

CASE REPORT

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Acute Pancreatitis Complicated with Diabetic Ketoacidosis in a Young Adult without Hypertriglyceridemia: A Case Report

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Systemic complications related to acute pancreatitis include acute respiratory distress syndrome, multiple organ dysfunction syndrome, disseminated intravascular coagulation, hypocalcemia, hyperglycemia, and insulin dependent diabetes or diabetic ketoacidosis. In practice, the development of diabetic ketoacidosis induced by acute pancreatitis is rare and generally associated with hypertriglyceridemia. However, herein we report a case of a 34-year-old female without hypertriglyceridemia, who was diagnosed with acute pancreatitis complicated with diabetic ketoacidosis. The patient was admitted with complaints of febrile sensation, back pain, and abdominal pain around the epigastric area. Levels of serum amylase and lipase were elevated to 663 U/L and 3,232 U/L. Contrast-enhanced abdominal CT showed pancreatic swelling, peri-pancreatic fat infiltration and fluid collection. The patient was initially diagnosed with simple acute pancreatitis. Though the symptoms were rapidly relieved after initiation of treatment, severe hyperglycemia (575 mg/dL), severe metabolic acidosis (pH 6.9), and ketonuria developed at four days after hospitalization. However, serum triglyceride levels remained within the normal range (134 mg/dL). Finally, the patient was diagnosed with acute pancreatitis complicated with diabetic ketoacidosis unrelated to hypertriglyceridemia. She recovered through insulin and fluid therapy, and receives insulin therapy at the outpatient clinic. (*Korean J Gastroenterol* 2016;68:274-278)

Key Words: Pancreatitis; Diabetic ketoacidosis; Hypertriglyceridemia

INTRODUCTION

Acute pancreatitis, an inflammatory response of the pancreas to factors like gallstones, alcohol or hypertriglyceridemia, can produce a spectrum of locoregional or systemic complications. Locoregional complications include necrosis, abscess, pseudocyst, and ascites, while systemic complications include acute respiratory distress syndrome, multiple

organ dysfunction syndrome, disseminated intravascular coagulation, gastrointestinal hemorrhage, hyperglycemia, hypocalcemia, hypertriglyceridemia, and insulin dependent diabetes or diabetic ketoacidosis.^{1,2}

In clinical practice, the development of diabetic ketoacidosis secondary to acute pancreatitis is rare. Case reports and clinical studies often note an association of diabetic ketoacidosis induced by acute pancreatitis with hypertrigly-

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ceridemia.^{3,4} In a patient without hypertriglyceridemia, the development of acute pancreatitis complicated by diabetic ketoacidosis is unusual.⁵

Herein, we report the case of a 34-year-old female diagnosed with diabetic ketoacidosis secondary to acute pancreatitis, unrelated to hypertriglyceridemia.

CASE REPORT

A 34-year-old female visited the emergency department with complaints of febrile sensation, lower back pain, and abdominal pain around the epigastric area for four days. Her symptoms worsened for another two days after the onset of the initial symptoms. The patient took over-the-counter drugs and received treatment at a local clinic, but the symptoms were not relieved. The patient had no underlying diseases such as diabetes and hypertension. Her family history was unremarkable. She was a full-time housewife. She had one-pack year history of smoking and consumed 24 g of alcohol per month (two bottles of beer). There was no history of medication except analgesics.

On physical examination, an acute ill appearance, alert mental status, and direct tenderness at epigastric area and left costovertebral angle were noted. The initial vital signs were blood pressure 120/80 mmHg, heart rate 90 beats/min, respiration rate 20 breaths/min, and body temperature 37.1°C. The patient's body weight was 51 kg, and height was 1.53 m (BMI, 21.8 kg/m²). The initial laboratory evaluation of peripheral blood revealed white blood cell (WBC) 6,400 cells/ μ L (poly, 73.4%), hemoglobin 14.4 g/dL (hematocrit, 43.2%), platelet 2.91×10^5 cells/ μ L, prothrombin time 11.5 sec, aspartate aminotransferase 71 U/L, alanine aminotransferase 44 U/L, gamma glutamyl transpeptidase 68

