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Case Report

Diabetic Ketoacidosis Without Diabetes Mellitus in Acute Pancreatitis

Duha Zaffar, MD [1,*], Aditi Rawat, MD [2], Robert T. Chow, MD [1], Kashif M. Munir, MD [3]

[1] Department of Internal Medicine, University of Maryland Medical Centre Midtown Campus, Baltimore, Maryland
[2] Student of Medicine, American University of Antigua College of Medicine, Antigua
[3] Department of Endocrinology, University of Maryland School of Medicine, Baltimore, Maryland

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ABSTRACT

Background/Objective: Diabetic ketoacidosis (DKA) is typically but not exclusively seen in patients with a history of diabetes mellitus.
Case Report: This is a case of 39 year-old male who was diagnosed with acute pancreatitis based on characteristic symptoms and positive CT findings on presentation. Laboratory testing revealed elevated serum glucose 251 mg/dL, low serum bicarbonate 8 mmol/L, increased anion gap 21, and elevated serum beta-hydroxybutyrate 9.62 mmol/L. Diagnosis of DKA was made, however patient did not carry a diagnosis of diabetes mellitus. His hemoglobin A1c in hospital was normal at 5.4%. Additionally, follow-up hemoglobin A1c at 4 months and 10 months postdischarge did not imply diabetes mellitus, 5.8% at both time points. The patient who was initially managed with intravenous insulin required no insulin or oral diabetic medication on discharge. All these findings argued against new onset diabetes mellitus.
Discussion: This case explores the potential pathophysiology that underlies this phenomenon including possible transient insulin insufficiency due to beta cell dysfunction from pancreatic inflammation. It also highlights the reversibility and transiency of possible beta cell dysfunction during acute pancreatitis and emphasizes the importance of closely assessing the patients' insulin requirements upon discharge, especially when a prior history of diabetes mellitus is absent.
Conclusion: DKA can occur as a rare complication of acute pancreatitis in a nondiabetic patient. Hyperglycemia associated with acute pancreatitis-induced DKA can be temporary and these patients might not necessarily require insulin upon discharge. Therefore, careful discharge planning is very important in such patients.

Introduction

Diabetic ketoacidosis (DKA) is typically but not exclusively seen in diabetic patients. Cases of acute pancreatitis-induced DKA in nondiabetic patients have been previously reported.[1,2] In general, identifying acute pancreatitis in individuals with DKA poses a diagnostic challenge due to overlap of symptoms, thus potentially resulting in one of the diagnoses going unnoticed. In a prospective study involving 100 DKA patients, the prevalence of acute pancreatitis was 11%.[3] We report a case of DKA precipitated by acute pancreatitis in a patient with history of chronic alcoholism and no known underlying diabetes. This case highlights the fact that DKA should be considered in the differential diagnosis of a patient presenting with high anion gap metabolic acidosis and hyperglycemia with acute pancreatitis even without a history of diabetes mellitus.

Case Report

A 39-year-old male with a history of multiple episodes of alcoholic pancreatitis in the past and no prior history of diabetes mellitus (DM) presented with nausea, vomiting and severe epigastric pain radiating to the back for 3 days. Vitals signs demonstrated heart rate of 113 beats/minute, blood pressure of 135/67 mm Hg, body temperature of 36.8 C, and body mass index of 32 kg/m2. On

Abbreviations: BAL, blood alcohol level; DKA, diabetic ketoacidosis; DM, diabetes mellitus; HbA1c, hemoglobin A1c.

Informed consent was obtained for this case report.

* Address correspondence to Dr Duha Zaffar, Department of Medicine, 827 Linden Avenue, Baltimore, Maryland 21201.
E-mail address: Duha.Zaffar@umm.edu (D. Zaffar).

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physical examination, the patient appeared dehydrated with generalized abdominal tenderness. Laboratory testing (Table) revealed elevated serum glucose 251 mg/dL, low serum bicarbonate 8 mmol/L, increased anion gap 21, and elevated serum beta-hydroxybutyrate 9.62 mmol/L. Work-up for the etiology of ketoacidosis revealed the patient last consumed alcohol 2 weeks prior with the blood alcohol level (BAL) on admission being undetectable. Therefore, alcoholic ketoacidosis was ruled out. He denied recent starvation and had an intact appetite, making starvation ketoacidosis unlikely. He was not on any home medications. Hemoglobin A1c (HbA1c) was normal at 5.4%. Given that patient fulfilled the diagnostic criteria [4] and in the absence of any other identifiable etiology, his ketoacidosis was deemed secondary to DKA.

Serum lipase was elevated at 458 U/L (normal range 0–160 U/L), and computed tomography abdomen showed edema of the pancreatic head with adjacent peripancreatic fat stranding consistent with acute pancreatitis (Fig.). Diagnosis of acute pancreatitis was made based on characteristic symptoms and positive computed tomography findings. Work-up for etiology of acute pancreatitis revealed no gallstones on imaging. Serum calcium was normal at 9.6. Serum triglycerides were moderately elevated at 589. There was no prior history of smoking.

