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Case Report

Fulminant type 1 diabetes mellitus associated with heavy drinking: a case report

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Abstract: Background: Fulminant type 1 diabetes is a new sub-type of type 1 diabetes with a remarkably acute onset. It is characterized by an intrinsic insulin deficiency resulting from a markedly and severe destruction of pancreatic cells. Because this disease progress rapidly, early detection is critical for initiating timely interventions. Here we report a rare case of Fulminant type 1 diabetes associated with excessive alcohol use. Case presentation: A 34-year-old Chinese man was admitted to our hospital due to refractory diarrhea. His blood glucose level was 24.6 mmol/L (442.8 mg/dl) and he was positive for urine ketone bodies. Immediate treatment actively reduced the blood glucose level and corrected his electrolyte disturbance and acid-base imbalance. Fulminant type 1 progresses rapidly and the prognosis is extremely poor. Conclusion: Clinicians and patients must be aware that early diagnosis and treatment are important to the outcome of patients.

Keywords: Diabetes, autoimmunity, pancreatic cells

Introduction

The etiology and pathogenesis of Fulminant type 1 diabetes are still not fully understood. Several factors such as viral infection, genetic susceptibility, autoimmunity, pregnancy and others seem to be involved. The Committee of the Japan Diabetes Society reported the FT1DM diagnostic criteria in 2012, and FT1DM should have the following characteristics: (1) Rapid onset of hyperglycemia symptoms and development of diabetic ketoacidosis or ketosis within 1 week. (2) Fasting blood glucose ≥ 16.0 mmol/L, glycated hemoglobin <8.7%. (3) Serum fasting C-peptide <0.10 nmol/L (0.3 ng/mL), 120 min C peptide <0.17 nmol/L (0.5 ng/mL). Compared with classic type 1 diabetes, these patients usually require high doses of insulin and are more prone to hypoglycemia and acute complications. Diabetic ketoacidosis should be corrected immediately when the disease is highly suspected clinically. After the condition is stabilized, insulin replacement therapy is gradually transitioned to a chronic phase. Generally, an insulin pump or ultra-short-acting insulin combined with medium long-acting insulin intensive therapy is selected, and the insulin dose is 0.4-0.8 IU/kg. However, due to the rapid destruction of islet β cells and the almost complete and irreversible loss of islet function, the patients' blood sugar fluctuates greatly, and the incidence of hypoglycemia is high.

Case presentation

A 34-year-old Chinese man presented to our hospital due to diarrhea for 8 days. He had no significant past medical history. The patient developed diarrhea after drinking 500 ml of alcohol 8 days before admission, 4-6 times a day, and there was no obvious mucus and pus blood in the stool. There was no fever, abdominal pain, nausea or vomiting on admission. The patient has a normal body mass index (20.1 kg/m^2) with a height of 174 cm and a weight of 61.5 kg. After admission, a physical examination was performed and the results were as follows: Temperature (T), 37.1°C; Pulse rate (P), 102 bpm; Respiration rate (R) 20/min; Blood Pressure (BP), 118/86 mmHg. The patient was conscious but showed slow verbal responses.

Table 1. Results of the laboratory tests

Test	Results					Normal Range
Routine Blood Analysis	Day 1	Day 2	Day 4	Week 1	Week 2	
WBC	11.22 × 10^9/L	10.32 × 10^9/L	8.4 × 10^9/L	NA	9.48 × 10^9/L	(3.5-9.5) × 10^9/L
N%	90%	89%	69%	NA	61.20%	40-75%
HGB	112 g/L	99 g/L	127 g/L	NA	109 g/L	110-160 g/L
PLT	68 × 10^9/L	58 × 10^9/L	149 × 10^9/L	NA	191	125-350 × 10^9/L
Blood Chemistry Tests						
ALT	401 U/L	305 U/L	184 U/L	116 U/L	27 U/L	9-50 U/L
AST	664/L	574 U/L	86 U/L	89 U/L	45 U/L	15-40 U/L
AMY	45	37	NA	NA	NA	40-130 U/L
LPA	25	23	NA	NA	NA	0-180 U/L
GGT	1423 U/L	1567 U/L	1354 U/L	1274 U/L	45 U/L	10-60 U/L
Urea	19.36 mmol/L	22.5 mol/L	6.6 mmol/L	2.4	NA	2.8-8.2 mmol/L
CRE	394.7 umol/L	347 umol/L	99 umol/L	48.4	NA	44-133 umol/L
GLU	24.46 mmol/L	20.46 mmol/L	8.3	6.38	6.38 mmol/L	3.89-6.11 mmol/L
TG	4.85 mmol/L	2.93 mmol/L	NA	NA	NA	0.23-1.7 mmol/L
LDH	815 U/L	NA	213	NA	NA	120-250 U/L
CK	4634 U/L	1402 U/L	230 U/L	57 U/L	22 U/L	50-310 U/L
CKMB	NA	29.3 U/L	13.0 U/L	13.4	9	0-24 U/L
CRP	257.25 mg/L	169.88 mg/L	68.36 mg/L	17.15 mg/L	13.93 mg/L	0-3 mg/L
Na^+	141.3	129.6 mmol/L	NA	NA	NA	137-147 mmol/L
HbA1c	NA	5.20%	NA	NA	NA	5-6.3%
UA	1131 u/L	975 u/L	NA	239 u/L	237 u/L	208-428 u/L
ESR	41 mm/h	NA	NA	NA	32	0-20 mm/h
Blood Gas Analysis						
PH	7.29	7.4	NA	NA	NA	7.35-7.45
BE	-15.2	-10	NA	NA	NA	-2-3 mmol/L
Routine Urine Analysis						
PH	5.5	NA	5	NA	NA	5-7.5
Glucose	3+	NA	-	NA	NA	-
Protein	1+	NA	-	NA	NA	-
Ketone bodies	1+	NA	-	NA	NA	-