IU/L, alkaline phosphatase 77 IU/L, lactate dehydrogenase 541 IU/L, total bilirubin 0.3 mg/dL, direct bilirubin 0.1 mg/dL, total protein 7.6 g/dL, albumin 4.1 g/dL, amylase 663 U/L, lipase 3,232 U/L, blood urea nitrogen 8.9 mg/dL, creatinine 0.68 mg/dL, glucose 95 mg/dL, calcium 10.5 mg/dL, total cholesterol 199 mg/dL, HDL-cholesterol 35 mg/dL, and triglyceride 142 mg/dL. The high sensitivity-C reactive protein, an acute phase reactant, was increased to 11.63 mg/L. Erythrocyte sedimentation rate was also elevated to 36 mm/hr. The urinary analysis revealed no glycosuria or proteinuria. Viral markers on hepatitis A, B and C were all negative. Anti-nuclear antibody, anti-mitochondrial antibody and rheumatoid factor were negative. In addition, serum immunoglobulin G4 level was 33.1 mg/dL (reference range, 32.4-115.9 mg/dL). Electrocardiogram and chest X-ray were unremarkable. The initial contrast-enhanced abdominal CT revealed diffuse edematous change of pancreas, peri-pancreatic fat infiltration and peri-pancreatic fluid collection (Fig. 1).

The patient was diagnosed with acute pancreatitis based on the specific clinical symptoms, high elevation of amylase and lipase, and abdominal CT findings. The severity of pancreatitis of the patient was estimated as Ranson's score 1 and Acute Physiologic and Chronic Health Evaluation (APACHE) II score 2 on admission day.^{6,7} However, the Balthazar CT score of acute pancreatitis was rated at grade E, more severe than the Ranson's and APACHE II scores, by the radiologist.⁸ The patient was admitted to the general ward. Fluid replacement over 3,000 mL daily including crystalloid fluid and total parenteral nutrition, and alimentary abstinence were ordered. The patient complained frequently of severe abdominal pain. Fever higher than 38°C developed after admission. Thus, meperidine was intravenously injected for pain control and prophylactic antibiotics (third generation

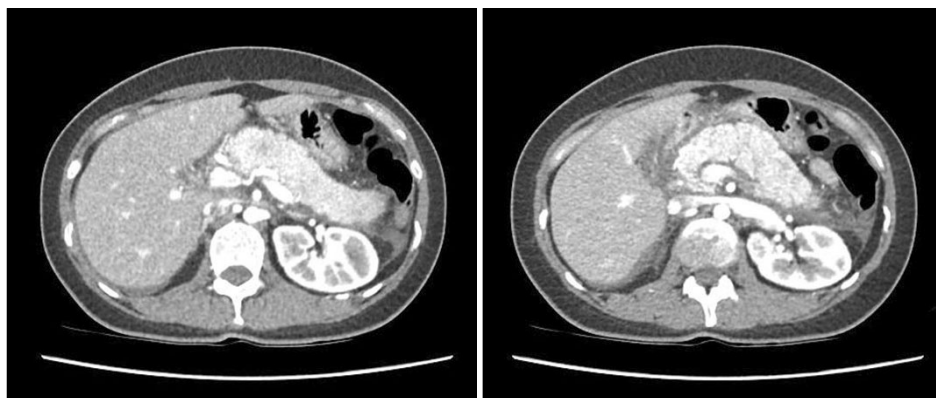


Fig. 1. Contrast-enhanced abdominal CT scans at admission showed a diffuse edematous change of the pancreas, peri-pancreatic fat infiltration, and peri-pancreatic fluid collection.

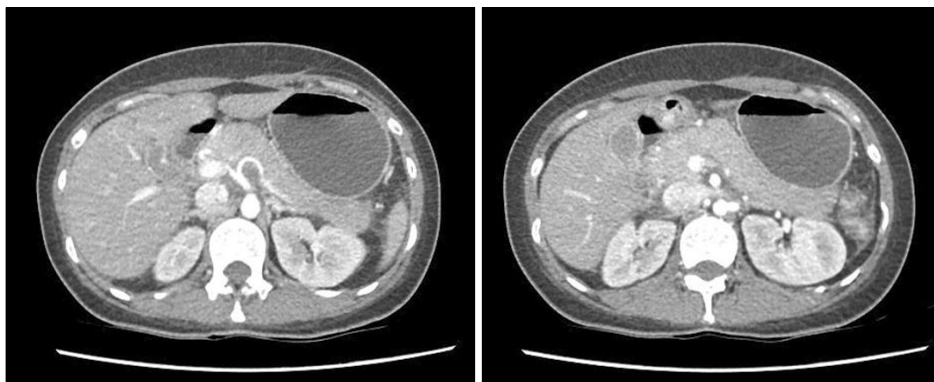


Fig. 2. Contrast-enhanced abdominal CT scans at the time of diagnosis of diabetic ketoacidosis revealed slightly swelling of the pancreas, and no evidence of necrosis and newly developed complications.

cephalosporin) were administered. Her symptoms and signs improved during the initial two days.

