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CASE REPORT

Acute pancreatitis masked by diabetic ketoacidosis – case reports

Katarzyna Pochodowicz, Michał A. Okruszko, Maciej Szabłowski, Artur Bossowski, Barbara Głowińska-Olszewska

Department of Paediatrics, Endocrinology, and Diabetology with Cardiology Division, Medical University of Bialystok, Bialystok, Poland

ABSTRACT

We present 2 cases of diabetic children who developed acute pancreatitis (AP) in the course of diabetic ketoacidosis (DKA). A 14-year-old girl, diagnosed with diabetes type 1 (DT1), poorly metabolically controlled so far, was admitted with DKA. Her pancreatic enzymes were increased. In ultrasound (USG), her pancreas was enlarged. This evidence indicated AP co-existing with diabetic ketoacidosis. An 8-year-old girl, suffering from DT1, was admitted with DKA, in a diabetic coma, without verbal contact. Her pancreatic enzymes were elevated. Her pancreas was hyperechoic in USG. Criteria of AP were confirmed.

DKA is a frequent severe condition occurring in children with DT1. Acute pancreatitis is a life-threatening condition. Association between AP and diabetic ketoacidosis is rare. We wish to propose with this presentation the need to check the level of pancreatic enzymes in addition to the basic tests for patients with DKA.

KEY WORDS:

acute pancreatitis, diabetes mellitus type 1, diabetic ketoacidosis.

INTRODUCTION

Diabetic ketoacidosis (DKA) occurs as the result of decreased insulin level. DKA can co-exist with new-onset diabetes mellitus type 1 (DT1). 15% to 67% of newly diagnosed DT1 is complicated by DKA [1]. It may also occur in long-lasting DT1. The risk of DKA in these cases is 1% to 10% per patient-year. The main reasons are stress, inadequate doses of insulin, or infections.

DKA is characterized by abdominal pain, polyuria, polydipsia, vomiting, dehydration, and polyphagia, which may cause weakness and even lethargy. DKA could progress rapidly, masking the signs and symptoms of other co-existing diseases.

Acute pancreatitis (AP) is not as common in the paediatric population as in adults. However, the incidence of AP in children is increasing. It occurs in 1 in 10,000 paediatric patients [2]. The diagnosis of AP may require at least 2 of the following: abdominal pain, an increase of pancreatic enzymes more than 3 times the upper limit, and imaging results indicating AP. Nowadays obesity has become one of the most common reasons for AP [3]. The other mentioned causes of AP are biliary tract diseases, traumas, or autoimmunity. Diabetic ketoacidosis is has not been mentioned as a possible reason or accompanying condition for acute pancreatitis so far.

According to the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN), acute pancreatitis can be divided into mild, moderately severe, and severe. Mild AP is the most common in paediatrics, and in this kind of AP, there is no organ failure, or local or systemic complications. It is classified as severe AP if it lasts longer than or develops after 48 hours [4].

ADDRESS FOR CORRESPONDENCE:

Prof. Barbara Głowińska-Olszewska, Department of Paediatrics, Endocrinology, and Diabetology with Cardiology Division, Medical University of Bialystok, 7 Waszyngtona St., 15-274 Bialystok, Poland, e-mail: barbara.glowinska-olszewska@umb.edu.pl

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Clinically apparent pancreatitis rarely occurs in children with DKA. The first symptoms are abdominal pain and emesis. Interestingly, severe abdominal pain, which requires visiting a paediatrician, occurs in up to 25% of school-age children [5]. In differential diagnosis, pancreatitis and DKA are uncommon in children. The reason for the pain is often due to a mild cause, so detecting the life-threating condition is even more important [6]. It is essential to check the localization, duration, onset, additional symptoms, and other factors that could be the reason for the pain [5]. Blood studies, abdominal X-ray, and ultrasound scans of the abdomen can be helpful. Computer tomography with contrast is suitable when the USG is inconclusive. Frequent reasons for acute abdominal pain in school age are acute gastroenteritis, urinary tract infection, inflammatory bowel disease, appendicitis, pneumonia, viral syndromes, constipation, liver abscess, cholangitis, Meckel's diverticulitis, testicular or ovarian torsion, and trauma [6].

