Diabetic Ketoacidosis Caused by Acute Pancreatitis Results in Severe Hypertriglyceridemia: A Case Report

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Clinical Medicine Insights: Endocrinology and Diabetes
Volume 18: 1–5

DOI: 10.1177/11795514251323826
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ABSTRACT: Diabetic ketoacidosis (DKA) is an acute complication of diabetes that mainly occurs in type 1 diabetes. However, it can also occur in type 2 diabetes, although less commonly. One of the rare causes of this condition is acute pancreatitis. While hypertriglyceridemia is a known complication of DKA, triglyceride levels higher than 2000 are an unusual finding. We present a case of undiagnosed type 2 diabetes mellitus in a patient who came to the hospital with epigastric pain, nausea, and vomiting. Subsequent blood tests revealed hyperglycemia, ketonuria, metabolic acidosis, and increased levels of amylase and lipase, leading to a simultaneous diagnosis of DKA, acute pancreatitis, and very severe hypertriglyceridemia. In patients experiencing abdominal pain and severe diabetic complications, acute pancreatitis should always be considered as a possible diagnosis, and triglyceride levels should be tested to identify hypertriglyceridemia as a potential cause of pancreatitis or complications of DKA.

Plain Language Summary

Diabetic ketoacidosis (DKA) is a serious condition mainly seen in people with type 1 diabetes, but it can also occur in type 2 diabetes, though less often. An uncommon cause of DKA is acute inflammation of the pancreas. While high triglyceride levels can occur with DKA, very high levels above 2000 mg/dL are unusual.

We describe a case of a patient with undiagnosed type 2 diabetes who came to the hospital with stomach pain, nausea, and vomiting. Blood tests showed high blood sugar, the presence of ketones in urine, metabolic acidosis, and high amylase and lipase levels. These results led to the diagnosis of DKA, acute inflammation of the pancreas, and very high triglyceride levels.

When patients have stomach pain and serious diabetes-related problems, it is important to consider acute pancreatitis as a possible cause. Checking triglyceride levels is also essential to determine if high triglycerides may contribute to pancreatitis or worsen DKA.

KEYWORDS: Diabetes mellitus, diabetic ketoacidosis, acute pancreatitis, hypertriglyceridemia, epigastric pain, ascites

RECEIVED: October 18, 2024. **ACCEPTED:** February 1, 2025.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

COMPETING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Introduction

Patients with type 2 diabetes mellitus experience various complications related to the disease over their lifetime. One effect of diabetes is on lipid metabolism, leading to prolonged metabolism of lipoproteins after eating. This can result in fasting hypertriglyceridemia and poor blood glucose control. The abnormality is caused by the disruption of the activity of lipoprotein lipase (LPL), which is a key enzyme in breaking down triglyceride-rich lipoproteins.[1]

Diabetic ketoacidosis (DKA) is an acute complication of diabetes that mainly occurs in type 1 diabetes (T1DM) and less commonly in type 2 diabetes (T2DM), with an incidence of less than 2 per 1000 patient-years.[2] The main etiologies in T2DM, like T1DM, are severe infections, but they can also occur due to trauma, cardiovascular events, or other severe conditions. In uncommon cases, it can happen following acute pancreatitis.[3,4] It may also present as the primary sign of a subset of T2DM identified as ketosis-prone diabetes mellitus.[5]

One of the complications of improper blood sugar (BS) control is the occurrence of acute complications, such as diabetic ketoacidosis (DKA). Hypertriglyceridemia is observed in 30% to 50% of DKA cases; still, triglyceride levels exceeding 2000 are uncommon in these patients.[6] This finding is often linked to type 1 diabetes or poorly controlled diabetes with severe insulin deficiency in various studies.[7,8]

Case Description

We report a 41-year-old Caucasian woman referred to the hospital with complaints of abdominal pain, nausea, and vomiting. She initially experienced nausea and vomiting in the morning. Three to 4 hours later, she also developed a loss of appetite and pain in the epigastric pain. She experienced a decrease in her epigastric abdominal pain when sitting but an increase in discomfort when lying down, with the pain radiating to her back and left side of the chest. She initially self-medicated with antacid drugs but sought medical attention when the pain persisted. She had a history of gestational diabetes mellitus (GDM) during her pregnancy 2 years ago and was treated with insulin detemir at that time. Her insulin was discontinued after delivery, and she ceased her monthly medical visits after being in remission for 1 year with normal blood sugar levels in all post-pregnancy tests. She had no prior history of fungal or viral infections before her hospital visit. She had not undergone any laboratory tests for about a year and showed no signs of

Table 1. Laboratory findings.

