Diabetic Ketoacidosis Associated with Recurrent Pulmonary Edema and Rhabdomyolysis in a Patient with Turner’s Syndrome

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Abstract

Turner’s syndrome is a condition involving total or partial absence of one X chromosome and has been associated with a number of diseases including non insulin dependent diabetes mellitus, abnormalities of glucose metabolism and hypothyrosis. There have been many case reports in which Turner’s syndrome is associated with type 2 diabetes, but the association with type 1 diabetes and/or life threatening complications is very rare. We present an unusual case of a patient with Turner’s syndrome who has type 1 diabetes and is complicated with ketoacidosis, severe acute and recurrent pulmonary edema and rhabdomyolysis.

Key words: type 1 diabetes, AaDO2

Introduction

Ketoacidosis is a common metabolic disturbance in patients with uncontrolled type 1 diabetes. Despite aggressive fluid replenishment in the initial management of the ketoacidotic state, pulmonary edema is a rare complication (1, 2). Rhabdomyolysis is often seen in patients with uncontrolled diabetes but the cause is still unknown (3, 4).

Turner’s syndrome is a condition involving total or partial absence of one X chromosome in all or part of the cells. Turner’s syndrome has been associated with a number of diseases including non-insulin-dependent diabetes mellitus (NIDDM), abnormalities of glucose metabolism and hypothyrosis, and thyroid antibody formation (5–7). There have been many case reports in which Turner’s syndrome is associated with type 2 diabetes. In these cases insulin resistance is a prominent feature (6, 7). The association with type 1 diabetes is very rare, with only one Italian case of Turner’s syndrome with type 1 diabetes in the literature (8). And furthermore diabetic patients with severe and life threatening complications were not found in the patients with Turner’s syndrome. We present an unusual case of a patient with Turner’s syndrome who has type 1 diabetes and is complicated with ketoacidosis, severe acute and recurrent pulmonary edema and rhabdomyolysis.

Case Report

A 28-year-old woman was brought to our hospital because of vomiting and disturbance of consciousness. She was semicomatose, without localizing neurological signs. The initial examination disclosed the following values: temperature, 35.8°C; blood pressure, 80 mmHg; pulse rate, 100 beats per minute; and respiratory rate, 30/min. The lung was clear. Cardiac examination showed no cardiomegaly and heart murmur. Her skin and tongue were dry. Initial laboratory studies showed leukocyte count of 21,400 × 10⁴/mm³, Hb 16.4 mg/dl, CRP 7.6 mg/dl and glycosuria and 4+ ketones on the urinalysis. Blood chemistry revealed fasting plasma glucose 50.6 mmol/l, urea nitrogen 22.9 mmol/l, creatinine 221 μmol/l, serum myoglobin 450 ng/ml, amylase 4,295 IU/l (S 84.2%) and elastase I 1,090 ng/dl. An arterial blood gas analysis in room air showed pH 6.94, PO₂ 125 mmHg, PCO₂ 10.5 mmHg, HCO₃⁻ 2.1 mmol/l, BE -28.2 mmol/l and oxygen saturation (SaO₂) 94.7%. Blood ketone was 15,500 μmol/l. A chest X-ray examination (CXR) was unremarkable. She was diagnosed as diabetic ketoacidosis with severe dehydration and rhabdomyolysis. The patient was treated with hydration (mainly 0.9% NaCl, 8 l/first 24 hours) and continuous insulin infusion (1–5 U/h) during the first 24 hours. After these treatments, BP increased to normal range and blood glucose decreased to 13.8 mmol/l. Ketoacidosis was resolved and she became alert. Late on the second hospital day, she developed dyspnea and hypoxia. Arterial blood gas analysis in room air showed pH 7.35, PO₂ 61.0 mmHg, PCO₂ 21.1 mmHg, HCO₃⁻ 11.3 mmol/l and
SaO₂ 93.4%. Alveolar-arterial O₂ gradient (AaDO₂) was elevated to 62.7 mmHg (11.4 mmHg on admission, normal 5–15). A CXR was consistent with pulmonary edema without cardiomegaly. An echocardiogram revealed slightly impaired systolic function with an ejection fraction of 60%. The main condition appeared noncardiogenic pulmonary edema. The hypoxemia gradually worsened and AaDO₂ was widened over 100 mmHg despite the aggressive use of diuretics and oxygenation. On the third hospital day, she was intubated and mechanically ventilated with 10 cm of positive endo-expiratory pressure (PEEP). In spite of these treatments, the pulmonary edema was not improved. The systolic BP again went down to 80 mmHg and the urinary volume decreased. Then continuous hemodiafiltration (CHDF) was introduced for 17 hours, with rapid improvement of hypoxemia. On the eighth hospital day mechanical ventilation was discontinued and the use of digitalis and diuretics was discontinued on the 12th hospital day. Her condition was constant until the 14th hospital day. On the 14th hospital day, she developed dyspnea and severe pulmonary edema again. The clinical course is summarized in Fig. 1. It took 20 days for the renal function to be normalized, because the diabetes was complicated with rhabdomyolysis. There was no family history of diabetes mellitus; she had been diagnosed as Turner’s syndrome at age 16. Her medical record at the age of 16 years was not obtained. She was in good health for at least the previous 10 years. Her height was 136 cm, weight 38 kg and body mass index 22. She was sexually immature, with stage 3 breast and stage 3 pubic hair development according to Turner’s classification. Skeletal abnormalities included a webbed neck, shield chest, cubits valgus and brachydactylyia. The serum estrogen (undetectable) and progesterone (0.4 ng/ml) were low and LH (33.8 mU/ml) and FSH (137.3 mU/ml) levels elevated. The other anterior pituitary hormones were normal. The chromosomal karyotype was 45XO/46, X, idic (X) and she was diagnosed as Turner’s syndrome. The islet cell autoantibodies (ICAs), autoantibodies to insulin (IAAs) and autoantibodies to glutamic acid decarboxylase (GAD) were negative. Urinary C-peptide excretion was measured daily for three days between the 30 and 32nd hospital days when the metabolic disturbance improved by intensive insulin therapy (the blood glucose levels controlled between 8.3–13.9 mmol/l) and the mean value was as low as 2.4 µg/day.

