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Diabetic Ketoacidosis Complicated by Hypertriglyceridemia-Induced Pancreatitis: A Case Report

Imran Khan[1], Adrienne Kwong[2], Caitlin Richler[1], Christine Landry[1], Sydney Morin[1] and Pierre Thabet[3]*

[1]*Department of Clinical Pharmacology, University of Ottawa School of Pharmaceutical Sciences, Canada*

[2]*Department of Palliative Care and Critical Care, Ottawa Hospital, Ottawa, Canada*

[3]*Department of Critical Care, University of Ottawa School of Pharmaceutical Sciences, Canada*

Abstract

Background: Diabetic Ketoacidosis (DKA) is a severe complication of diabetes characterized by hyperglycemia, metabolic acidosis, and ketosis. It can lead to complications such as hypertriglyceridemia-induced pancreatitis due to increased lipolysis and triglyceride formation.

Case Presentation: A 28-year-old female presented with symptoms consistent with diabetic ketoacidosis (DKA), including polyuria, polydipsia, polyphagia, and unintentional weight loss. Laboratory results revealed severe hyperglycemia (glucose 22.9 mmol/L, HbA1c 14.5%), metabolic acidosis (pH 7.15), and elevated beta-hydroxybutyrate (6.75 mmol/L). Further evaluation showed markedly elevated triglycerides (45 mmol/L) and lipase (2928 IU/L), indicating mild pancreatitis. Upon reviewing her clinical presentation and lab findings, poorly controlled diabetes was determined to be the primary cause, leading to DKA and secondary hypertriglyceridemia. The patient was managed in the ICU with insulin therapy, fluid resuscitation, and Fenofibrate to address hypertriglyceridemia. Identifying the primary precipitant through this comprehensive assessment is crucial for directing management toward aggressive control of hyperglycemia, ketosis, and triglyceride levels.

Conclusions: This case underscores the complex interplay between DKA, hypertriglyceridemia, and pancreatitis. Accurate clinical evaluation is essential to tailor management strategies focusing on aggressive control of hyperglycemia and triglyceride levels to prevent complications and optimize patient outcomes.

Keywords: Diabetic ketoacidosis; Hypertriglyceridemia; Pancreatitis; Insulin therapy; Fenofibrate

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Correspondence:
Imran Khan, Department of Clinical Pharmacology, University of Ottawa School of Pharmaceutical Sciences, Institut du Savoir Montfort, Ottawa, Canada,

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Introduction

Diabetic Ketoacidosis (DKA) is a serious complication of diabetes characterized by hyperglycemia, metabolic acidosis, and elevated ketone levels. It is commonly seen in patients with type 1 diabetes but can also occur in individuals with type 2 diabetes under certain conditions [1]. DKA can cause hypertriglyceridemia due to increased lipolysis and release of free fatty acids converted into triglycerides [2]. Elevated triglyceride levels, exacerbated during DKA by increased lipolysis, can directly contribute to pancreatitis by promoting fat accumulation in pancreatic cells. Approximately 7% of acute pancreatitis cases are attributed to hypertriglyceridemia as a secondary cause [3]. This relationship is bidirectional; DKA can predispose to hypertriglyceridemia and pancreatitis, while severe hypertriglyceridemia can worsen insulin resistance, potentially triggering or worsening DKA. This case report presents a unique instance of the triad of DKA, hypertriglyceridemia and pancreatitis offering insights into their intricate interrelationships and management approaches.

Case Presentation

A 28-year-old female presented to the Emergency Department (ED) with symptoms of polyuria, polydipsia, polyphagia, and unintentional weight loss over the past few weeks. She had a significant history of feeling unwell for the past year, gaining approximately 20 pounds, and recently losing weight due to her catabolic state. Her past medical history included depression and an appendectomy and her home medications included Venlafaxine, Aripiprazole and Pantoprazole. She reported occasional cigarette smoking and occasional use of THC and alcohol but denied significant chronic

alcohol use. Her family history was notable for type 2 diabetes in her mother. Upon admission, her laboratory results were significant for severe hyperglycemia, with a random serum glucose on admission of 22.9 mmol/L (412 mg/dL), hemoglobin A1c (HbA1c) of 14.5%, Beta-Hydroxybutyrate (BHB) level of 6.75 mmol/L, and a pH of 7.15, consistent with DKA. Additionally, she had markedly elevated triglycerides at 45 mmol/L (4000 mg/dL). A CT abdomen revealed mild pancreatitis, likely secondary to hypertriglyceridemia, and an abdominal ultrasound showed no evidence of kidney stones with a normal common bile duct size

