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CASE REPORT

A Case Report of an Elderly Type 2 Diabetes Mellitus Complicated with Fulminant Type 1 Diabetes Mellitus

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SUMMARY

Background: **Fulminant type 1 diabetes mellitus (FT1DM) is a new subtype of type 1 diabetes mellitus, first proposed by Japanese scholars. Its main clinical features include acute onset (< 1 week), pancreatic islet function failure, negative islet-related autoantibodies, and concurrent ketosis or diabetic ketoacidosis. A recent study in Japan indicated that the incidence of FT1DM accounts for 15 - 20% of all ketosis or ketoacidosis-related type 1 diabetes mellitus. However, cases of type 2 diabetes mellitus complicated with FT1DM are rarely reported.**

Methods: **A comprehensive analysis of the clinical characteristics and diagnosis-treatment process was conducted by monitoring key indicators such as the patient's blood glucose, glycated hemoglobin, pancreatic islet function, amylase levels, and diabetic autoantibodies, and integrating this data with the patient's medical history and relevant literature.**

Results: **The patient was diagnosed with type 2 diabetes mellitus complicated with fulminant type 1 diabetes mellitus.**

Conclusions: **Clinicians should enhance their understanding of fulminant type 1 diabetes to achieve early diagnosis and treatment.**

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KEYWORDS

type 1 diabetes mellitus, type 2 diabetes mellitus, fulminant type 1 diabetes mellitus

INTRODUCTION

Fulminant type 1 diabetes mellitus (FT1DM), as a new subtype of type 1 diabetes mellitus, has received increasing attention in recent years. The clinical features of FT1DM are rapid disease progression. Ketosis or ketoacidosis often occurs within one week, with a significant increase in blood glucose, but normal or slightly elevated glycated hemoglobin. The function of pancreatic β cells is completely destroyed, resulting in absolute deficiency of insulin secretion, and the diabetic autoantibody is negative. Many patients can have the characteristics of both type 1 diabetes and type 2 diabetes. In 2013, FT1DM developed on the basis of type 2 diabetes was first reported in Japan [1]. Currently, there are still relatively few case reports of type 2 diabetes combined

Case Report accepted May 8, 2025

with FT1DM. This article reports a case of elderly type 2 diabetes mellitus complicated with fulminant type 1 diabetes mellitus and analyzes its clinical characteristics and diagnosis and treatment process in combination with relevant literature.

CASE PRESENTATION

A 70-year-old male presented to the Endocrinology Clinic of Shaoxing Central Hospital on June 29, 2021, with a history of "elevated blood glucose discovered 2 years ago and poor glycemic control over the past 3 days." Two years prior, during a routine physical examination, the patient was diagnosed with elevated fasting blood glucose (7.6 mmol/L) accompanied by symptoms of dry mouth, polydipsia, and polyuria. Oral hypoglycemic therapy with metformin and glimepiride sustained-release tablets was initiated. However, the patient did not adhere to a regular medication schedule or routinely monitor his blood glucose levels. One month prior, due to blurred vision, the patient was hospitalized in the Endocrinology Department of Shaoxing Central Hospital. During this admission, glycated hemoglobin (HbA1c) was measured at 9%, diabetes autoantibodies were negative, and urine ketones were negative. The results of the oral glucose tolerance test (OGTT) were as follows: fasting blood glucose 6.95 mmol/L, 0.5-hour postprandial blood glucose 7.62 mmol/L, 1-hour postprandial blood glucose 14 mmol/L, 2-hour postprandial blood glucose 20.71 mmol/L, and 3-hour postprandial blood glucose 19.48 mmol/L. The C-peptide release test showed: fasting C-peptide 0.49 ng/mL, 0.5-hour postprandial C-peptide 0.97 ng/mL, 1-hour postprandial C-peptide 1.43 ng/mL, 2-hour postprandial C-peptide 3.44 ng/mL, and 3-hour postprandial C-peptide 3.84 ng/mL. Based on these findings, the patient was diagnosed with type 2 diabetes mellitus (T2DM). Treatment included subcutaneous injections of protamine zinc recombinant lispro insulin (25R) at doses of 18 IU before breakfast and 12 IU before dinner, along with oral metformin tablets (500 mg twice daily). Following discharge, the patient adhered to the prescribed regimen and maintained regular eating habits. Fasting blood glucose was controlled between 5 - 6 mmol/L, and 2-hour postprandial blood glucose was controlled between 9 - 11 mmol/L. Three days prior to the current presentation, the patient experienced a significant increase in blood glucose levels, with fasting blood glucose reaching 16 mmol/L and 2-hour postprandial blood glucose reaching 27 mmol/L. At that time, the patient reported mild nasal congestion but no chills, fever, cough, sputum production, abdominal pain, diarrhea, nausea, or vomiting. Physical examination revealed: body temperature 36.5°C, pulse rate 60 beats/minute, blood pressure 95/57 mmHg, respiratory rate 19 breaths/minute, BMI 25.04 kg/m². No significant enlargement of the thyroid or lymph nodes was noted. Lung auscultation revealed clear breath sounds without rales. Cardiac rhythm was regular with no murmurs. The abdomen was soft, with no tenderness or rebound tenderness, and there was no edema in the lower extremities. Auxiliary examinations included: outpatient re-evaluation of HbA1c at 8.6%, serum amylase at 312 U/L, negative diabetes autoantibodies, normal blood routine and CRP, negative urine ketones, and an abdominal CT scan showing no abnormalities. The OGTT results were as follows: fasting blood glucose 10.93 mmol/L, 2-hour postprandial blood glucose 23.03 mmol/L. The C-peptide release test showed: fasting C-peptide 0.01 ng/mL and 2-hour postprandial C-peptide 0.01 ng/mL.

