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Diabetic Ketoacidosis in Chronic Kidney Disease Masquerading as Acute Pancreatitis

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Abstract:

Diabetic ketoacidosis (DKA) is a life threatening acute complication of type 1 diabetes. Since diabetic patients may have hypertriglyceridemia, they are at risk of developing acute pancreatitis (AP). Hyperamylasemia may suggest a diagnosis of AP, but levels may be elevated in DKA. Hence, serum lipase levels correlate better with the diagnosis of AP. However, pancreatic enzymes are excreted by the kidneys and their levels are elevated in patients with chronic kidney disease (CKD). This report describes a patient with type 1 diabetes and CKD stage 4, not on hemodialysis, who presented with DKA and had very high levels of pancreatic enzymes in the absence of pancreatitis.

Key words: Diabetes Ketoacidosis, Kidney, Renal Insufficiency, Pancreatitis, Hypertriglyceridemia.

Introduction

Acute pancreatitis (AP) is an acute inflammatory disorder of the pancreas. In 10-15% cases, the condition is life threatening. Epigastric pain is the predominant symptom, which may radiate to the back, chest, flanks or lower abdomen. Serum amylase and lipase levels are elevated in AP. Abdominal contrast enhanced computed tomography (CT), abdominal ultrasound, magnetic resonance imaging (MRI) are radiological methods which aid in diagnosis of AP [1]. However, elevated pancreatic enzyme levels have been noted in CKD patients [2,3]. Features like epigastric pain and elevated pancreatic enzymes are also seen in DKA [4]. Moreover, AP can present or coexist with DKA [5,6].

This case report aims to highlight the importance of elevated pancreatic enzymes in DKA and CKD, and the diagnostic dilemma posed by such elevations in patients with these two illnesses.

Case Report

A 27 year old lady, a known type 1 diabetic, hypertensive and CKD stage 4, presented to emergency department at night with 6-8 episodes of non-bloody, non-projectile, non-bilious vomiting since morning, associated with mild epigastric discomfort. She had history of low grade fever and mild burning micturition since 2 days and history of skipping her insulin for past 2 days.

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She was on nifidipine retard 20 mg twice daily, iron and calcium supplements. On admission, the patient was conscious, oriented with 42 kg weight and height of 150 cms. Her heart rate was 120/ min, blood pressure 100/60 mmHg (right arm supine position), respiratory rate of 28/min and temperature of 100^0F. Physical examination revealed dehydration, mild tenderness in the epigastrium with normal bowel sounds. There was no palpable mass or skin discoloration. Other systemic examinations were normal.

Initial laboratory investigations showed anemia (Hb 9.6 g/dL) with normal leucocyte and platelet counts. Peripheral smear showed microcytic hypochromic red cells. Her urea was 114 mg/dL, creatinine 3.88 mg/dL, sodium 137 mEq/L, potassium 4.1 mEq/L and bicarbonate 10 mEq/L. Her blood glucose was 500 mg/dL and urinary ketones were positive. Her total cholesterol was 327 mg/dL with triglycerides 126, LDL 192, VLDL 25 and HDL 94 mg/dL. Serum calcium, liver functions and prothrombin time values were within normal range. Although urine microscopy showed pus cells, culture was sterile. Chest X-ray and ECG were normal. Arterial blood gas analysis revealed pH 7.1, pCO_2 13 mmHg, HCO_3 9 mEq/L. She was managed on the lines of DKA with intravenous. fluids and insulin infusion and injection ceftriaxone for urinary tract infection.

On day 2, her heart rate, BP and respiratory rate normalized and she was afebrile. However, in view of her persistent abdominal discomfort, possibility of AP was considered and serum amylase and lipase levels were checked which came as 388 U/L and 6603 U/L respectively. Her ultrasound abdomen revealed presence of fatty liver. A plain CT abdomen was taken, as the patient is a known CKD, which was normal. She was kept nil per oral on days 2, 3 and 4. Her abdominal symptoms started to improve during these days. On day 5, she was started on light oral diet and remained asymptomatic. Her fasting blood sugar was 150 mg/dL with normal electrolytes and improving renal parameters (urea 50 mg/dL and creatinine 2.4 mg/dL). She continued to be asymptomatic with normal vitals during her remaining hospital stay. On day 10, prior to her discharge, the repeated levels of amylase and lipase were 368 U/L and 2941 U/L respectively.