On hospital day 3, the patient's abdominal pain nearly subsided, and fever did not develop. Her bowel sound was also normoactive. Though the levels of amylase and lipase were still over normal range, oral intake was planned to start the next day. However, the patient complained of dyspnea, tachypnea, and dizziness at night. Oxygen through nasal prong was supplied. Arterial blood gas analysis revealed pH 7.25, pCO_2 21.2 mmHg, pO_2 171.8 mmHg, HCO_3^- 9.1 mEq/L, base excess -13.1, and O_2 saturation 99%. Despite these laboratory results, only 500 mL of normal saline solution was administered additionally. On hospital day 4, the patient again complained of serious dyspnea, tachypnea, lightheadedness, and agitation. Acute ill appearance, slightly drowsy mentality, and dry skin and tongue were observed on physical examination. The vital signs were blood pressure 100/60 mmHg, heart rate 101 beats/min, respiration rate 24 breaths/min, and body temperature 36.8°C. After starting resuscitation by crystalloid solution, laboratory tests were conducted. Tests revealed WBC 25,500 cells/ μ L (poly, 83.5%), hemoglobin 12.7 mg/dL (hematocrit, 41.1%), platelet 4.61×10^5 cells/ μ L, prothrombin time 12.0 sec, amylase 510 U/L, lipase 883 U/L, blood urea nitrogen 25.5 mg/dL, creatinine 0.97 mg/dL, glucose 575 mg/dL, triglyceride 134 mg/dL, and $Na^+/K^+/Cl^-$ 129/6.8/101 mEq/L. Venous blood gas analysis was estimated to pH 6.925, pCO_2 15.7 mmHg, pO_2 57.7 mmHg, HCO_3^- 3.2 mEq/L, base excess -28.0, O_2 saturation 70.8%. In addition, serum and urine ketone values were all positive.

To rule out the development of locoregional complications of acute pancreatitis such as abscess, pseudocyst, and hemorrhage, contrast-enhanced abdominal CT was performed

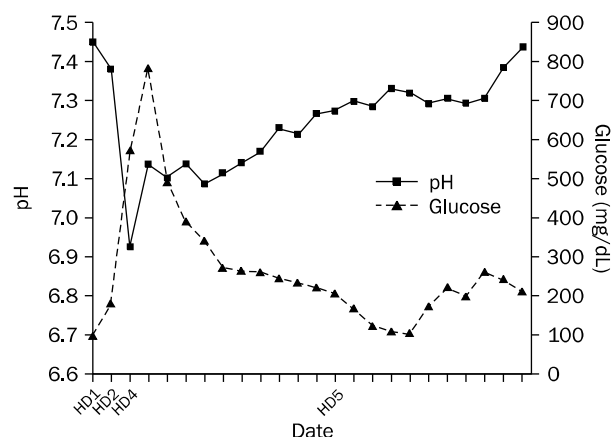


Fig. 3. Changes in the patient's arterial pH and serum glucose levels. HD, hospital day.

again. The repeat abdominal CT showed slightly decreased swelling of the pancreas and no evidence of complications (Fig. 2). The patient was diagnosed as having diabetic ketoacidosis associated with acute pancreatitis. Intravenous insulin and crystalloid solution were rapidly administered according to the results of serum glucose and arterial blood gas analysis at the intensive care unit. The level of serum glucose decreased to approximately 250 mg/dL within a day, but metabolic acidosis improved only slowly (Fig. 3). The patient fully recovered after four days of treatment for diabetic ketoacidosis. The diabetes-related laboratory tests conducted in course of treatment of diabetic ketoacidosis revealed HbA_{1c} 5.8%, insulin 55.23 μ U/mL (reference range, 0-28 μ U/mL), and C-peptide 0.01 ng/mL (reference range, 0.78-1.89 ng/mL). The patient was discharged from the hospital after a full recovery from acute pancreatitis complicated with severe diabetic ketoacidosis. At the time of discharge, the laboratory tests associated with diabetes showed insulin 19.06 μ U/mL, and C-peptide 0.04 ng/mL. At this time, the patient

is still on insulin therapy for diabetes at the outpatient clinic.