NA: Not Available.

There were no obvious skin rashes or other symptoms. Clear breathing was heard in both lungs. The heart rhythm was irregular. Arrhythmia including audible and premature beats was detected. Routine admission laboratory tests performed immediately, and the results were summarized in **Table 1**. Peripheral blood examination revealed elevated high blood glucose (24.6 moll/L (442.8 mg/dl)), ketosis, elevated leukocyte count, metabolic acidosis with a pH level of 7.29 and elevation of liver function tests. Fulminant type 1 diabetes mellitus is often accompanied by elevated amylase and lipase, and patients have a history of alcohol consumption, but patients with amylase and lipase are normal. The urinalysis showed a very high level of sugar (3+), presence of protein (+) and Ketone bodies (1+) in his urine. Patient was suspected to have Fulminant Type 1 diabetes mellitus and received immediate treatment. Treatment includes administration of adequate liquid infusion, intravenous injection of regular insulin to reduce blood glucose, and correction of electrolyte disturbance, acid-base imbalance. Twelve hours after admission, the urinary ketone bodies were negative, and the blood Ph increased to 7.37. To further control his glucose level, the patient was admitted to our department. On day 2, the HbA1c was 5.2%. Laboratory examinations were repeated on day 2, day 4, week 1 and week 2 (**Table 1**). On week one, the patient received the oral glucose tolerance test (OGTT), the insulin releasing test (IRT) and C-peptide release test (CRT)

Table 2. Results of OGTT, IRT and CRT at week 1

Time (min)	OGTT (Glucose, mmol/L)	IRT (Insulin, uIU/mL)	CRT (C-peptide, ng/mL)
0	6.38 (114.84 mg/dl)	2.38	0.07
30	10.47 (118.46 mg/dl)	4.79	0.05
60	14.39 (259.02 mg/dl)	6.40	0.02
120	17.65 (316.08 mg/dl)	6.16	0.07
180	12.46 (224.28 mg/dl)	5.97	0.02

OGTT: Oral Glucose Tolerance Test; IRT: Insulin Release Test; CRT: C-Peptide Releasing Test. The normal range of OGTT (0 min, 120 min) 3.9-6.0 mmol/L (70.2-108 mg/dl)/<7.8 mmol/L (140.4 mg/dl). The normal range of IRT (0 min, 30 min-60 min, 180 min) 5-20/25-200/5-20 uIU/mL. The normal range of CRT (0 min, 30 min-60 min, 120 min, 180 min) 0.3-1.3/1.5-13/<30/10-20 ng/mL.

(**Table 2**). The results of these tests further confirmed the increased glucose level and β-Cell dysfunction resulting in decreased insulin secretion in this patient. On week two, results from the blood chemistry tests showed normal liver and kidney function suggesting that the liver and kidney damage was transient and controlling the glucose level was able to reverse liver and kidney damage. Negative results were obtained from urine amylase test, blood lipase test, thyroid gland function test, blood coagulation test, stool culture, and measurement of the islet autoantibodies including islet cell antibody (ICA), glutamic acid decarboxylase (GAD) and insulin autoantibodies (IAA). After 16 days' treatment, the patient was discharged but continued with insulin (34 u/d) treatment for six months. After 2 months of telephone follow-up after discharge, the patient still maintained the above treatment protocol, tested FPG 8-10 mmol/L (144-180 mg/dl), 2hPG10-15 mmol/L (180-270 mg/dl), no acute complications of hypoglycemia or hyperglycemia and uncomfortable symptoms occurred.

Discussion and conclusion

Fulminant Type 1 diabetes mellitus is a novel subtype of Type 1 diabetes [1]. This subtype is characterized by its sudden onset of diabetic ketoacidosis, absence of insulin secretion and diabetes-related antibodies and high serum pancreatic enzyme concentrations [1, 2]. In China, fulminant type 1 diabetes accounts for ~10% of the ketosis-onset type 1 diabetes cases [3].

