Diabetic Ketoacidosis as the First Manifestation of New Onset Juvenile Type 2 Diabetes

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Diabetic ketoacidosis (DKA) is considered a cardinal feature of type 1 DM. However, several reports have indicated that ketosis can occur spontaneously in type 2 diabetes patients. We report a rare case of new-onset non-obese juvenile type 2 diabetes presenting as DKA without a precipitating event. The patient was first misdiagnosed as having type 1 diabetes. A previously healthy 15-year-old girl was sent to the emergency room in a drowsy state of consciouness. Laboratory data revealed marked hyperglycemia, ketonemia and metabolic acidosis. DKA was the preliminary diagnosis, and she was treated with intravenous saline and continuous insulin infusion. Eight days later, she was discharged on a regimen of subcutaneous insulin injections twice daily. Two months following acute presentation, the insulin dose was decreased to once daily. Fasting C-peptide was 2.6 ng/mL (normal range 0.9 to 4 ng/mL). Insulin was discontinued and good glycemic control was achieved with gliclazide and metformin therapy. DKA in non-obese juvenile patients with new-onset diabetes does not necessarily imply the presence of type 1 diabetes. Type 2 diabetes should also be considered in non-obese juvenile patients presenting with DKA. **(Mid Taiwan J Med 2006;11:267-70)**

Key words

diabetic ketoacidosis, juvenile type 2 diabetes, new-onset diabetes

INTRODUCTION

Diabetes has been classified into two major forms: type 1 and type 2. Diabetic ketoacidosis (DKA) is traditionally regarded as the first manifestation of new-onset type 1 diabetes. This condition is common in pediatric and young patients. Winter et al [1] were the first to report an atypical form of diabetes in young obese Africa-Americans who showed ketoacidosis at the time of presentation followed by the absence of insulin dependence months to years later. This atypical subset of type 2 diabetes has also been reported in young obese Japanese and Canadian aboriginal youth [2-7]. However, new-onset non-obese juvenile type 2 diabetes presenting as DKA is rare. Here, we report a juvenile type 2 diabetic patient who initially presented with DKA.

Received : 10 March 2006. Revised : 10 April 2006.
Accepted : 19 April 2006.

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CASE REPORT

A 15-year-old junior high school student presented to our emergency room (ER) in a drowsy state of consciousness. She had been well until 4 days prior to admission, when she began to suffer from dizziness and generalized weakness. She visited a local medical clinic where a common cold was diagnosed. Some medications were prescribed, but her condition got worse. She was dehydrated and craved sugar-containing soft drinks. The day before admission, she complained

of nausea, vomiting, and abdominal pain. On the morning of admission, the patient had shortness of breath and was lethargic. Her family immediately sent her to our ER. On arrival, her blood pressure was 50/39 mmHg in a supine position. Her pulse was 153/min, respiration 30/min and temperature 37.6 °C. Physical examination revealed a drowsy young girl weighing 49 kg and measuring 154 cm tall. Her heart beat was rapid without murmur and her breathing was rapid. A fruity odor emitted from the patient's mouth. Bowel sounds were absent and she had generalized abdominal tenderness without rebounding pain. Her skin and mucous membranes were dry. Neurologic examination was normal.

Laboratory data consisted of the following: blood glucose 637 mmol/L (1158 mg/dL), serum ketone 40 mg/dL, osmolarity 366.4 mOsm/kgH_2O, BUN 17.9 mmol/L (50 mg/dL), Cr 168 μmmol/L (1.9 mg/dL), Na^+ 148 meq/L, K^+ 5.0 meq/L, Cl^- 109 meq/L, Hb 11.0 mmol/L (17.8 gm/L), WBC 9330/mm^3, Arterial blood gas analysis revealed a pH of 7.171, Pco_2: 18.3 mmHg, Po_2: 111.3 mmHg and $HCO3^-$ 6.7 mEq/L.

DKA was diagnosed. Hydration with intravenous normal saline was started. She also received an intravenous bolus of 10 units of regular insulin and an intravenous insulin drip at 5 units per hour. Approximately 5 hours later, she was lucid and her abdominal pain had subsided. Blood glucose was 14.3 mmol/L (260 mg/dL). Her insulin drip was continued at 2 units per hour and a mixture of 5% dextrose with normal saline was given. The next morning the patient was feeling much better. She was hungry and was able to take liquids. Her blood glucose was 15.4 mmol/L (280 mg/dL), the blood urine nitrogen and creatinine had returned to normal. She was started on 16 units of NPH insulin and 8 units of regular insulin and 1 hour later the insulin drip was discontinued. The insulin dose was adjusted to achieve good glycemic control. She also received dietary counseling and instructions on insulin administration and blood glucose monitoring. On the fifth day of hospitalization, her clinical condition had markedly improved. She was discharged on a regimen of 28 units of NPH insulin and 14 units of regular insulin before breakfast and 12 units of NPH insulin and 10 units of regular insulin before supper. The discharge diagnosis was type 1 diabetes.