Investigations

Laboratory investigations on admission revealed significant abnormalities. The patient's glucose level was markedly elevated at 25 mmol/L (450 mg/dL). Hemoglobin A1c (HbA1c) was 14.5%, indicating chronic hyperglycemia. Beta-Hydroxybutyrate (BHOB) was 6.75 mmol/L (pending during initial examination), suggestive of significant ketonemia. Arterial blood gas analysis showed a pH of 7.15, a partial Pressure of Carbon Dioxide (pCO2) of 23.8 mmHg, and a Bicarbonate (HCO3) at 8.3 mmol/L consistent with metabolic acidosis. Electrolyte imbalances included sodium at 125 mmol/L, potassium at 4.2 mmol/L, chloride at 84 mmol/L, and total carbon dioxide at 11 mmol/L. Additional laboratory findings included urea at 3.3 mmol/L (92.42 mg/d), creatinine at 87 μmol/L (0.98 mg/dL), and plasma lactate at 1.2 mmol/L. The anion gap was significantly elevated at 30 mmol/L, supporting the diagnosis of DKA. Triglycerides were markedly elevated at 45 mmol/L (3985 mg/dL). Urinalysis showed 4+ ketones, negative nitrite, trace leukocytes, and a negative beta HCG. Imaging studies included a lipase level of 1474 U/L, which is highly suggestive of pancreatitis. Given the patient presented with abdominal pain, a CT abdomen confirmed mild pancreatitis, and an ultrasound of the abdomen showed no evidence of kidney stones with a normal common bile duct size.

Treatment

Upon admission to the ICU on day 1, the patient underwent treatment following the hospital DKA protocol which included intravenous insulin therapy, fluid resuscitation, and electrolyte management. Fenofibrate was initiated to address her hypertriglyceridemia alongside supportive measures for DKA and acute pancreatitis. After 24 hours of intravenous insulin and fluid therapy, she transitioned to subcutaneous basal and bolus insulin therapy, receiving insulin glargine at bedtime and insulin aspart with meals. By day 4, following a three-day ICU stay, the patient's condition stabilized, prompting transfer to the medical floor. Despite initial concerns about Cushing's syndrome due to weight gain and central obesity, normal results from a 24-hour cortisol test ruled out this diagnosis. Ongoing diabetes management included adjusting insulin glargine and aspart doses, with plans for dietitian consultation and insulin education upon discharge. The patient responded well to treatment throughout her hospitalization, leading to stabilization and preparation for continued diabetes care post-discharge. Upon discharge, prescriptions were provided for insulin aspart with meals and insulin glargine at bedtime, with instructions for basal insulin titration. Fenofibrate was continued to manage hypertriglyceridemia, with a scheduled follow-up at the diabetes clinic in two weeks under the care of an internist. Notes from her follow-up in the hospital diabetes clinic two weeks post-discharge indicated that despite central obesity and negative anti-GAD antibodies, the most probable diagnosis remained type 1 diabetes. With risk factors for ongoing severe insulin deficiency including family history, age at presentation, and marked hyperglycemia at her presentation for DKA, the patient was counselled to continue insulin therapy indefinitely. She remained on her basal/bolus insulin regimen and Fenofibrate, with plans for ongoing follow-up at the diabetes clinic.