It is important to measure serum lipase and pancreatic amylase because the increased levels of these enzymes are valuable in the diagnosis of AP. Checking the level of serum lipase is more critical than other laboratory (pancreatic) or screening tests (USG, CT) alone [3, 7]. However, the combination of measurement of lipase and amylase and ultrasound is even more relevant to satisfactory diagnostics of AP.

In this report, we present 2 cases of diabetic ketoacidosis with confirmed AP.

CASE DESCRIPTION

FIRST PATIENT

A 14-year-old girl with a 3-year history of poorly controlled DT1 (glycated haemoglobin values up to 10%) was admitted to the Department of Gastroenterology, where AP and DKA were diagnosed. She had complained of acute abdominal pain, emesis, and loss of appetite for two days. Her last glycated haemoglobin was 8.4% (normal range 4.8–5.9%) with average 30-day glycemia of 326 mg%. She was treated with intensive insulin therapy with analogues. She was diagnosed with depression 1.5 years earlier. Her condition was a contraindication for use of an insulin pump. In the past, she had been hospitalized in an emergency unit several times because of DKA.

On admission to the hospital this time, the blood tests showed hyperglycaemia (272 mg/dl) and increased inflammation parameters – C-reactive protein (CRP) was 193.76 mg/l and procalcitonin (PCT) was 1.74 ng/ml. Arterial blood gas test after being admitted showed that $PaCO_2$ was 27.5 mm Hg, PaO_2 was 75.1 mm Hg, HCO_3 was 17.2 mmol/l, BE was – 7.4 mmol/l, and pH was 7.414. The activity of pancreatic enzymes was 498 IU/l for lipase (normal range 13–60 IU/l) and 309 IU/l for amylase (normal range 28–100 IU/l). The level of triglycerides was 498 mg/dl. Ultrasonography (USG) showed enlargement of the pancreas and lots of fluid in the peritoneal cavity. Computed tomography (CT) confirmed the ultrasound scan findings – the contours of the pancreatic tail and body were irregular. There were hypodense changes in the pancreas, which correspond with necrosis. These findings indicated AP. The CT scans also showed enlargement of the liver. Cooperation between the diabetologist and gastrologist was vital to introduce the appropriate treatment regimen. She was managed with a strict diet combined with antibiotics, parental hydration, electrolyte supplementation, intravenous insulin, and pancreatic enzymes. After 4 days, oral nutrition was started with Peptamen and rice porridge. Her condition improved. She was transferred to the Department of Diabetology. Next, control tests were performed: CT, USG, and measurement of pancreatic enzyme activity. The enzyme activity was normalizing, and the condition of the patient improved. A low-fat diet was implemented. After reeducation, the girl was discharged.

SECOND PATIENT

An 8-year-old girl with a 1.5-year history of DT1 was admitted to the hospital because of weakness and loss of verbal contact coexisting with hyperglycaemia (250–300 mg/dl) lasting for 2 days. Her last diabetes check-up visit was about one year ago. She was treated with subcutaneous insulin pen injections with insulin analogues. Her metabolic control before the hospitalization was unknown due to the lack of regular visits.

The physical examination showed dry, pale skin, a subfebrile state, and tachycardia (130 beats/min). Abdominal palpation was restricted because of difficult communication with the patient. Blood tests showed increased glucose levels, CRP, creatine kinase MB isoenzyme (CK-MB), and D-dimers. Her HbA_{1c}% was 7.9%. Arterial blood test showed that the level of $PaCO_2$ was 15.7 mm Hg, PaO_2 was 58.3 mm Hg, HCO_3 was 6.5 mmol/l, BE was – 21 mmol/l, and pH was 7.235. The activity of pancreatic enzymes was more than 3 times above the normal range (amylase was 864 UI/l and lipase 2769 UI/l). Urinalysis showed glucosuria and ketonuria. An ultrasound scan showed that the pancreas was slightly hyperechogenic. The criteria of AP were achieved (Table 1), and treatment was introduced with the cooperation of a diabetologist and a gastrologist.

