


A Rare Triad: Hypercalcemia-Induced Necrotizing Pancreatitis Presenting as Severe Diabetic Ketoacidosis

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Abstract

Primary hyperparathyroidism (PHPT) typically occurs in persons above 45 years, with a female predominance. PHPT induces a state of hypercalcemia, but acute pancreatitis is a rare sequelae of this hypercalcemia. We report a case of a 31-year-old man with no known medical history who presented in diabetic ketoacidosis with electrolyte abnormalities. His clinical course progressed to multi-organ dysfunction despite correction of metabolic derangements. Further workup led to the discovery of the uncommon triad by which previously undiagnosed PHPT precipitated severe diabetic ketoacidosis.

Keywords

acute pancreatitis, hypercalcemia, primary hyperparathyroidism, diabetic ketoacidosis

Introduction

Health care expenditure for diabetic ketoacidosis (DKA) exceeds US\$1 billion each year.^{1,2} Acute pancreatitis (AP) can be an underlying cause or a differential diagnosis of DKA. If DKA delays the detection of other medical conditions, such as AP, this can increase morbidity, length of hospital stay, and cost of hospitalizations. This case presentation highlights primary hyperparathyroidism (PHPT) as an unusual etiology of both DKA and AP, along with the importance of searching for a unifying diagnosis when symptoms persist despite correction of metabolic derangements.

Case Presentation

A 31-year-old man with no known medical history was brought to the emergency room by his sister for lethargy. History was obtained from his sister due to the patient's altered mental status. He was not known to be on any medications and there was no known history of recreational drug or alcohol use. He was confused that morning after complaining of increased thirst and urination earlier in the week. His sister was unable to provide further details on his symptoms.

On presentation, the patient was tachycardic and tachypneic, with other vital signs within normal limits. Physical examination was significant for a lethargic and dehydrated appearance, with diffuse tenderness on palpation of the abdomen. Laboratory workup revealed glucose of 1310 mg/dL, anion gap of 31 mmol/L, bicarbonate of 7 mmol/L, blood urea nitrogen of 28 mg/dL, creatinine of 1.8 mg/dL,

calcium of 14.0 mg/dL, phosphate of <1.0 mg/dL, potassium of 3.6 mEq/L, and β -hydroxybutyrate of >9 mmol/L. Continuous insulin infusion and intravenous fluids were started. However, he developed hypotension, worsening tachycardia, and became obtunded requiring intubation. He was transferred to the intensive care unit.

Hemodynamics improved, but he was noted to have persistent abdominal tenderness and an episode of emesis after extubation. Further investigations were done, revealing lipase 1302 U/L and amylase 708 U/L. Computed tomography scan of the abdomen revealed evidence of AP with extensive necrosis (Figure 1). He clinically improved with medical management of AP, but hypercalcemia persisted on serial laboratory tests despite aggressive intravenous fluid resuscitation. Further workup revealed elevated parathyroid hormone of 260.7 pg/mL and urinary calcium of 399 mg/24 h. A Tc-99m labeled sestamibi scan was unremarkable. He was started on cinacalcet for hypercalcemia and discharged home. He was started on cinacalcet for hypercalcemia and discharged home with outpatient follow-up with endocrinology.

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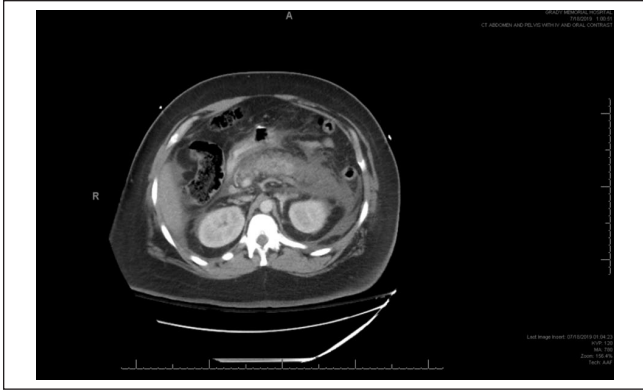


Figure 1. Computed tomography imaging showing enlarged, edematous pancreas with decreased enhancement of the pancreatic tail and significant surrounding inflammatory change.