LABORATORY PARAMETER		NORMAL RANGE	RESULTS					
			FIRST DAY	SECOND DAY	THIRD DAY	FOURTH DAY	FIFTH DAY	SIXTH DAY
WBC		4000-10 000/μL	14 000	11 200	10 500	10 800	9500	10 000
Hemoglobin		12-16 g/dL	14.8	13.7	12.8	12.2	11.8	12.2
Hematocrit		36-45 mL/dL	40.2	37.2	32.6	31.3	29.3	30.8
Platelet		150-450 × 10^3/μL	340	280	270	260	275	395
Amylase		<100 U/L	170	140	68	52		
Lipase		13-60 U/L	120	83	78	68		
Triglyceride		<200 mg/dL	2100	1600	610	550	280	242
CRP		<6 mg/dL	55.4	88		80	75	
ESR		Age + 10/2 mm/h	16	15	19	18		
Urea		21-43 mg/dL	24	25	26	22	25	27
Creatinine		0.6-1.3 mg/dL	0.7	0.8	1.0	0.7	0.8	1.0
Sodium		135-145 meq/L	128	132	135	134	136	137
Potassium		3.5-4.5 meq/L	4.3	4.8	4.2	4.4	3.7	4.0
Calcium		8.2-10.7 mg/dL	10.7	8.2	8.0	7.8	7.8	8.8
Phosphorus		2.5-5 mg/dL	17.3	7.2	4.4	2.3		
Magnesium		1.6-2.5 mg/dL	4.1	2.4	2.0	1.9	1.8	
Albumin		3.5-5.5 g/dL	5.5	4		3.4		3.2
AST		<35 U/L	42	45	35	28	34	
ALT		<31 U/L	34	42	28	22	25	
ALP		64-306 U/L	230	215	150	142	210	
Hb A1C		5.6%-6.4%	12.3					
cTnI		<0.1 ng/mL	<0.1					
ABG	PH	7.33-7.44	7.28	7.37	7.35	7.37	7.38	7.36
	Pco2	35-45 mmHg	25	23.1	37	36	43	40
	HCO3	22-26 mmol/L	12	14	22	23	25	23

Abbreviations: ABG, arterial blood gas; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; cTnI, cardiac troponin-I; ESR, erythrocyte sedimentation rate; HbA1C, hemoglobin A1C; WBC, white blood cells.

hyperglycemia. She was diagnosed with hypertension in the past 6 months, which was effectively controlled with a regimen of 25 mg of losartan twice daily. She did not disclose any history of alcohol consumption. Additionally, she had a family history of hypertension but did not report any instances of diabetes or hypertriglyceridemia in her family. When she visited the emergency room, her vital signs were as follows: blood pressure of 135/80mmHg, pulse rate of 98 beats/min, respiratory rate of 17 per minute, body temperature of 36.6°C, and oxygen saturation of 92% without oxygen. Her body mass index was 28. She was alert and oriented but lethargic, pale, and not jaundiced. During the oral examination, the oral mucous was dry. There were no skin lesions on the face, palms, and soles. Lung auscultation revealed clear breath sounds without any additional sounds. Heart auscultation was normal, with no murmurs or extra sounds detected. The abdomen was soft with tenderness in the epigastric and upper left quadrant, and shifting dullness or organ enlargement was not detected. During the examination of the genitalia, no signs of fungal infections were observed. In the laboratory tests, evidence of DKA (BS of 560 mg/dL, positive urinary ketones, metabolic acidosis), acute pancreatitis (amylase and lipase levels of 170 U/L and 120 U/L, respectively), and hypertriglyceridemia (triglyceride level of 2100 mg/dL) were detected (Table 1).[9,10] During the