The therapeutic regimen consisted of eating restriction combined with typical diabetic ketoacidosis treatment, antibiotics, rehydration, electrolytes supplementation, and pancreatic enzyme supplementation. The insulin therapy had to be modified due to AP. After 4 days, the condition of our patient improved, and a low-fat diet was introduced. Our patient and her mother were informed about diet and modification of insulin doses

TABLE 1. Manifestations of diabetic ketoacidosis co-existing with acute pancreatitis

Patient	Diabetes mellitus type 1	DKA on admission	Abdominal pain	Emesis	Dehydration	Duration of clinical signs and symptoms	Activity of serum lipase on admission	Activity of pancreatic amylase on admission	Imaging tests on admission
1	Present for 3 years	+	+	+	+	2 days	498 IU/l	309 IU/l	In USG and CT, the pancreas was enlarged, and the fluid was presented in the peritoneal cavity
2	Present for 1.5 years	+	±*	+	+	2 days	2769 IU/l	864 IU/l	In USG, the pancreas was hyperechogenic

CT – computed tomography, DKA – ketoacidosis, USG – ultrasound
** Limited contact with the patient*

due to changed glycaemia. After attending a meeting with a diabetic educator, the patient was discharged home.

DISCUSSION

DKA occurs in a quarter to almost half of cases with diagnosed DT1 [8]. It is more common than AP and is a well-recognized complication of diabetes, with accepted recommendations for recognition and treatment. However, the first symptoms AP are similar to those of acidosis, which we noticed in our patients (Table 1). Nevertheless, in the latest recommendations announced by the leading diabetologists associations, there is no mention of AP as a DKA complication [9, 10]. Only AP co-existing with hypertriglyceridaemia is described.

DKA management is patient hydration, managing hyperglycaemia with intravenous insulin, and electrolyte supplementation. It is important to measure blood glucose levels every hour and adjust the appropriate dose of insulin. If the arterial blood pH is 6.9 or lower, administration of bicarbonate and low-molecular-weight heparin should be considered [1, 9].

Despite the growing incidence of AP in paediatric patients, few guidelines provide information about managing this illness in the mentioned population. The authors of available publications emphasize hydration, pain control, and nutrition. Enteral nutrition is preferred at one-fourth to one-eighth of the total requirement of calories. Parenteral feeding should be considered only in cases where oral feeding is contraindicated. Once the clinical state of the patient has improved, a low-fat diet is recommended. However, recent studies have shown no difference in outcomes (such as discharge time) between a full-fat diet in children with mild-moderate AP and initial fasting and a low-fat diet [11].

Nevertheless, the stress connected with feeding and losing weight is not good for the patients [11]. For the first 24 hours, aggressive fluid management is recommended to reduce the complication rate. For pain control, opioid-sparing medicines should be considered. However, opioids could be used in severe pain. Antibiotics should be used only in cases of infected pancreatic necrosis [2].

Because there are 2 different ways of treating these diseases and not having one recommendation for co-existing AP and DKA, cooperation between the diabetologist and the gastrologist is necessary. The treatment may seem similar: hydration and electrolyte remediation. However, calculating the appropriate insulin dose depending on the amount of nutrition and the blood glucose level could be challenging. The diabetologist must calculate carbohydrate counting and modify the amount of insulin every day of treatment.

Co-working between doctors in paediatric cases with DT1 is relevant even in prevention of DKA. General practitioner or paediatricians should draw attention to modifiable risk factors such as the patient's mental condition, eating disorders, low socioeconomic structures, and extremes of glycated haemoglobin distribution. These triggers are especially important for patients who have had DKA in the past. Adolescent girls are more vulnerable to public opinion, which could be the reason for their mental disorder. These could be factors of recurrent DKA. The paediatrician should encourage patients to visit their diabetologist frequently [12].

