International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Exploring the Pathogenesis of Diabetic Ketoacidosis in the Context of Acute Pancreatitisand Hypertriglyceridemia

Mahvish Renzu[1*], Carly Hubers[2], Kendall Conway[2], Adam Manzoor Qazi[3], Alexander M Satei[4], Durga Yerasuri[5]

[1]Department of Internal Medicine, Wayne State University School of Medicine/ Trinity Health Oakland, Pontiac, MI, USA

[2]Wayne State University School of Medicine, Detroit, MI, USA

[3]Department of Internal Medicine, Wayne State University & Detroit Medical Center, Detroit, MI

[4]Department of Radiology, Trinity Health Oakland, Pontiac, MI 5. Department of Endocrinology,, Trinity Health Livonia, Livonia, MI, USA

Citation: *Mahvish Renzu , Carly Hubers , Kendall Conway , Adam Manzoor Qazi, Alexander M Satei , Durga Yerasuri. Exploring the Pathogenesis of Diabetic Ketoacidosis in the Context of Acute Pancreatitis and Hypertriglyceridemia. Int Clinc Med Case Rep Jour. 2024;3(7):1-6.*

Received Date: 15 June, 2024**; Accepted Date:** 05 July, 2024**; Published Date:** 10 July, 2024

[*]**Corresponding author:** Mahvish Renzu, Department of Internal Medicine, Wayne State University School of Medicine/ Trinity Health Oakland, Pontiac, MI, USA

ABSTRACT/SUMMARY

We present a perplexing case of a patient who developed diabetic ketoacidosis (DKA) concomitantly with acute pancreatitis (AP) and severe hypertriglyceridemia (HTG), without a prior diagnosis of diabetes. The absence of traditional diabetes markers and a transientdiabetes condition post-pancreatitis challenge the standard pathogenesis models for DKA. This case also underscores the critical importance of considering acute metabolic disturbances as potential precipitants of severe glycemic crises. It further highlights the complex interplay between these conditions, challenging the conventional understanding of their pathogenesis and raising important diagnostic and therapeutic considerations.

Keywords: Pathogenesis; Diabetic Ketoacidosis; Hypertriglyceridemia

BACKGROUND

The case of a patient presenting with a single episode of DKA in the absence of aprior diabetes history, amidst AP and significant HTG, embodies a unique and enlightening scenario for clinicians. Notably, the negative workup for type 1 diabetes mellitus (T1DM) markers, combined with the fleeting nature of his diabetes, challenges conventional understanding of DKA pathogenesis, suggesting acute metabolic disturbances like pancreatitis can precipitate DKA independently of chronic disease.

This case call attention to the complex interplay between AP, lipid metabolism disorders, and beta-cell function, emphasizing diagnostic and classification challenges in diabetes. This patient's story is of paramount interest as it presents a rare presentation of a common disease, DKA, offering new perspectives on disease pathogenesis, diagnostic difficulties, and the impactof socioeconomic factors on healthcare access and outcomes.

CASE PRESENTATION

A male in his early 20s with a past medical history significant only for a speech impediment presented to the emergency department, under the care of his sister, with altered mental status. His symptoms commenced approximately four days prior, characterized by nausea, vomiting, diarrhea, and abdominal pain without any fever, respiratory, or urinary complaints. Notably, he had no known personal or family history of diabetes at this time.

Upon arrival, he was tachycardic, tachypneic, with an initial point of care glucose exceeding 550 mg/dL. Laboratory findings revealed significant hyperglycemia with a blood glucose level of 1182 mg/dL, an elevated anion gap of 30, bicarbonate of 5 mmol/L, and an acute kidney injury with a creatinine of 2.27 mg/dL. Further tests showed a lipase level of 842 U/L, indicative of AP,and triglycerides were markedly elevated at 1267 mg/dL. His condition necessitated admission tothe intensive care unit (ICU) for aggressive management of DKA, AP, and associated complications.

Throughout his ICU stay, our patient encountered challenges in closing the anion gap, attributedin part to persistent hypokalemia. A nephrology consult posited renal tubular acidosis (RTA) type 1, for which sodium bicarbonate therapy was initiated. His diabetes management transitioned from an insulin drip to subcutaneous insulin as his anion gap normalized, and he began tolerating oral intake. Imaging studies confirmed the presence of AP without specifying the etiology [Figure 1A and 1B], alongside findings of severe hepatic steatosis [Figure 2]. The patient denied any alcohol use, but did admit to having an overall poor diet.