He was admitted to the intensive care unit and started on normal saline infusion and intravenous (IV) insulin that was later transitioned to sub-cutaneous insulin, following the institutional DKA protocol. As the serum glucose levels decreased, serum beta-hydroxybutyrate levels returned to normal, which further supports DKA as the etiology for his ketoacidosis. As there was clinical improvement in the pancreatitis, insulin requirements continued to decrease. Patient stayed in the hospital for 6 days while requiring insulin for first 5 days. Insulin was not required at the time of discharge. C peptide and islet cell antibodies were obtained after hyperglycemia had resolved. While C peptide was mildly elevated at 5.1 ng/mL (normal 0.5–2.0 ng/mL), islet cell antibodies were normal. Additionally, follow-up HbA1c at 4 months and 10 months post-discharge did not imply diabetes mellitus, 5.8% at both time points. No insulin or oral diabetic medications were prescribed on discharge. All these findings argued against new onset diabetes mellitus.

Highlights

- Diabetic ketoacidosis (DKA) is typically but not exclusively seen in patients with a history of diabetes mellitus.
- DKA should be considered in a patient with high anion gap metabolic acidosis and hyperglycemia with acute pancreatitis even without a history of diabetes mellitus.
- Hyperglycemia associated with acute pancreatitis induced DKA can be temporary, therefore, careful discharge planning is important in such patients.

Clinical Relevance

Early identification and management of diabetic ketoacidosis in acute pancreatitis is important especially since both can have a similar clinical presentation. Hyperglycemia associated with acute pancreatitis-induced DKA can be temporary and these patients might not necessarily require insulin upon discharge. Therefore, careful discharge planning is very important in such patients.

Discussion

Typical causes of acute pancreatitis include gallstones, alcohol consumption, hypertriglyceridemia, hypercalcemia, medications, and smoking.[5] In our patient, not only was abdominal imaging negative for gallstones, his last consumed alcoholic drink was 2 weeks ago ruling out these etiologies. His serum calcium levels were normal and he was not on any home medications. In the absence of any identifiable triggers for acute pancreatitis, this case was categorized as hypertriglyceridemia-related-acute pancreatitis vs idiopathic acute pancreatitis.[6]

The patient's ketoacidosis was attributed to DKA and his management involved IV insulin in the critical care setting. In general, ketoacidosis is characterized by the accumulation of ketones, primarily beta-hydroxybutyrate and acetoacetic acid, leading to metabolic acidosis with increased anion gap. These metabolic derangements are directly attributed to deficiency of insulin, resulting in unregulated lipolysis and the oxidation of free fatty acids. Ultimately, the production of ketone bodies results in metabolic acidosis with elevated anion gap.[7] The potential diagnoses of alcoholic and starvation ketoacidosis were considered; however, the (BAL) was nondetectable on admission, and the most recent consumption of alcoholic beverage was 2 weeks prior to presentation. While BAL is not necessarily a dependable indicator in cases of alcoholic ketoacidosis, a key characteristic of alcoholic ketoacidosisis the absence of hyperglycemia in individuals with a confirmed history of alcohol consumption; their serum glucose levels can be low, within the normal range, or slightly elevated.[8] Given that this patient's blood glucose levels reached 251 mg/dl, the likelihood of alcoholic ketoacidosis was deemed low. Starvation ketoacidosis typically manifests with a background of inadequate food intake, low or normal blood glucose levels.[9] Our patient denied poor oral intake and had an intact appetite on presentation. Furthermore, beta hydroxybutyrate is rather mildly elevated in starvation ketoacidosis typically unlike the 13x times elevation seen in our case. Lastly, serum bicarbonate concentration, in starvation ketosis is usually not lower than 18 mEq/l unlike 8 mEq/l in our case.[10] With no home medications on board, the possibility of euglycemic DKA from medications such as SGLT-2 inhibitors was unlikely.

Despite no history of DM, our patient fulfilled the criteria for DKA, which requires a blood pH < 7.3, serum bicarbonate < 19, elevated anion gap, and serum blood glucose > 249 mmol/L.[5] The HbA1c level of 5.4% implies satisfactory glycemic control over the

Table
Laboratory Values with Normal Reference Range

Labs	Blood glucose	Serum bicarbonate	Anion gap	Serum beta hydroxy butyrate	HbA1c	Lipase	Serum calcium	Serum triglycerides
Values	251 mg/dL (high)	8 mmol/L (low)	21 (high)	9.62 mmol/L (high)	5.4% (normal)	458 (high)	9.6 (normal)	589 (elevated)
Normal reference range	<140 mg/dL	22-28 mmol/L	10-14	<0.60 mmol/L	<5.7%	0-160 U/L	8.4-10.2 mg/dL	<150 mg/dL

Abbreviation: HbA1c = hemoglobin A1c.