Discussion

About one third of DKA presentations occur in persons without a medical history of diabetes mellitus (DM).¹³ These patients may either have newly diagnosed diabetes mellitus or a differential diagnosis such as AP, gastroenteritis, starvation ketosis, or use of medications such as corticosteroids or antipsychotics.³ In the patients with AP who present with DKA, the diagnosis of AP can be hidden as 19% to 46% of patients with DKA have abdominal pain.⁴⁻⁶ This was seen in our patient whose electrolyte derangements and abdominal pain initially masked his diagnosis of AP.

Serum lipase and amylase levels are not considered standard initial investigations in patients with DKA. Elevation of serum lipase and amylase may also be a nonspecific occurrence in 24.7% to 79.0% of patients with DKA.⁷ However, this case highlights the benefits of ordering serum lipase and amylase early in patients with DKA, and a possible need for including these tests in standardized management guidelines. In patients being managed for AP, the presence of other comorbidities including DKA can further raise mortality to as high as 80%.⁸ When AP and DKA coexist, more aggressive volume resuscitation is generally needed, which was administered in this case.⁶

Approximately 80% to 90% of cases of AP are caused by cholelithiasis or alcohol use, which were absent in our patient.⁹ There was also no known history of causes such as illicit drug use, recent infection, abdominal trauma, abnormalities of the pancreatic anatomy, autoimmune disorder, or medication use.¹⁰ It has been estimated that hypertriglyceridemia accounts for 36% in AP with DKA.^{11,12} A previous triad of hypertriglyceridemia-induced AP with DKA was described in 1997.¹³ In our case, the patient had a normal lipid panel. His initial laboratory test results were significant for hypercalcemia and hypophosphatemia, and additional laboratory test results revealed PHPT. Hypocalcemia is the expected feature in AP and constitutes one for scoring criteria for grading severity of AP.¹⁴ Therefore, PHPT may be

suspected when a patient presenting with a flare of pancreatitis has paradoxical hypercalcemia.

A state of hypercalcemia in patients with PHPT may lead to AP, but this is infrequent with an estimated prevalence of 1.5% to 13%.¹⁵ The sex distribution of AP in PHPT shows a male preponderance with a ratio of 2:1,¹⁶ in contrast to the female preponderance seen in PHPT without associated pancreatic disease.⁹ Most cases of AP associated with PHPT present as a life-threatening illness.¹⁷ The pathogenesis of hypercalcemia-mediated pancreatic injury is still unclear, but various mechanisms have been proposed including the following: (1) hypercalcemia causing a de novo activation of trypsinogen to trypsin, which triggers an inflammatory cascade resulting in autodigestion, edema, and necrosis of the pancreas¹⁸; (2) hypercalcemia can precipitate formation of pancreatic calculi, leading to pancreatic duct obstruction. This obstruction can modify pancreatic secretions and subsequently cause recurrent bouts of pancreatitis.¹⁹ (3) Certain genetic risk factors can predispose patients with PHPT to AP.²⁰

Our case highlights a rare triad of hypercalcemia-induced pancreatitis leading to DKA. Clinicians should be aware of hypercalcemia-induced AP in DKA patients with persistent abdominal pain despite euglycemia. This case presentation also highlights PHPT in a young man, as an unusual etiology of the hypercalcemia leading to both DKA and AP. PHPT should be suspected when a patient with acute pancreatitis has hypercalcemia on initial laboratory workup, instead of the characteristic hypocalcemia.

Declaration of Conflicting Interests

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Ethics Approval

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

Informed Consent

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

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References

- Maldonado MR, Chong ER, Oehl MA, Balasubramanyam A. Economic impact of diabetic ketoacidosis in a multiethnic indigent population: analysis of costs based on the precipitating cause. *Diabetes Care*. 2003;26:1265-1269.