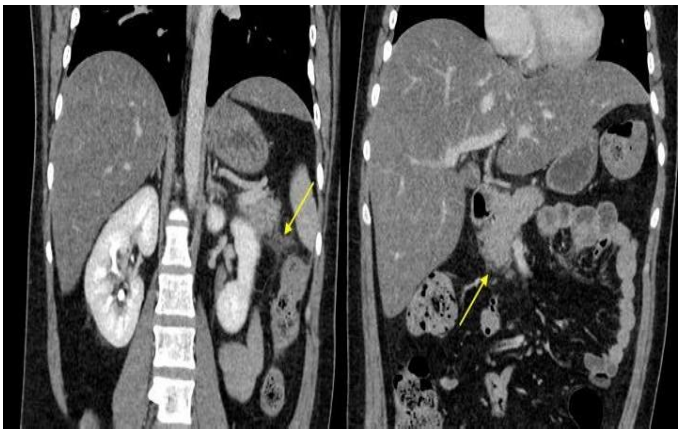

Figure 1A and 1B: Fat stranding and inflammation at the tail (figure 1A) and head (figure1B) of the pancreas. Severe hypoattenuation of the liver is compatible with hepatic steatosis.

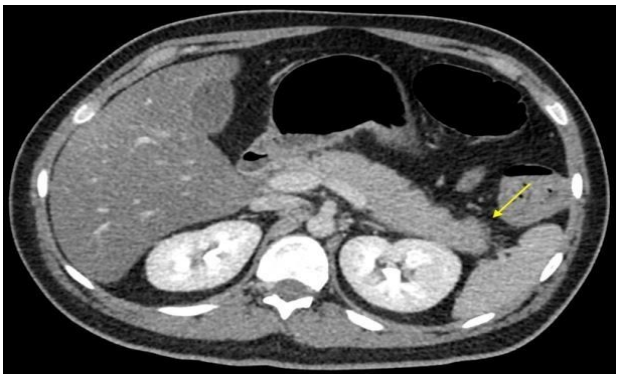

Figure 2: Axial CT of the abdomen and pelvis with IV contrast demonstrates fat stranding and inflammation near the tail of the pancreas. No pancreatic ductal dilation or peripancreatic fluid collection. Severe hypoattenuation of the liver is compatible withhepatic steatosis.

On hospital day 5, he was stabilized and discharged with diagnoses of DKA, new-onset diabetesmellitus suspected to be T1DM, AP with hypertriglyceridemia of 175 mg/dL , RTA type 1, and acute kidney injury secondary to prerenal azotemia. The patient was referred for endocrinology follow-up to manage his newly diagnosed diabetes and to clarify the type of diabetes. His outpatient management involved transitioning to a basal-bolus insulin regimen and addressing HTG with statin and fibrate therapy.

Differential Diagnosis: The patient's presentation with DKA initially raised the obvious differential diagnosis of T1DM versus T2DM. However, the lack of autoimmune markers typical of T1DM and the temporary nature of the hyperglycemia pointed away from a chronic condition.The concurrent significant HTG and AP further complicated the clinical picture, leading to the consideration of a secondary cause of diabetes.

The intricate relationship between DKA, HTG, and AP in this case led to a diagnostic challenge. While DKA is commonly associated with diabetes, the presence of severe HTG and AP raises the possibility that one of these conditions may have precipitated the others. The resolution of DKA following the management of pancreatitis suggests a potential causal link, yet it remains unclear whether the pancreatitis led to DKA or vice versa. This ambiguity calls attention to the need for a careful and comprehensive approach in evaluating patients with this complex triad of conditions.

Outcome and Follow-up: At subsequent follow-up visits, the patient has reported no symptoms of polyuria, polydipsia, nocturia, blurry vision, or lower extremity paresthesias. There have continued to be no signs of autoimmune diabetes, as evidenced by adequate C-peptide levels andnegative GAD and islet cell antibodies. Despite his BMI of 20 kg/m2 and a clinical presentation suggesting a T1DM picture, the absence of autoimmune markers and his response to treatment have led to the consideration that AP or HTG may have been the culprit of his DKA.

The patient has resumed his daily activities and work as a landscaper. He has been educated on the symptoms of hypoglycemia and what to look out for. The follow-up period has been ongoing since his hospital admission several years ago, with regular monitoring of his glycemic and lipid profiles to ensure optimal management of his health. Overall, the patient is doing well, with no evidence of disease recurrence or complications related to his initial presentation of DKA in the setting of AP and HTG.

At the time of this writing, the patient is only on a single dose of metformin. Interestingly, throughout his care, his HbA1c has never been elevated. His most recent HbA1c was 5.5%, indicating good glycemic control. The atypical presentation, characterized by DKA in the absence of diabetes mellitus, and the subsequent finding of significant HTG and AP, reinforcethe complexity of his case.

The ongoing management and monitoring of this patient, now in his mid 20s, is geared towardsoptimizing his glycemic control, managing his lipid profile, and closely observing his clinical course to refine his diagnosis and treatment plan over time.