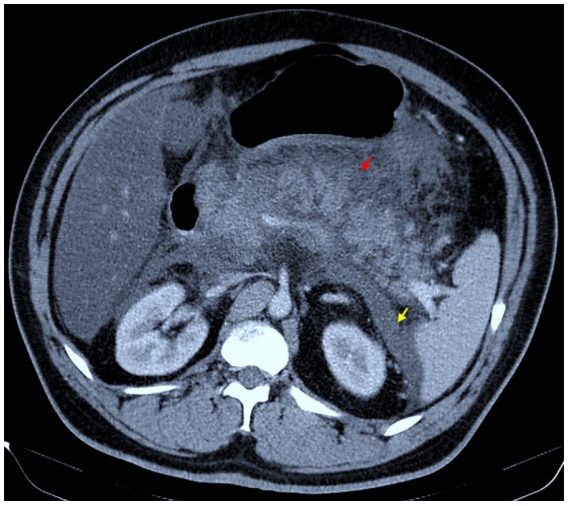

Figure 1. The abdominopelvic CT scan indicated the presence of acute pancreatitis, with observed swelling and edema surrounding the pancreas, as well as notable fat stranding (red arrow) and ascites (yellow arrow).

ultrasound examination, everything appeared normal, and no fluid was found in the peritoneum. However, due to excessive intestinal gas, examining the pancreas was impossible. The patient was transferred to the intensive care unit and started on the following treatments: intravenous antibiotics (Levofloxacin 500 mg daily, metronidazole 500 mg 3 times a day), intravenous insulin, hydration with 4 L of ringer lactate on the first day and 3 L daily thereafter, and pethidine ampoule 25 mg for pain relief when needed. Antibiotics were initiated because of the elevated leukocyte count and high levels of C-reactive protein. An abdominopelvic CT scan with intravenous enhancement revealed swelling and severe inflammatory changes in the fat around the pancreas. Additionally, mild free fluid was observed in the peritoneal spaces of the abdomen and pelvis (Figure 1).

The ejection fraction was within the 55% to 60% range during the cardiology consultation. Based on the negative troponin results (<0.1 ng/mL) and normal findings in the ECG and echocardiography, the possibility of acute coronary syndrome was ruled out. The detailed laboratory test results are presented in Table 1.

The following day, in addition to abdominal pain, abdominal distention was evident. The pain did not intensify compared to before, and the mucosa dehydration had resolved. The Shifting dullness examination (The examination reveals fixed dullness in the left flank and splenic region, which shifts to the right flank during percussion when the patient assumes a right oblique position, eliminating the dullness from the left flank[11]) yielded positive results, while the blood pressure and oxygen saturation remained normal. Normal defecation was reported. In the second ultrasound examination, no signs of pancreatic necrosis were observed. However, mild to moderate interloop fluid in the abdominal cavity, particularly on the left side, and mild to moderate free fluid in the pelvis were noted.

Despite the recommendation for ascites fluid paracentesis, she did not consent. The patient's BS gradually decreased from the second day, and metabolic acidosis responded to the treatment. On the third day of hospitalization, the abdominal pain decreased, and the abdomen was mildly tender in the epigastric region, distended with shifting dullness, and without rigidity and guarding. Her appetite for food and liquids returned, and the liquid diet was started.

On the fourth day of hospitalization, the patient's triglyceride levels decreased to less than 500 mg/dL. As a result, after 4 hours of changing the subcutaneous insulin, the insulin infusion was stopped, and the gemfibrozil capsule 600 mg twice a day was started. The patient's abdominal distention gradually decreased, and she was able to tolerate a solid diet. Consequently, she was transferred to the internal disease ward. By the sixth day, all symptoms had been alleviated, and insulin doses were optimized, leading to the patient's discharge with a prescription for gemfibrozil 600 mg twice a day, subcutaneous pen insulin glargine, and aspart, and dietary recommendations. During the 2-month follow-up, the patient did not experience any gastrointestinal symptoms, and her triglyceride tests were within normal limits. Due to low sugar levels, insulin aspart was stopped, and the dose of insulin glargine was reduced. Figure 2 illustrates the clinical course of the patient from diagnosis to discharge.