Discussion

Hypertriglyceridemia plays a pivotal role in the pathogenesis of acute pancreatitis, particularly when serum levels surpass 1000 mg/dl [4]. This condition arises from pancreatic lipase-mediated hydrolysis of triglycerides TGs into toxic free fatty acids, which can induce pancreatic injury through mechanisms involving lipotoxicity. In the context of DKA, there may be a pronounced elevation in serum triglycerides, further exacerbating the risk of Acute Pancreatitis (AP). The convergence of DKA, AP, and hypertriglyceridemia represents a clinically challenging triad, characterized by its rarity and significant morbidity and mortality [5]. Management strategies typically involve aggressive control of hypertriglyceridemia and DKA, alongside supportive measures aimed at mitigating pancreatic inflammation and dysfunction. Determining whether DKA triggered hypertriglyceridemia leading to pancreatitis or if hypertriglyceridemia-induced pancreatitis precipitated DKA requires a careful evaluation of the clinical timeline. A key factor is the sequence of symptom onset and laboratory results. Whether hyperglycemia and ketonemia are present before abdominal pain and elevated pancreatic enzymes, may help suggest that DKA was the primary event, which then led to hypertriglyceridemia and subsequent pancreatitis. On the other hand, if the patient initially presents with symptoms of acute pancreatitis (e.g., severe abdominal pain, nausea, vomiting) followed by hyperglycemia and ketonemia, hypertriglyceridemia-induced pancreatitis may be given considered as the primary trigger for DKA [6]. Additionally, the typical progression of these conditions can offer clues. DKA often develops rapidly within hours to days, whereas hypertriglyceridemia-induced pancreatitis may have a variable onset depending on the severity [7]. An elevated hemoglobin A1c further supports DKA as the primary driver, reflecting a prolonged period of poorly controlled hyperglycemia. A thorough review of the patient's diabetes history, lipid levels, and prior episodes of DKA or pancreatitis is essential for establishing a clear timeline and identifying the primary precipitant. Importantly, these conditions can also have a bidirectional relationship, where one exacerbates the other, creating a vicious cycle that complicates management [8]. In this particular case, our patient's presentation suggests a complex interplay of conditions, with DKA likely being the primary precipitant. As stated above, her symptoms of polyuria, polydipsia, polyphagia, and unintentional weight loss, along with severe hyperglycemia (HbA1c of 14.5%) and significant ketonemia (BHOB of 6.75 mmol/L), are hallmark features of DKA. The markedly elevated triglycerides of 45 mmol/L (4000 mg/dL) suggest secondary hypertriglyceridemia, which is a common complication of DKA due to increased lipolysis and free fatty acid conversion. This hypertriglyceridemia likely led to the development of mild pancreatitis, as confirmed by the elevated lipase levels and CT findings. To rule out other causes of pancreatitis, a review of her lab results showed no overt abnormalities. Her home medications of venlafaxine, aripiprazole, and pantoprazole were evaluated using the Naranjo Adverse Drug Reaction Probability Scale [9]. The scores indicated that these medications were unlikely to have significantly contributed to her pancreatitis, pointing instead to hypertriglyceridemia as the primary cause. Therefore, the sequence appears to be DKA causing

hypertriglyceridemia, which subsequently induced pancreatitis. However, the bidirectional relationship means that while DKA initiated this cascade, the resultant hypertriglyceridemia and pancreatitis could further exacerbate her metabolic derangements, creating a cyclical worsening of her condition. Our case reports have also documented managing this complex interplay between DKA, hypertriglyceridemia and pancreatitis [10-12]. In all of these cases, prompt diagnosis and comprehensive management, including CT scans and lipid panels, were critical in achieving successful outcomes. This triad, while rare, underscores the necessity for heightened clinical suspicion and tailored therapeutic approaches to effectively manage these interconnected conditions. There are limitations to this case report, most notably, the retrospective nature of the study may have impacted the thorough identification, reporting, and documentation in the patient's medical chart. The lack of genetic testing or more comprehensive family history limits the understanding of potential hereditary contributions to the patient's condition. In addition, not all potential contributing factors (such as detailed lipid panel, autoantibodies, or inflammatory markers) were evaluated, potentially overlooking other underlying conditions. Finally, the documented short follow-up period post-discharge limits the assessment of long-term management efficacy and patient outcomes, including potential recurrences of DKA or pancreatitis. This case underscores the critical importance of recognizing intricate bidirectional relationships: DKA can induce hypertriglyceridemia leading to pancreatitis, and severe hypertriglyceridemia can exacerbate DKA. Identifying the primary cause through detailed clinical evaluation is crucial for developing tailored management strategies, which should focus on aggressive control of hyperglycemia, ketosis, and triglyceride levels.

Conclusion

In summary, this case highlights the intricate relationship involving DKA, hypertriglyceridemia, and pancreatitis. The potential bidirectional exacerbation between DKA and hypertriglyceridemia emphasizes the necessity for thorough clinical assessment to identify the underlying precipitant. Accurate identification is crucial for tailored therapeutic strategies, emphasizing comprehensive monitoring and long-term management to prevent recurrence and enhance patient outcomes.

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