Histocompatibility antigens were A-11, A-31, B-62, B-61, CW-3, CW-8, DR-9, and DQ-3. Mitochondria gene abnormality was not observed. Regular insulin (20–24 U) and NPH insulin (8–10 U) were necessary to control the blood glucose at discharge and thereafter. She was diagnosed type 1 diabetes in consideration of the clinical course (acute onset of ketoacidosis), low urinary C-peptide (lack of insulin secretion), and HLA DR-9 positive. Diabetic retinopathy, neuropathy and nephropathy were not observed. The HbA1c level improved up to 8% at the time of discharge (54th hospital day) from 11% on admis-

Figure 1. Clinical course of this case.
sion.

**Discussion**

This case illustrates an uncommon presentation of the ketoadicosis and recurrence of pulmonary edema found in the type1 diabetic patient with Turner’s syndrome. Turner’s syndrome afflicts approximately 50 per 100,000 females and is characterized by retarded growth, gonadal dysgenesis and infertility. Less is known about the natural course of this syndrome, especially in adulthood (9, 10). Women with this disease seem to have an increased incidence of osteoporotic fractures in adulthood, diabetes mellitus, mainly type 2 diabetes, ischemic heart disease, hypertension and stroke. In Turner’s syndrome, the increased incidence of diabetes mellitus is well known, and most reported cases were type 2 diabetes associated with insulin resistance (6, 7) and only one case was type 1 diabetes (8). This Italian case was a 16.5-year old female with ketoacidosis and the insulin secretion was almost nil and islet cell autoantibody was positive. According to the Danish epidemiological study from 1984 to 1993 in Denmark (9), not only type 2 diabetes but also type 1 diabetes was found at a markedly increased incidence in Turner’s syndrome, although islet cell antibodies were not reported with an increased frequency. In a literature search however, only one case report could be found on type 1 diabetes with Turner’s syndrome and there was no case report on Turner’s syndrome with severe and life threatening type 1 diabetes. Turner’s syndrome is frequently associated with metabolic disturbance and autoimmune disorders and these abnormalities might be related to a subgroup with an isochromosome of the long arm of X chromosome (i(Xq)) (11). In the present case, the chromosomal karyotype was 45X0/46, X, idic(X). The type 1 diabetes might be related to the presence of an isochromosome of the long arm of X chromosome.

The American Diabetes Association and the World Health Organization have proposed that type 1 diabetes be subdivided to autoimmune (immune-mediated) diabetes (type 1A) and idiopathic (no known etiology, no evidence of autoimmunity) diabetes (type 1B) (12, 13). Imagawa et al recently reported the characteristics of Japanese cases of Type 1A and 1B (14). According to their report, some patients with type 1B diabetes are characterized by a remarkably abrupt onset, a higher mean plasma glucose concentration, remarkably diminished urinary excretion of C peptide, a more severe metabolic disorder and higher serum pancreatic enzyme concentrations compared with those of type 1A diabetes. Although ICAs, IAAs and GAD antibodies were negative, the present case showed a severe metabolic acidosis, a high plasma glucose and abrupt onset, and insulin secretion was still very low when the metabolic disturbance was improved by intensive insulin therapy, and furthermore serum amylase and elastase I levels were elevated on admission. Taken altogether, the present case might be type IB. The capacity of insulin secretion and the appearance of diabetes-related autoantibodies must be closely followed. And further study would clarify the association between the metabolic and autoimmune disturbance seen in Turner’s syndrome and gene abnormalities.

In the present case, the recurrent pulmonary edema was another unusual and interesting point. Only one case report on recurrent pulmonary edema with type 1 diabetes by Jain et al was found in the literature (2). They propose that the rapid administration of crystalloids and altered capillary permeability may have been its contributing mechanisms. High glucose and/or metabolic factors related to acidosis are thought to induce a change of vascular permeability. In the prezent case, the initial pulmonary edema might have occurred through rapid overhydration and altered capillary permeability by acidosis and rhabdomyolysis. The use of digitalis and diuretics was discontinued on the 12th hospital day. The early discontinuation of such drugs in conjunction with slightly diminished cardiac and pulmonary function may have induced the second pulmonary edema on the 14th hospital day.

**References**