Discussion

The inflammatory process of AP is caused by an intracellular activation of digestive enzymes. Gallstones, alcoholism and hypertriglyceridemia are some of the common causes of AP. According to 1992 Atlanta Symposium, AP is best defined clinically by a patient presenting with two of the following criteria : a) symptoms such as epigastric pain, consistent with the disease; b) a serum amylase or lipase greater than 3 times the upper limit of normal; or c) radiological imaging consistent with diagnosis, usually using CT or MRI. In 85-90% of patients, the condition is self-limiting and subsides within 4-7 days. The management of these patients is supportive, with therapy aimed at reducing pancreatic enzyme secretion, fluid resuscitation, electrolyte replacement and analgesics.

In selected circumstances endoscopic retrograde cholangiopancreatography (ERCP), antibiotics and surgical drainage are required. The Ranson scoring system is used to assess the severity of AP. The scoring system uses a series of 11 prognostic signs, where three or more criteria indicate severe AP [7]. The Balthazar score assesses the severity of pancreatitis based on abdominal CT appearance of the pancreas [8].

In AP, the serum amylase levels increase within 2-3 hours, peaks at 12-24 hours, and returns to normal after 3-5 days [9]. Pancreatic pseudocyst should be suspected if the levels remain elevated after 5 days. In order to distinguish AP from non-pancreatic hyperamylasaemia, isoenzyme determination of pancreatic (P-type) amylase and non-pancreatic (S-type) amylase is used [10]. The serum lipase levels rise within 4-8 hours, peak at 24 hours and remain elevated for 10-14 days [11]. Since the pancreas is the only source of lipase, estimation of serum lipase are specific for pancreatic injury.

Chronic kidney disease (CKD) reflects a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate. Pancreatic enzymes are rapidly excreted by the kidneys, hence the patients with CKD have elevated levels of amylase and lipase. These levels rarely show more than threefold rise [2,3]. Furthermore, the serum lipase levels increase with hemodialysis, probably due to the lipolytic effect of heparin used during the procedure [12].

DKA, an acute complications of diabetes, was formerly considered a hallmark of type 1 diabetes. Nausea and vomiting are often prominent with abdominal pain, which may be severe and can resemble AP. Patients are dehydrated and can have Kussumaul's breathing. Inadequate insulin administrations and infections like pneumonia, urinary tract infection, gastroenteritis are some of the common precipitating events. DKA is characterized by hyperglycemia (250-600 mg/dL), ketosis and metabolic acidosis along with a number of secondary metabolic abnormalities. Pancreatic enzymes are elevated in DKA, but the source remains unclear. Pancreatic acinar cells may undergo subtle injury and thereby liberating pancreatic enzymes into the circulation. Another possibility is an extrapancreatic origin, like salivary glands, which are triggered by the dysmetabolic state [12]. Increase in lipase may be due to non-pancreatic lipolytic enzymes from sources like stomach, small bowel, liver, tongue and oesophagus [13].

As mentioned earlier, AP may predispose or coexist with DKA. AP can induce hyperglycemia and ketosis in a diabetic patient and thereby cause DKA [14,15]. In DKA, there is activation of lipolysis in adipose tissue due to insulin deficiency, thereby releasing free fatty acid (FFA) and accelerating the formation of VLDL. In addition, there is decreased removal of VLDL from the plasma due to reduced activity of lipoprotein lipase in peripheral tissue. These two mechanisms can result in hypertriglyceridemia which in turn generates cytotoxic FFA in pancreatic circulation leading to AP [16,17].

A prompt diagnosis of AP is important in a patient presenting with DKA. Firstly, the severity of ketoacidosis can be aggravated by AP, by worsening intravascular volume depletion, thus requiring more aggressive fluid replacement. Secondly, the glucose homoestasis can be altered by AP, thus making hyperglycemic control more difficult. Thirdly, once the ketoacidosis is under control, oral diet may be initiated in DKA, which can be detrimental in AP. Moreover, epigastric pain, like in AP, may be experienced by a patient with DKA which can be the result of gastritis or hepatomegaly. Therefore, AP should be considered in a DKA patient with severe abdominal pain which fails to resolve following correction of fluid volume and acidosis.

Abdominal ultrasound is an ideal initial imaging tool for the diagnosis of AP. Pancreatic enlargement and hypoechogenicity can be picked up on ultrasound [18]. Abdominal CT with contrast is considered the gold standard

for diagnosing pancreatic necrosis and peri-pancreatic collections.

Conclusion

CKD patients have elevated serum levels of amylase and lipase, due to their poor excretion. DKA shares features of AP in terms of epigastric pain, acidosis and elevated pancreatic enzyme levels. Moreover, AP can coexist or predispose to DKA. Hence, when a CKD patient with type 1 diabetes presents with DKA, an elevated amylase and lipase levels may mislead to the diagnosis of AP. In such a situation, imaging should be relied upon to arrive at a correct diagnosis.

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