Acute Necrotizing Pancreatitis Caused by Transient Hypertriglyceridemia in a Patient With DKA and Normal Serum Amylase and Lipase

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Abstract
We report a case of diabetic ketoacidosis (DKA), severe hypertriglyceridemia (HTG), and acute necrotizing pancreatitis in a previously healthy male who presented with epigastric pain. Transient HTG triggered by DKA was the likely cause of his acute pancreatitis (AP). On admission, his serum pancreatic enzymes were within normal limits. He was treated successfully with intravenous insulin therapy and volume resuscitation. This triad of DKA, HTG, and AP has rarely been reported in the literature, but not with normal enzyme levels. Persistent epigastric pain in a patient with DKA and severe HTG should warrant the consideration of AP, even if the pancreatic enzymes are within normal limits.

Keywords
acute pancreatitis, diabetic ketoacidosis, hypertriglyceridemia, normal serum amylase and lipase

Introduction
Acute hypertriglyceridemia (HTG) has been described as a complication of diabetic ketoacidosis (DKA). Severe HTG, defined by The Endocrine Society as serum triglyceride (TG) levels above 11.3 mmol/L, is an uncommon cause of acute pancreatitis (AP). Normal serum amylase and lipase in AP is rare, but has been reported in HTG-induced AP.

Case Report
A 31-year-old male presented to the emergency department on August 13, 2021 with 3 days of severe epigastric pain and exertional dyspnea. He also reported symptoms of polyuria and polydipsia over the past one and a half months. He had no past medical history and was a non-drinker. A screening lipid panel performed 1 year ago by his primary care practitioner was normal.

Upon presentation, the vital signs were temperature 36.7°C, blood pressure 145/87 mmHg, pulse rate 140 beats per minute, respiratory rate 20 breaths per minute, and oxygen saturation 98% on room air. He was alert, but dehydrated. There were no xanthelasmata or eruptive xanthomas. His abdomen was soft with epigastric tenderness. There was no guarding or rebound tenderness. Bowel sounds were normoactive. Grey-Turner’s, Cullen’s, and Fox’s signs were negative.

His relevant serum biochemistry profiles were as follows: urea 3.5 mmol/L, sodium 127 mmol/L, potassium 4.3 mmol/L, chloride 96 mmol/L, glucose 26.1 mmol/L, creatinine 55 μmol/L, albumin 42 g/L, bilirubin 6.2 μmol/L, AST 14 IU/L, ALT 38 IU/L, ALP 101 IU/L, amylase 12 U/L (13–53 U/L), lipase 59 U/L (10–60 U/L), and CRP 379.8 mg/L. His full blood count showed hemoglobin of 16.5 g/dL, total white count of 20,700 cells/μL with 87.8% neutrophils and platelet count of 307,000 cells/μL. Coagulation profiles were normal.

His venous blood gas result revealed a metabolic acidosis: pH 7.221, pCO2 25.3 mmHg, pO2 < 40 mmHg, and bicarbonate 10.1 mmol/L. Urine ketones were 4+. His venous blood gas result revealed a metabolic acidosis: pH 7.221, pCO2 25.3 mmHg, pO2 < 40 mmHg, and bicarbonate 10.1 mmol/L. Total white count of 20,700 cells/μL with 87.8% neutrophils and platelet count of 307,000 cells/μL. Coagulation profiles were normal.

Following his admission, the laboratory notified the inpatient team that his serum was turbid and lipemic (Figure 1).

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Lipid panel was performed which yielded the following results: TG 20.76 mmol/L (<2.2 mmol/L), total cholesterol 11.57 mmol/L (<5.2 mmol/L), measured low density lipoprotein cholesterol 1.78 mmol/L (<3.3 mmol/L), and high density lipoprotein cholesterol 0.57 mmol/L (1.0–1.6 mmol/L).

Since severe HTG is known to cause pseudohyponatremia, the laboratory was consulted about this possibility. They clarified that the hyponatremia was “true,” since they employ the direct ion-selective electrode potentiometry (DSE) method to measure sodium.

Computed tomography (CT) imaging of the abdomen was performed on admission, in view of severe epigastric pain. This revealed evidence of AP with areas of necrosis involving the pancreatic tail despite normal serum amylase and lipase levels. There was peripancreatic and retroperitoneal fluid, without overt loculation. This was suggestive of grade D AP according to the Balthazar CT severity index (Figure 2).

He was admitted to the high dependency unit and administered normal saline and intravenous insulin. His hemoglobin A1c was 11.3%. Anti-glutamic acid decarboxylase antibodies and anti-islet cell antibodies were negative. The pancreatic enzymes were repeated 2 days later and were still normal.

On the third day of admission, he was commenced on an oral diet, together with a subcutaneous insulin regimen and fenofibrate. His serum amylase and lipase were repeated on day four; both remained within normal limits. He was discharged without complications on day six.

Discussion

The prevalence of AP among DKA patients is low; estimates range from 2% to 11%.2,3 HTG has been postulated as a trigger for AP in DKA patients.

Even in the absence of AP, non-specific elevations of amylase and lipase may be observed in up to 25% of DKA cases, although the exact mechanisms are not known.4 Several mechanisms have been proposed which include leakage from pancreatic acini and release of salivary amylase.5,6

HTG-induced AP in DKA patients was first described in 1997 by Nair et al. as an “enigmatic triangle,” where the authors highlighted the complex relationship between these three entities.7 HTG during DKA has been attributed to the insulinopenic state, causing a release of free fatty acids from adipocytes and enhanced very-low-density-lipoprotein production.3,7 Although the exact mechanism by which HTG causes AP is not known, it is believed that the release of free fatty acids within pancreatic capillaries leads to trypsinogen activation and pancreatic damage.5,9 Also, increased plasma viscosity from the high lipid levels may cause ischemia of the pancreas.

Conversely, AP induced by HTG can cause acute beta cell dysfunction, leading to the insulinopenic state, which can trigger DKA.10 In our patient, we believe that the DKA caused his HTG, since his recent lipid panel was normal.

Elevated amylase and lipase levels are the hallmark of AP. However, normal levels have been reported in HTG-induced AP and guidelines on AP do recognize this phenomenon.11,12 The exact mechanism has not been clearly elucidated. It has been proposed that in-vitro interference with assays of amylase activity by elevated TG levels might be responsible.13

Pseudohyponatremia has been known to occur in cases of severe hyperlipidemia or hyperproteinemias in laboratories which employ the indirect ion-selective electrode potentiometry method to measure serum sodium.14 This is attributed to displacement of serum water by elevated concentrations of serum lipids or proteins leading to an artefactual error. Even in these cases, significant pseudohyponatremia is not observed until serum TG is greater than 16.9 mmol/l.15

This error is not seen when DSE is used to measure serum sodium. With increasingly widespread adoption of DSE in modern hospital laboratories, pseudohyponatremia should no longer be a cause of confusion.
**Conclusion**

The triad of DKA, HTG, and AP is an uncommon event. Even if pancreatic enzymes are normal, persistent epigastric pain in a patient presenting with DKA should warrant consideration of a CT scan. The diagnosis of pseudohyponatremia should no longer be considered in laboratories using DSE potentiometry.

**Author Contributions**

HSC and WHHH collected data and drafted the manuscript. VP revised the manuscript.

**Data Availability**

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

**Declaration of Conflicting Interests**

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

**Funding**

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

**Ethical Approval**

Our institution does not require ethical approval for reporting individual cases.

**Informed Consent**

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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