At follow-up one week after discharge, her fasting blood glucose level was 4.5 mmol/L (82 mg/dL). The insulin dose was decreased. Two months later, the insulin dose was decreased to once daily. Fasting C peptide was checked and the level was 2.6 ng/mL (normal fasting range 0.9 to 4 ng/mL). Therefore, insulin was discontinued and gliclazide 80 mg once daily and metformin 500 mg twice daily were begun. Her diabetes was under control and the blood glucose ranged from 5.5 mmol/L to 6.6 mmol/L (100 to 120 mg/dL) before meals. She had gained 3 kg two months after the episode of DKA.

DISCUSSION

Several reports have described an atypical group of patients with type 2 diabetes who initially presented with DKA [1-7]. The patients ranged in age from 10 to 42 years, and most of them were quite obese. None of the patients had a history of diabetes or obvious precipitating factors for DKA. However, a positive family history was found. After the resolution of DKA, these patients had a clinical course more typical of type 2 diabetes. Our patient was a normal weight female (BMI = 22 kg/m^2) and her father had type 2 diabetes. She was the first patient with new-onset non-obese juvenile type 2 diabetes to present with DKA in our hospital.

A previous study indicated that patients with obese type 2 diabetes with spontaneous DKA have defects in both insulin secretion and insulin action. It appears that an acute and severe impairment of insulin secretion is the primary event involved in the development of DKA in these patients [2]. The possible mechanism of impaired insulin secretion is chronic hyperglycemia in obese-DKA type 2 diabetes. This phenomenon is termed glucose toxicity. Control of severe hyperglycemia with insulin for several days or weeks results in improved β cell function and insulin action, and allows

discontinuation of insulin therapy in most cases [8]. Our patient self-administered insulin injections for about 2 months and maintained good glycemic control. The glucose toxicity was then corrected by insulin therapy and her diabetes was controlled with oral antidiabetic drugs (OADs).

It is difficult to differentiate between type 1 and type 2 diabetes in the juvenile population, particularly when DKA is the chief presenting clinical feature. However, this distinction is important because long term treatment strategies differ between the two types [6]. Africa-American patients with DKA have negative titers for islet cell antibodies (ICA) or glutamic acid decarboxylase (GAD) [1,2,9]. We did not check ICA and GAD antibodies, because these assays are not available in our hospital. The fasting C peptide in our patient was 2.6 ng/mL. In several different studies, fasting C-peptide levels of less than 0.54 ng/mL are widely accepted as cut off values for type 1 diabetes [10,11]. Type 2 diabetes was defined as fasting C-peptide levels greater than 1.1 ng/mL [12]. Although there is some overlap between type 1 and type 2 diabetes, C-peptide up to 2.6 ng/mL is unlikely in type 1 diabetes, even in the honeymoon phase. Another study of ketone-prone type 2 diabetes found that subjects who have DKA can have exogenous insulin discontinued during follow-up if the fasting C-peptide level is greater than 0.99 ng/mL [13]. Total remission for insulin treatment is rarely seen in the honeymoon phase and the duration of the honeymoon phase usually lasts for a few months to 2 years [14]. Our patient took OADs for about 5 years during the follow-up period without developing DKA. Therefore, type 2 diabetes was diagnosed.

The presence of DKA in non-obese juvenile patients dose not necessarily imply the presence of type 1 diabetes. DKA can occur in non-obese juveniles with type 2 diabetes. Fasting plasma C-peptide level, subsequent clinical course in these patients and family history of diabetes can help the physician to correctly diagnose type 2 diabetes in non obese juvenile patients who first present with DKA.

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以糖尿病酮酸血症為初表現的青少年第2型糖尿病

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糖尿病酮酸血症被認爲是第1型糖尿病的主要特徵，然而，幾篇報告指出肥胖非裔美國成年人、青少年及肥胖日本年輕第2型糖尿病患者，會自發性的出現酮酸血症。本文提出一例罕見的病例報告，一位15歲非肥胖新發生的第2型糖尿病女孩，以糖尿病酮酸血症爲初表現，而且沒有任何造成酮酸血症的誘發原因，以致最初被誤診斷爲第1型糖尿病。因此，我們強調以糖尿病酮酸血症爲表現的非肥胖青少年糖尿病患，並非一定是第1型糖尿病，也必須考慮第2型糖尿病的可能。（中台灣醫誌 **2006;11:267-70**）

關鍵詞

糖尿病酮酸血症，青少年第2型糖尿病，初發的糖尿病

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收文日期：2006年3月10日　　修改日期：2006年4月10日

接受日期：2006年4月19日