DISCUSSION

With acute pancreatitis, development of complications is associated with increased total hospital stays, costs, in-hospital deaths. As a leading cause of hospitalization for gastrointestinal diseases in many countries, including the United States and Korea, acute pancreatitis is the second highest cause of total hospital stays and is the largest contributor to aggregate costs. It is also the fifth leading cause of in-hospital deaths in the United States.⁹ Many articles on pancreatitis-related complications focus on development of necrosis, pseudocysts, ductal disruption, peri-pancreatic vascular complications, and extra-pancreatic infections including pneumonia and urinary tract infection.^{9,10} Thus, most clinicians tend to pay attention to these well-characterized complications. However, hyperglycemia related to acute pancreatitis is rare in clinical practice, and diabetic ketoacidosis associated with pancreatitis seldom occurs. Conversely, acute pancreatitis or asymptomatic hyperamylasemia may develop as a result of diabetic ketoacidosis, and this is not as rare.¹¹

Hyperglycemia induced by acute pancreatitis is associated with the destruction of pancreatic beta cells, which are the sources of insulin in the body. Complete destruction of the pancreatic beta cells may lead to diabetic ketoacidosis secondary to the loss of insulin source from the pancreas. However, acute pancreatitis precipitates a more severe episode of diabetic ketoacidosis due to marked depletion of the intravascular volume.¹² In our case, serum blood urea nitrogen of the patient rose from 8.9 mg/dL to 25.5 mg/dL on hospital day 4. This elevation of serum blood urea nitrogen reflects fluid administration deficiency. Insufficient fluid resuscitation might cause more secretion of counter-regulatory hormones such as glucagon, catecholamines, and cortisol, in comparison with the amount of insulin secretion. As a result, the increased counter-regulatory hormones might produce hyperglycemia and metabolic derangement. In other words, if the patient had undergone aggressive resuscitation with more crystalloid solution and received more intensive care, the complicated diabetic ketoacidosis might have not occurred.

To our knowledge, the link between diabetic ketoacidosis and acute pancreatitis is mediated through hypertrigly-

ceridemia.¹³ The association among diabetic ketoacidosis, acute pancreatitis, and hypertriglyceridemia has been reported in several case reports since 1980.^{12,14,15} Hypertriglyceridemia is a common sequela in diabetic ketoacidosis and is hypothesized as the most common factor triggering acute pancreatitis.¹¹ In diabetic ketoacidosis, insulin deficiency activates lipolysis in the adipose tissue, leading to the release of free fatty acids, which accelerates formation of very low-density lipoproteins in the liver. The reduced activity of lipoprotein lipase in the peripheral tissue decreases removal of very low-density lipoproteins from the plasma, resulting in hypertriglyceridemia.¹⁵ Hypertriglyceridemic pancreatitis is an uncommon condition, mostly associated with poor glycemic control. However, in this case, the patient had no past medical history of diabetes or familial history of diabetes, and the levels of triglyceride were within normal range at initial assessment and when diabetic ketoacidosis developed.

At initial admission, Ranson's score and APACHE II score based on laboratory results and vital signs, and Balthazar CT grade based on the radiologic images showed marked differences. Although Ranson's score and APACHE II score of the patient were 1 point and 2 point, respectively, Balthazar CT grade was grade E. The discrepancy of Ranson's score or APACHE II score and Balthazar CT grade may be attributed to blood sampling from the patient at an early stage of acute pancreatitis, when blood lab results may not accurately reflect the severity of radiologic pancreatitis by CT grade. A review of the patient's medical records revealed that Ranson's score changed from 1 point to 4 points and APACHE II score changed from 2 points to 11 points 48 hours after admission. If the discordance of laboratory and radiologic assessments was thoroughly considered, the development of severe complications might have been avoided. We believe that when treating acute pancreatitis, the clinicians should pay attention to changes in risk parameters including Ranson's criteria or APACHE II score during the initial 48 hours. In addition, especially in the early stage of acute pancreatitis, radiologic risk assessment should receive more attention.

In conclusion, this case is important in that severe diabetic ketoacidosis may develop after acute pancreatitis in a patient without hypertriglyceridemia despite the clinical improvement of acute pancreatitis. Thus, the physicians should consider the possibility of development of diabetic ketoacidosis associated with acute pancreatitis, regardless of trigly-

ceride levels.

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