The etiology and pathogenesis of Fulminant type 1 diabetes are still not fully understood. Several factors such as viral infection, genetic susceptibility, autoimmunity, pregnancy etc. seem to be involved [4-6]. In our case, the patient had a long history of excessive alcohol use 500-750 g of pure alcohol a day for 8 years. The patient presented to our hospital with persistent diarrhea without abdominal pain. According to the classification of diabetes mellitus by the American Diabetes Association or the World Health Organization [7], Fulminant type 1 diabetes has the following clinical characteristics: (i) duration of hyperglycemic symptoms is 4 days on average; (ii) there is a high prevalence of preceding common-cold-like and gastrointestinal symptoms; (iii) there is a near-normal level of glycated hemoglobin (HbA1c) in spite of very high plasma glucose levels associated with ketoacidosis; (iv) the disease is sometimes related to pregnancy; and (v) there are increased serum pancreatic enzyme levels, absent C-peptide levels, but virtually no detectable autoantibodies against constituents of pancreatic beta cells. In our case, the patient is (i) a young male with normal BMI and no family history of diabetes; (ii) characterized by the rapid onset of disease; (iii) has signs of gastrointestinal infection caused by excessive drinking; (iv) findings on admission includes hyperglycemia levels but normal HbA1c levels; (v) ketoacidosis at onset and transiently increased liver and kidney function tests, muscle enzymes and uric acid; (vi) after correction of ketoacidosis, symptoms improved; (vii) the levels of C-peptide and insulin were significantly reduced with the progression of the disease; (viii) during treatment with insulin, the blood glucose levels of the patient fluctuated significantly.

Treatment of the disease is similar to autoimmune diabetes [2]. Once diagnosed with ketoacidosis, it should be treated immediately. After the acute phase of treatment, long-term glycemic control by insulin therapy is required, but it is difficult to make the blood glucose control ideal for conventional insulin intensive treatment [1]. In our case, 4 days after treatment, results from routine blood test and kidney function tests were normal. One week after treatment, his blood uric acid level returned to a normal value. Two weeks after treatment, the liver function was fully recovered. FT1D progresses rapidly and the prognosis is extremely poor. Compared with classic type 1 diabetes,

these patients usually require high doses of insulin and are more prone to hypoglycemia and acute complications. Therefore, early diagnosis and treatment are important to the outcome. At the same time, pay attention to long-term blood glucose control after stabilization to delay the occurrence of complications and reduce the disability rate.

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Disclosure of conflict of interest

None.

Abbreviations

FT1DM, fulminant type 1 diabetes mellitus; T, temperature; P, pulse rate; R, respiration rate; BP, Blood Pressure; OGTT, Oral glucose tolerance test; IRT, Insulin releasing test; CRT, C-peptide release test; ICA, Islet cell antibody; GAD, Glutamic acid decarboxylase; IAA, Insulin autoantibodies; HbA1c, glycated hemoglobin.

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References

[1] Imagawa A, Hanafusa T, Awata T, Ikegami H, Uchigata Y, Osawa H, Kawasaki E, Kawabata Y, Kobayashi T, Shimada A, Shimizu I, Takahashi K, Nagata M, Makino H and Maruyama T. Report of the Committee of the Japan Diabetes Society on the research of fulminant and acute-onset type 1 diabetes mellitus: new diagnostic criteria of fulminant type 1 diabetes mellitus. J Diabetes Investig 2012; 3: 536-539.

[2] American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2021. Diabetes Care 2021; 44 Suppl 1: S15-S33.

[3] Hosokawa Y, Hanafusa T and Imagawa A. Pathogenesis of fulminant type 1 diabetes: genes, viruses and the immune mechanism, and usefulness of patient-derived induced pluripotent stem cells for future research. J Diabetes Investig 2019; 10: 1158-1164.

[4] Imagawa A and Tachibana M. Fulminant type 1 diabetes: recent research progress and future prospects. Diabetol Int 2020; 11: 336-341.

[5] Hayakawa T, Nakano Y, Hayakawa K, Yoshimatu H, Hori Y, Yamanishi K, Yamanishi H, Ota T and Fujimoto T. Fulminant type 1 diabetes mellitus associated with Coxsackievirus type B1 infection during pregnancy: a case report. J Med Case Rep 2019; 13: 186.

[6] Okahata S, Sakamoto K, Mitsumatsu T, Kondo Y, Noso S, Ikegami H and Shiba T. Fulminant type 1 diabetes associated with Isolated ACTH deficiency induced by anti-programmed cell death 1 antibody-insight into the pathogenesis of autoimmune endocrinopathy. Endocr J 2019; 66: 295-300.

[7] American Diabetes Association. Erratum. Classification and diagnosis of diabetes. Sec. 2. In standards of medical care in diabetes-2016. Diabetes Care 2016; 39: 1653.