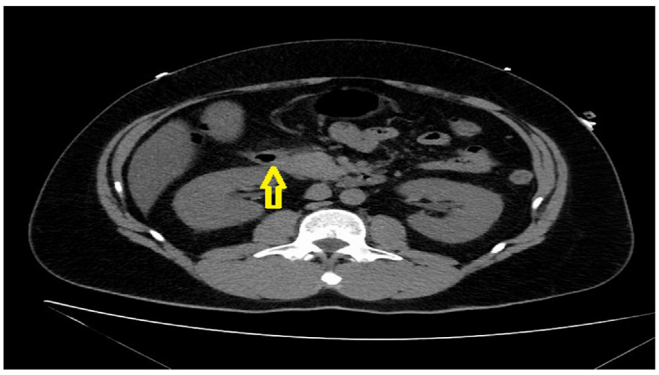

Fig. Computed tomography abdomen showing edema of the pancreatic head with adjacent peripancreatic fat stranding consistent with acute pancreatitis.

3 months prior to hospitalization. His HbA1c at 4 months and 10 months postdischarge was 5.8% on both occasions, arguing against new onset DM. Even though obtained after hyperglycemia had resolved, his mildly elevated C-peptide and normal islet cell antibodies argued against de novo onset of type 1 DM.

While DKA predominantly occurs in individuals with type 1 diabetes, including latent autoimmune diabetes of adulthood, other causes of pancreatic insult, such as cystic fibrosis and hemochromatosis, can also result in diabetes and potentially DKA. DKA also occurs in patients with advanced type 2 diabetes, as a relative lack of insulin can precipitate DKA in that setting.[11] In such patients, following resolution of DKA, the requirement for insulin therapy often persists. Interestingly, our patient did not require any insulin at the time of discharge, further making diagnosis of DM unlikely. Finally, DKA cases have rarely been observed in individuals with type 2 diabetes who were using SGLT-2 inhibitors.[12] Our patient was not taking any home medications.

Our patient's presentation suggests the coexistence of acute pancreatitis and DKA. The process of acute pancreatitis causing beta cell dysfunction, with transient insulin insufficiency resulting in DKA, has been previously described.[13,14] Another possible mechanism for acute pancreatitis-induced DKA is stress hyperglycemia, which can cause a rapid elevation in serum glucose levels. That scenario might provoke DKA in patients with acute pancreatitis who are inherently predisposed to insulin intolerance.[1] Additionally, the underlying mechanism for DKA in type 2 DM which involves glucose toxicity associated temporary beta cell dysfunction[13] can be projected as a possible cause for triggering DKA in our case as well. Lastly, a concept known as postpancreatitis diabetes mellitus has emerged in the literature, which can serve as another potential etiology for DKA after an episode of acute pancreatitis.[1] This phenomenon can be differentiated by the presence of prolonged hyperglycemia[15] which was not seen in our case.

DKA is a critical medical emergency often necessitating intensive care unit management. In a retrospective study of patients with acute pancreatitis, the presence of DKA increased the morbidity and mortality of acute pancreatitis, as evidenced by a higher incidence of severe acute pancreatitis cases in the group with DKA in comparison to the group without DKA.[16] Thus, prompt identification of the simultaneous occurrence of DKA and acute pancreatitis is meaningful due to unfavorable prognostic implications.[17] Another study demonstrated that individuals experiencing both DKA and acute pancreatitis exhibit more pronounced abnormalities in laboratory indicators of DKA severity, pancreatic inflammation, kidney function impairment, and metabolic profile disturbance.[17] Moreover, the coexistence of DKA and acute pancreatitis significantly impacts the utilization of healthcare resources, resulting in extended DKA duration, longer hospital stays, and a greater need for ICU support.[17] Enhanced awareness regarding this critical combination of life-threatening disorders can facilitate early identification and ultimately lead to improved clinical outcomes for patients with DKA.[17]

Lastly, in patients with DKA caused by acute pancreatitis, this case highlights the need to closely assess patients' insulin requirements upon discharge, especially when a prior history of diabetes is absent; insulin is not necessarily a mandatory component of their postdischarge treatment. In patients with DKA and acute pancreatitis, the loss of pancreatic beta cell function seems to be reversible. Our case postulates that pancreatic beta cells that temporarily lose function can potentially regain functionality after the attack of acute pancreatitis subsides. Theoretically, this should be supported by a deficiency in C peptide level. For our patient, C peptide was unfortunately not obtained during presentation but rather late when patient was already managed with insulin and normoglycemic.

Conclusions

DKA can occur as a rare complication of acute pancreatitis in a nondiabetic patient. Early identification and management of this critical medical emergency is important especially since both can have a similar clinical presentation. Management is similar to that of DKA associated with diabetes mellitus. However, hyperglycemia associated with acute pancreatitis-induced DKA can be temporary and these patients might not necessarily require insulin upon discharge. Therefore, careful discharge planning is very important in such patients.

Disclosure

The authors have no conflicts of interest to disclose.

Acknowledgment

This case report was presented in poster form at the Maryland Chapter of the American College of Physicians Annual Resident Conference, Baltimore, MD in May, 2023.

Author contributions

D. Z. was involved in clinical care of this patient, wrote the manuscript, and reviewed the literature. A. R. also contributed to the manuscript writing and literature review. D. Z., R. D. C., and K. M. M. reviewed and edited the manuscript. R. D. C. is the article guarantor.

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