DISCUSSION

The interrelationship between DKA, HTG and AP is complex and multifaceted. The case presented in this report emphasizes the uncertainty surrounding the causal relationship between these conditions.

HTG, a common cause of AP, may lead to more severe forms of pancreatitis. The excess triglycerides are hydrolyzed by pancreatic lipases, releasing free fatty acids that can cause direct toxicity to pancreatic cells. Furthermore, the increased blood viscosity due to elevated triglyceride levels can impair pancreatic blood flow, exacerbating the inflammatory process.[1]

In T1DM, the reduction in insulin production leads to decreased activity of lipoprotein lipase, resulting in elevated triglyceride levels. Conversely, in individuals with T2DM, hyperinsulinemia and insulin resistance contribute to increased triglyceride production and reduced clearance, further exacerbating the risk of HTG. Moreover, the development of HTG-induced AP can lead to transient beta cell dysfunction, creating a state of insulin deficiency.

This, coupled with the systemic inflammation associated with AP, can increase insulin resistance, potentially precipitating an episode of DKA.[1]

Imburgio et al. suggest that stress hyperglycemia, a common response to critical illnesses such as AP, may play a significant role in the development of DKA. The activation of the hypothalamic- pituitary-adrenal axis and the sympathetic nervous system, along with the presence of pro- inflammatory cytokines, can lead to elevated serum glucose levels through increased hepatic gluconeogenesis and glycogenolysis, as well as reduced glucose uptake in peripheral tissues.

This acute hyperglycemic state, coupled with the pancreatic inflammation and beta-cell dysfunction caused by AP, can precipitate DKA in susceptible individuals, such as our patient. The intricate interplay between these metabolic disturbances highlights the need for a comprehensive approach to managing patients presenting with this

presentation.[2]

The pathophysiological relationship between these three conditions is intricate. A case described by Kong et al. highlights a similar triad, where a 44 year old male patient presented with DKA concurrent with acute severe HTG-induced pancreatitis as the first manifestation of T2DM. Theircase emphasized the potential for DKA to be both a risk factor for AP and a consequence of HTG-induced pancreatitis.[3]

An additional case presented by Aung et al. adds another layer of complexity to the relationship between DKA, HTG, and AP. Their report describes a 70-year-old patient who presented with AP and ketoacidosis, but without a prior history of diabetes, much like our own patient. Their patient's ketoacidosis resolved quickly with minimal intervention, highlighting the fleeting natureof hyperglycemia and insulin deficiency in the context of AP.[4]

It is important to consider AP as a potential trigger for DKA, even in the absence of a formal diabetes diagnosis. The short-lived suppression of insulin secretion due to AP can lead to hyperglycemic ketoacidosis, as observed in the case reported by Aung et al. and potentially ourown as well. Furthermore, Aung et al.'s findings suggest that DKA can be induced by acute hyperglycemia secondary to pancreatitis, emphasizing the bidirectional relationship between these conditions.[4]

The case described by Aung et al. further notes the need for a comprehensive evaluation of patients presenting with ketoacidosis, as various factors, including alcohol consumption, malnutrition, and medication use, can contribute to the development of pancreatitis and subsequent ketoacidosis. A similar approach to care was taken with our own patient to ensureadequate care was being delivered.[4]

In our case, the patient's transient hyperglycemia and subsequent development of DKA in the context of AP and significant HTG illustrate the delicate balance between this triad of conditions. It stresses the importance of considering the potential bidirectional relationship between DKA and AP in the clinical evaluation and management of such cases.

Learning Points:

- AP can trigger DKA in individuals without prior diabetes, challenging traditionalpathogenesis models.
- The bidirectional relationship between DKA and AP shows the importance of considering each condition as both a potential cause and consequence in the clinicalevaluation and management of patients.
- Atypical presentations of hyperglycemia necessitate a comprehensive diagnostic approach, as standard classifications may not apply.

REFERENCES

1. Narala B, Al-Tkrit A, David S, Alataby H, Nfonoyim J. A Fatal Case of Hypertriglyceridemia-Induced Acute Pancreatitis in a Patient With DiabeticKetoacidosis. Cureus . 2021;13(5):e14968.
2. Imburgio S, Vedire A, Sanekommu H, Johal A, Taj S, Lesniak C, et al. Acute Pancreatitis as an Unusual Culprit of Diabetic Ketoacidosis in a Nondiabetic: A Case-Based Review. Case Reports in Endocrinology.

2023;2023:e9122669.

3. Kong MT, Nunes MP, Leong KF. Diabetic ketoacidosis with acute severe hypertriglyceridaemia-induced pancreatitis as first presentation of type 2 diabetes. BMJCase Reports. 2021;14(4):e239727.
4. Aung NL, Vakani V, Wassel M. A Case of Hyperglycemic Ketoacidosis in a Patient Without Diabetes. Cureus. 2022;14(4):e24560.