Discussion

Epigastric pain is a common complaint among patients referred to medical centers. Various conditions, including myocardial infarction, pancreatitis, gastroesophageal reflux disease, peptic ulcer disease, gastritis, duodenal ulcer disease, and stomach cancer, can cause it. A less noticeable cause of abdominal pain is diabetic ketoacidosis (DKA), making it challenging to differentiate from conditions like acute pancreatitis.[12,13] In the patient described, a normal ECG, the absence of severe rigidity and guarding of the abdomen, lack of response to antacid drugs, spreading pain to the back, partial improvement of symptoms in the sitting position, an increase in serum amylase and lipase, as well as imaging findings, all contribute to the diagnosis of acute pancreatitis along with DKA.[14] The distinguishing factor in this patient's case, compared to other studies, is the lack of a history of hypertriglyceridemia and diabetes diagnosed after pregnancy.

Elevated HbA1C in diabetic patients is associated with numerous complications. Therefore, prioritizing diabetes management in these patients is essential to mitigate the risk of severe complications.[15] The HbA1C level in our case was 12.3%, which should normally be below 5.6%,[16] indicates previously undiagnosed diabetes mellitus, with the absence of any symptoms prompting the patient to seek medical attention in the last year. Another specification of our case is the co-occurrence of acute pancreatitis, DKA, and hypertriglyceridemia, which is an uncommon finding observed in only 4% of cases.[17]

During diabetic ketoacidosis (DKA), the lack of insulin causes the breakdown of fat in adipose tissue, leading to

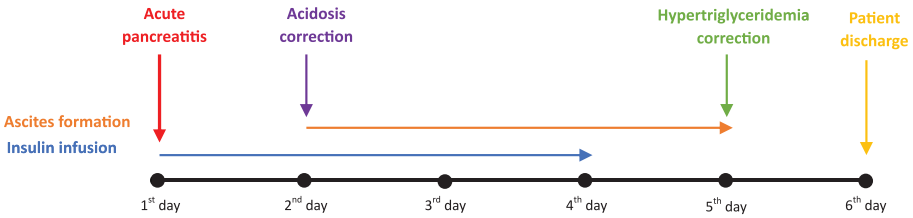

Figure 2. Time course of the patient's clinical events from the onset of symptoms to hospital discharge.

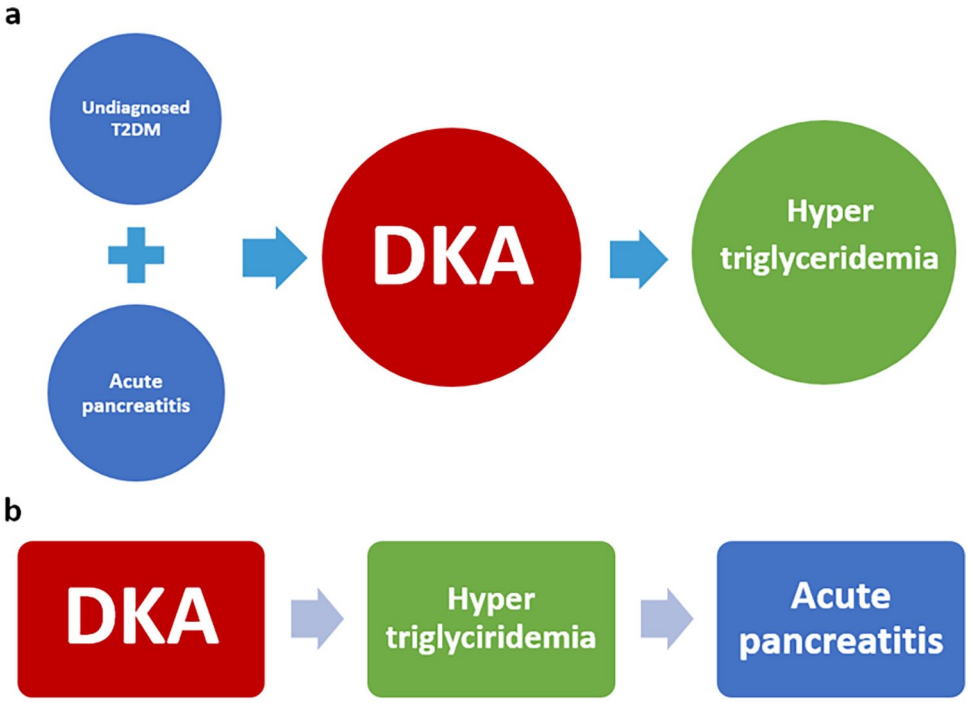

Figure 3. The process of patient's conditions. (a) represents the first theory, and (b) represents the second theory.

