FULMINANT TYPE 1 DIABETES WITH NORMAL SERUM AMYLASE: A CASE REPORT

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ABSTRACT

Fulminant type 1 diabetes (FT1D) is a subtype of type 1 diabetes characterized by abrupt onset, acidosis at diagnosis, negative status of islet-related autoantibodies, and nearly no C-peptide secretion. Our hospital admitted an 18-year-old man who had HbA1c 5.7%, Autoantibodies against pancreatic β cells were negative, serum amylase 92 U/L presented in diabetic ketoacidosis on admission. CT scan of the liver showed localized edema. After two weeks of intensive insulin therapy, his serum and urine amylases were still in the normal range, autoantibodies against pancreatic β-cells were still negative, and abdominal CT showed that the local liver edema disappeared. In this report, a case of fulminating type 1 diabetes with normal serum amylase is concerned.

Keywords: *fulminant type 1 diabetes, Serum amylase, diabetic ketoacidosis.*

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Introduction

First reported in 2000, fulminant type 1 diabetes is characterized by sudden onset and rapid progression to ketoacidosis, low HbA1c levels, and shortage of islet-related autoantibodies[(1)]. The most common symptoms of FT1D flu-like symptoms, including thirst and drowsiness; abdominal symptoms include nausea, vomiting, and abdominal pain[(2)]. FT1D is a subtype of idiopathic type 1 diabetes, which is also characterized by elevated serum pancreatic exocrine enzymes[(3)], and contains monocytes infiltration[(4)]. So far, Japan has made most reports of FT1D, and FT1D accounts for 3.04% of patients with new-onset type 1 diabetes in China[(5)]. Although the etiology of FT1D remains controversial, genetic factors, including human leukocyte antigen (HLA), and environmental factors, including viral infections, have been shown to influence the development of the disease[(6)]. Here, a case of FT1D with normal serum amylase is presented in contrast to previously reported findings.

Clinical description

Our hospital admitted an 18-year-old man on November 16, 2020.The patient presented with dry mouth, polydipsia, and polyuria 6 days before thethe onset of the disease and nausea, vomiting, and abdominal pain three days ago. After a visit to a nearby hospital, he was diagnosed with acute gastroenteritis. Despite the treatment with Pantoprazole, Metoclopramide and intravenous

fluid resuscitation, his symptoms did not abate. early in the morning of November 15, he was admitted to the emergency department of our hospital due to chest discomfort and unconsciousness. On examination, his heart rate was 110 beats/min and he had abdominal tenderness. Lab test results showed a significantly elevated fasting plasma glucose (43.29 mmol/L) level, pH value 7.153 and urine ketone ++. Although the patient has no history of diabetes, his grandmother suffered from diabetes at age 60.

Variable		Reference range
Complete blood count		
White blood cell, $\times 10^9$/L	9.9	3.5-9.5
Red blood cell, $\times 10^{12}$/L	4.47	4.3-5.8
Hemoglobin, g/L	142	130-175
Hematocrit, %	44.4	40-50
Platelets, $\times 10^9$/L	156	125-350
Artery blood gas analysis		
pH	7.417	7.35-7.45
pO_2, mmHg	89.2	83-108
pCO_2, mmHg	36.6	35-48
Lactate, mmol/L	1.27	0.5-2.2
Base excess, mmol/L	-1.0	-3.0-3.0
Anion Gap, mmol/L	17.1	8-16
Urinalysis		
pH	6.5	5.4-8.4
Ketone bodies	+++	-
Biochemistry		
Na, mmol/L	138.3	137-147
K, mmol/L	3.88	3.5-5.3
Islet-related autoantibodies		
IAA, COI	0.04	<1.0
GADA, IU/mL	4.21	<10
GADA, IU/mL(2 week)	3.67	<10
IA-2A, IU/mL	4.5	<10
ICA, COI	0.27	<1.0
ZnT8A, IU/mL	1.0	<10
Pancreatic amylase		
Urine amylase, U/L	358	50-875
Serum amylase, U/L	92	35-135
Urine amylase, U/L (2 week)	369	50-875
Serum amylase, U/L (2 week)	95	35-135
Serological testing for virus		
EBVCA IgM, U/mL	12.75	<20.00
EBVCA IgG, U/mL	744.00	<20.00
HSVIIgM	-	-
HSVIIgG	+	-
DNA typing		
HLA-DRB1*03:01-HLA-DQB1*02:01		
HLA-DRB1*12:02-HLA-DQB1*03:01		

Table 1: The laboratory results of an 18-year-old man with FT1D.

He was admitted to the hospital after being diagnosed as diabetic ketoacidosis (DKA). On examination, he was conscious but lethargic and smelled of ketones on breathing, and had a blood pressure of 118/76 mmHg. He had a waist circumference of 75cm, a body mass index (BMI) of 21.8 kg/m2, was well developed and moderately nourished. According to physical examination, no significant positive signs except poor skin elasticity were found. Other tests showed negative glutamic acid decarboxylase antibody (GADA), islet cell antibody (ICA), anti-insulin antibody (IAA), tyrosine phosphatase antibody (IA-2A) and zinc transporter 8 autoantibody (ZnT8A). Fasting C-peptide was less than 0.01 ng/ml and HbA1c was 5.7%. Serum lipase was normal (Table 1).