A proper diagnosis is the crucial for fast and non-complicated recovery. Abdominal pain, nausea, and emesis could suggest DKA and AP, or both co-existing, which is uncommon. Approximately 2% of children with DKA develop AP [13, 14]. AP co-existing with DKA was the diagnosis in our 2 cases. The patients did not have any infections or traumas and did not introduce new medication before the hospitalization. Nonetheless, hypertriglyceridaemia was presented [9]. The connection between DKA and hypertriglyceridaemia occurs in approximately 30–50% of cases [15]. A low insulin level causes lipolysis and an increase of TG in the blood [16]. An elevated level of triglycerides in DKA could cause acute pancreatitis [3, 4]. Their symptoms indicated that DKA was the reason for the appearance of AP.

DKA can be one of a few possible reasons for AP. Consideration of AP coexisting with DKA is very import-

ant for further treatment. Acute pancreatitis worsens the patient's condition. Moreover, AP reduces intravascular volume and disturbs glucose homeostasis, making control of glycaemia much more difficult. Also, treating ketoacidosis only with the continuation of oral feeding could aggravate the course of AP, which could worsen the severity of DKA [17]. Normalizing DKA without diagnosing AP and continuing oral feeding could worsen AP and cause recurrent DKA.

When similar symptoms occur, the physician should consider DKA and acute pancreatitis. When children have abdominal pain, ketoacidosis, and dehydration, pancreatic enzymes should be measured. In DKA, elevated serum lipase and amylase are frequent, but usually they do not meet the criteria of AP. The mechanism of this elevation is not precise. Evidence-based medicine confirms that high activity of pancreatic enzymes relates to poorly controlled diabetes [13, 14, 17]. However, metabolic or neural disorders of the pancreas could cause leakage of pancreatic enzymes from the acini. Additionally, non-pancreatic organs such as the stomach, liver, small bowel, tongue, oesophagus, and the gastroesophageal junction may release lipolytic enzymes into the bloodstream. Furthermore, during DKA, hypovolaemia with a decreased glomerular filtration rate may appear. In the conjunction with decreased amount of lipase in the urine and increase in the circulation. What is more, lower renal clearance of amylase causes its elevation in the bloodstream [13, 18].

If acute pancreatitis is recurrent, the doctor should consider chronic pancreatitis (CP). CP in childhood without obvious reasons demands further examination. The gastrologist should consider hereditary pancreatitis after mucoviscidosis has been excluded. In our cases the doctors did not perform genetic examinations because our patients had not had acute pancreatitis in the past [19].

If the pancreatic enzymes are 3 times higher than the upper limit, it is recommended that abdominal imaging be performed. In ultrasound, pancreas enlargement and hypoechogenicity are significant for acute pancreatitis, although the absence of this image cannot exclude AP. Abdominal ultrasonography is very important and may help find complications such as pseudocyst, pancreatic abscess, or necrosis [14, 17]. A more advanced way of imaging can be abdominal CT, especially in severe or complicated AP. It allows the detection of necrosis, pseudocysts, and peripancreatic fluid. Moreover, CT is easier to perform when the patient is obese, and it may be helpful when there are artefacts in the ultrasound scan. However, even a CT scan can appear normal in mild AP [2, 4].

CONCLUSIONS

It is important to consider acute pancreatitis in the differential diagnosis of diabetic ketoacidosis with co-existing abdominal pain and emesis. Acute pancreatitis is a life-threatening but uncommon disease in children, with DT1 patients among them. Symptoms are very similar to those appearing in typical diabetic ketoacidosis, and this may lead to misdiagnosis. We would like to propose with these case reports the need to add the level of pancreatic enzymes – lipase and amylase – to the basic tests for diagnosis of diabetic ketoacidosis, particularly in cases with ultrasonography examination, if needed. Screening for acute pancreatitis could help paediatricians detect this complication earlier, understand the severe clinical condition of the patients, and introduce the appropriate treatment to avoid severe morbidity. In managing patients with DKA and co-existing AP, cooperation between the diabetologist and gastroenterologist may be necessary.

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DISCLOSURE

The authors declare no conflict of interest.

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