increased levels of free fatty acids (FFA). This, in turn, speeds up the production of very low-density lipoprotein (VLDL) in the liver. Furthermore, reduced lipoprotein lipase (LPL) activity in peripheral tissues decreases the removal of VLDL from the blood, resulting in hypertriglyceridemia. According to Endocrine Society guidelines, hypertriglyceridemia is categorized as follows: normal is less than 150 mg/dL, mild is between 150 and 199 mg/dL, moderate is between 200 and 999 mg/dL, severe is between 1000 and 1999 mg/dL, and very severe exceeds 2000 mg/dL.[18] While moderate hypertriglyceridemia is common during DKA, very severe hypertriglyceridemia is uncommon.[3]

Hypertriglyceridemia can, in rare cases, lead to acute pancreatitis, with a prevalence of about 7%.[19,20] Acute pancreatitis occurring in the presence of hypertriglyceridemia typically manifests when triglyceride (TG) levels exceed 1000 mg/dL.[19] A study by Baranyai et al. examined patients with acute pancreatitis caused by hypertriglyceridemia. The study found that 54.5% of cases had amylase levels elevated to 3 times the normal range, while 58.8% had lipase levels that also reached 3 times the normal range. In our case, however, the amylase and lipase levels are within the range of 40% to 46%, and despite the significant imaging findings, the levels of both amylase and lipase did not increase as expected.[21]

A study conducted by Samanta et al. revealed that 38.5% of patients with acute pancreatitis developed ascites. The study indicated that these patients generally exhibited a poorer prognosis, with a higher incidence of organ failure and mortality. However, in our patient's case, despite the presence of ascites, the efficient treatment led to the resolution of the condition and prevented the failure of other organs.[22]

In our case, two hypotheses are being considered for the patient's condition (Figure 3). According to the first hypothesis, the patient's high HbA1C indicates poorly controlled diabetes, which, along with abrupt acute pancreatitis, may have triggered the development of DKA, followed by very severe hypertriglyceridemia. In the case presented by Hahn et al., a patient diagnosed with type 1 diabetes mellitus stopped using insulin and was subsequently admitted to the hospital. During the admission, the patient was found to have severe hypertriglyceridemia, similar to the situation in our case. However, in our case, the patient had only a history of gestational diabetes mellitus

(GDM) prior to the development of these conditions.[3] The second hypothesis indicates that DKA occurred first, leading to very severe hypertriglyceridemia, which subsequently caused acute pancreatitis, a situation that has been observed and documented in other cases as well (Figure 3).[23,24] In the case reported by Narala et al., the patient not only experienced hypertriglyceridemia but also consumed a significant amount of beer prior to admission. Sadly, the patient's condition was fatal in this case, but in our case, the patient was discharged in good health.

The first theory is considered more likely, as DKA in the setting of T2DM needs to be triggered by an acute condition such as pancreatitis. Also, the patient had either no personal or familial history of hypertriglyceridemia to explain this level of TG, so it seemed that a condition had caused it, like the occurrence of DKA. In our patient, when considering the first theory, the cause of acute pancreatitis may be classified as idiopathic, affecting 25% to 30% of patients with the condition. Following a thorough review of the patient's history, laboratory tests, and a gallbladder ultrasound, no evident cause can be determined.[25]

Conclusions

Abdominal pain can present numerous differential diagnoses. Two critical conditions that require immediate attention are Diabetic Ketoacidosis (DKA) and acute pancreatitis, both of which should be addressed promptly. Hypertriglyceridemia, a potential consequence of DKA and an implicated etiology of acute pancreatitis, may often be overlooked. It is advisable to conduct triglyceride level assessments in such cases to avert further complications.

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the patient to publish this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Consent for publication

Written informed consent was obtained from the patient to publish this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author contributions

AM Visited the patient in the ICU and drafted and revised the manuscript, SG drafted the manuscript.

Acknowledgements

Not applicable.

Availability of data and materials

The data used during the current case are available from the corresponding author upon reasonable request.

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