Based on these findings, the patient was diagnosed with FT1D. Upon admission, he was treated with continuous intravenous infusion of small amounts of insulin and fluid supplementation. After ketosis resolved, 100g standard steamed buns meal test was re-examined, and the levels of plasma glucose, C-peptide and insulin were assessed at baseline (0 minutes) and 120 minutes during the test.

	0 min	120 min
Blood glucose (mmol/L)	4.82	24.64
C-peptide (ng/mL)	<0.01	<0.01
Insulin (μIU/mL)	<0.20	<0.20

Table 2: Data of 100g steamed bread meal test.

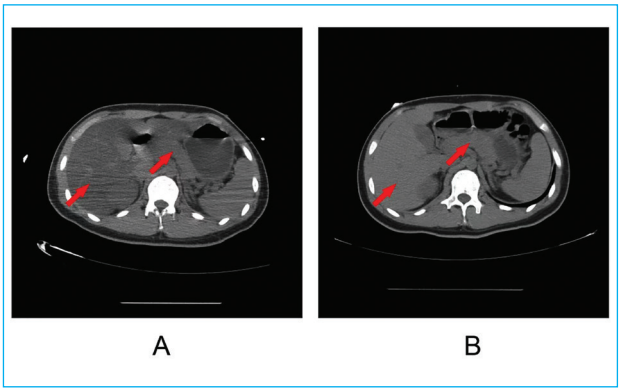

Figure 1: A There was local edema in the liver and normality in the pancreas during DKA. **B** After 2 weeks, the liver returned to normal and the pancreas was normal..

As shown in Table 2, the patient failed to regain islet function after inpatient treatment. During the course of the disease, abdominal CT scan indicated localized edema in the liver and no abnormalities in the pancreas (Fig1). Coxsackie A/B, EV71, EV common type, Measles virus, cytomegalovirus (CMV), adenovirus (ADV), herpes simplex virus(HSV)I/II , EB virus capsid antigen (EBVCA) were all negative except EBVCA IgG and HSVIIgG. According to HLA typing, the patient was heterozygous of HLA-DRB1*03:01-

HLA-DQB1*02:01 After the resolution of DKA, he was treated with continuous subcutaneous insulin injection. After inpatient treatment, the plasma glucose was controlled and stable, and the patient's insulin requirement was about 46.8 units per day. Three months after discharge, he required 32.2 units of insulin per day to achieve glycemic control. Tests for GADA, ICA, IAA, IA-2A, and ZnT8A were still negative. We observed that the patient's fasting serum C-peptide level remained less than 0.01 ng/mL and HbA1c was 7.3%.

Discussion

The case of a young male patient with FT1D and normal serum amylase was described. Our clinical findings in this case were consistent with the diagnostic criteria for FT1D. Genetic and environmental factors influence the pathogenesis of FT1D[7]. With regard to genetic factors, susceptibility to progress to FT1D is related to HLA class II genes. Commonly, most East Asian populations suffer from HLA DR4 haplotype, while the Korean population is unique in that the DR3 haplotype[8]. Our patient also exhibited this typical HLA type.

In terms of environmental factors, viral infections, especially enterovirus infections, can cause the co-expression of interferon (IFN)-g and CXCL10 in β cells in patients with FT1D. IFN-g can both destroy β cells and accelerate CXCL10 production by the remaining β cells. The autoimmune response is activated until the β-cells are completely destroyed. Thus, the destruction of β-cells in FT1D is the result of a vicious cycle[9]. Among several patients with type 1 diabetes caused by viral infections, a significant elevation of amylase can be observed, and it is thought that the mechanism is not autoimmunity, but rather antiviral inflammation exerting an etiopathological effect on fulminant type 1 diabetes[10]. In this case, multiple viruses were tested and there was no recent viral infection.

One of the characteristics of FT1D is the elevation in the level of serum pancreatic enzymes, which is believed to be related to autoimmune inflammation of the pancreas[11]. The patient did not show signs of acute pancreatitis, his serum amylase was normal, and abdominal CT did not show pancreatic inflammation. A survey on FT1D found that 42% of patients did not increase serum amylase[12]). The reason may be that FT1D may only trigger an immune response against pancreatic islet cells within a few months after the onset, without causing pathological changes in pancreatic inflammation. Such as edema changes, necrosis, hemorrhage, cyst formation, and exocrine pancreatic atrophy[13]. This indicates that elevated serum amylase may not be a specific marker of FT1D. Some studies believe that the increase in serum amylase is related to the degree of DKA. In patients with severe DKA, serum amylase can account for 60%. During DKA, blood volume decreases, and glomerular filtration rate decreases, resulting in decreased pancreatic enzymes[14]. Although the patient's DKA was accompanied by weakened skin elasticity, the serum amylase did not increase. It may be that the patient's blood pressure has been normal, indicating that his blood volume has not decreased significantly.

Conclusion

These indicate that the patient has no evidence of FT1D caused by common viral infections and has not reached the level of severe DKA. Therefore, this may be the reason why the serum amylase is within the normal range.

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Author Contributions

JY: completed the background research and drafted and edited the manuscript. ST and ZM: drafted the manuscript. ZS and QJ: edited the manuscript. KY: edited the manuscript and approved the final manuscript.

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