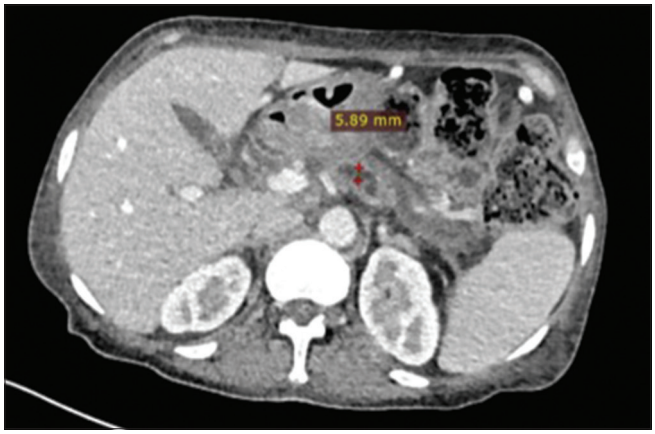

Figure 1: Axial contrast-enhanced CT of the abdomen showing atrophic pancreas with dilated main pancreatic duct (MPD) (arrows) and non-enhancing necrotic areas

DKA develops due to relative or absolute insulin deficiency with upregulation of stress hormones such as glucagon, cortisol, catecholamines, and growth hormone. Glucagon enhances lipolysis, which in turn increases the supply of fatty acids to the liver. Glucagon's main effect is on liver, where it activates the carnitine acyltransferase system through inhibition of malonyl-CoA synthesis.[7] This results in mobilization and oxidation of fatty acids for the formation of ketoacids. DKA is typically seen in DM type 1 where the levels of glucagon are high secondary to insulin deficiency. DKA becomes a rare entity in cases of chronic pancreatitis as glucagon is a major stress or counter-regulatory hormone needed for ketogenesis, which is absent in such patients. The plausible explanation is that in such patients, the levels of catecholamines is enhanced; this upregulates ketone production by stimulating lipolysis in adipocytes and providing free fatty acids to the liver to produce ketones.[8] In our case, the patient presented with DKA for the first time and after subsequent investigation she was found to have chronic pancreatitis with DM3c. Hence for clinicians, it is crucial to recognize DM3c at an early stage so that life-threatening complications like DKA can be better managed and prevented.

Conclusion

Chronic pancreatitis is a major cause of pancreatogenic diabetes (type 3c DM), and it should be suspected in any patient with clinical features suggestive of the same along with the development of diabetes. Autoimmune workup to rule out type 1 DM should be done to establish the diagnosis. Managing hyperglycemia in such cases is difficult due to complex hormonal changes and first-time treatment should be metformin which also reduces the incidence of pancreatic carcinoma. Early recognition of this entity and appropriate management can avoid rare complications like DKA.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other

clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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