2. Kitabchi AE, Umpierrez GE, Murphy MB, et al. Management of hyperglycemic crises in patients with diabetes. *Diabetes Care*. 2001;24:131-153.
3. Westerberg DP. Diabetic ketoacidosis: evaluation and treatment. *Am Fam Physician*. 2013;87:337-346.
4. Singla AA, Ting F, Singla A. Acute pancreatitis secondary to diabetic ketoacidosis induced hypertriglyceridemia in a young adult with undiagnosed type 2 diabetes. *JOP*. 2015;16:201-204.
5. Umpierrez G, Freire AX. Abdominal pain in patients with hyperglycemic crises. *J Crit Care*. 2002;17:63-67.
6. Wang Y, Attar BM, Bedrose S, et al. Diabetic ketoacidosis with hypertriglyceridemia-induced acute pancreatitis as first presentation of diabetes mellitus: report of three cases. *AAACE Clin Case Rep*. 2017;3:e195-e199.
7. Pak S, Cha D, Jazayeri-Moghaddas O, et al. Diabetic ketoacidosis with acute necrotizing pancreatitis as first presentation in latent autoimmune diabetes in adult. *J Med Cases*. 2017;8:356-358.
8. Nielsen OS, Simonsen E. A case of transient diabetes mellitus in connection with acute pancreatitis. *Acta Med Scand*. 1969;185:459-461.
9. Valenzuela JE, Segura EB, Torres AS, Alvarez FC. Acute pancreatitis associated with hypercalcemia. A report of two cases [in Spanish]. *Rev Esp Enferm Dig*. 2009;101:65-69.
10. Whitcomb DC, Yadav D, Adam S, et al; North American Pancreatic Study Group. Multicenter approach to recurrent acute and chronic pancreatitis in the United States: the North American Pancreatitis Study 2 (NAPS2). *Pancreatol*. 2008;8:520-531.
11. Nair S, Yadav D, Pitchumoni CS. Association of diabetic ketoacidosis and acute pancreatitis: observations in 100 consecutive episodes of DKA. *Am J Gastroenterol*. 2000;95:2795-2800.
12. Seth A, Rajpal S, Saigal T, et al. Diabetic ketoacidosis-induced hypertriglyceridemic acute pancreatitis treated with plasmapheresis—recipe for biochemical disaster management. *Clin Med Insights Gastroenterol*. 2014;7:51-53.
13. Nair S, Pitchumoni CS. Diabetic ketoacidosis, hyperlipidemia, and acute pancreatitis: the enigmatic triangle. *Am J Gastroenterol*. 1997;92:1560-1561.
14. Dias C, Carreira LM. Serum ionised calcium as a prognostic risk factor in the clinical course of pancreatitis in cats. *J Feline Med Surg*. 2015;17:984-990.
15. Koppelberg T, Bartsch D, Printz H, Hasse C, Rothmund M. Pancreatitis in primary hyperparathyroidism (pHPT) is a complication of advanced pHPT [in German]. *Dtsch Med Wochenschr*. 1994;119:719-724.
16. Carnaille B, Oudar C, Pattou F, Combemale F, Rocha J, Proye C. Pancreatitis and primary hyperparathyroidism: forty cases. *Aust N Z J Surg*. 1998;68:117-119.
17. Prinz RA, Aranha GV. The association of primary hyperparathyroidism and pancreatitis. *Am Surg*. 1985;51:325-329.
18. Haverback BJ, Dyce B, Bundy H, Edmondson HA. Trypsin, trypsinogen and trypsin inhibitor in human pancreatic juice: mechanism for pancreatitis associated with hyperparathyroidism. *Am J Med*. 1960;29:424-433.
19. Cope O, Culver PJ, Mixter CG Jr, Nardi GL. Pancreatitis, a diagnostic clue to hyperparathyroidism. *Ann Surg*. 1957;145:857-863.
20. Felderbauer P, Karakas E, Fendrich V, et al. Pancreatitis risk in primary hyperparathyroidism: relation to mutations in the SPINK1: trypsin inhibitor (N34S) and the cystic fibrosis gene. *Am J Gastroenterol*. 2008;103:368-374.