The patient underwent hypoglycemic treatment at the outpatient clinic, receiving insulin aspart 6 IU subcutaneously before each meal and insulin degludec 8 IU subcutaneously before bedtime. After one week of this four-times-daily insulin regimen, the patient returned to our outpatient clinic for follow-up. At that time, the blood amylase level was 123 U/L, urine amylase was 1,566 U/L, fasting blood glucose was 6.7 mmol/L, and 2-hour postprandial blood glucose was 9.8 mmol/L. Following two months of continued treatment, the patient revisited our outpatient clinic on September 12, 2021. During this period, the patient adjusted the insulin dosage in accordance with fluctuations in blood glucose levels. Glycated hemoglobin was measured at 7.7%, and both blood and urine amylase tests were negative. Additionally, diabetes autoantibody testing results were negative. The steamed bun meal test was repeated, revealing a fasting blood glucose level of 6.34 mmol/L and a 2-hour postprandial blood glucose level of 20.76 mmol/L. The C-peptide release test indicated fasting C-peptide levels of < 0.01 ng/mL and 2-hour postprandial C-peptide levels of < 0.01 ng/mL, suggesting pancreatic β-cell failure. Based on the patient's medical history and changes in pancreatic function (Table 1), the final diagnosis was type 2 diabetes mellitus complicated by fulminant type 1 diabetes mellitus.

DISCUSSION

Fulminant type 1 diabetes mellitus (FT1DM), first described by Japanese scholars Imagawa et al. in 2000, represents a distinct subtype of type 1 diabetes mellitus (T1DM) [2]. The exact pathogenesis of FT1DM remains elusive but is believed to involve multiple factors, including autoimmunity, viral infections, and environmental triggers. It has been hypothesized that viral infection of pancreatic islets and exocrine acinar cells initiates antiviral immune responses, subsequently activating the host's immune system and leading to the rapid and near-complete destruction of pancreatic islet cells, predominantly β-cells [3,6]. The implicated viruses are acute cytopathic viruses, typically belonging to the Picornaviridae family, such as enteroviruses (EV), human herpesvirus 6, influenza B virus, Coxsackie virus, and cytomegalovirus [4,5]. Key pathological features of FT1DM include insulitis and exocrine pan-

Table 1. The process of pancreatic function changes in response to the steamed bread meal test.

	Time	0 hour	0.5 hour	1 hour	2 hours	3 hours
Duration of hospital stay	**blood glucose (mmol/L)**	**6.95**	**7.62**	**14**	**20.71**	**19.48**
	C-peptide (ng/mL)	**0.49**	**0.97**	**1.43**	**3.44**	**3.84**
The initial outpatient follow-up visit	**blood glucose (mmol/L)**	**10.93**	**/**	**/**	**23.03**	**/**
	C-peptide (ng/mL)	**0.01**	**/**	**/**	**0.01**	**/**
The subsequent outpatient follow-up visit	**blood glucose (mmol/L)**	**6.34**	**/**	**/**	**20.76**	**/**
	C-peptide (ng/mL)	**< 0.01**	**/**	**/**	**< 0.01**	**/**

creatitis, with evidence of viral infection observed in both islet cells and exocrine tissues [6,7]. FT1DM predominantly affects East Asian populations, and certain genetic predispositions, particularly human leukocyte antigen (HLA) class II genes, are strongly associated with disease susceptibility [8,9]. Genome-wide association studies conducted on Japanese patients with fulminant type 1 diabetes mellitus have demonstrated that single nucleotide polymorphisms within the HLA region, especially in the class II DR locus, play a critical role in the onset and progression of FT1DM [10]. Additionally, pregnancy, medications, and immunosuppressive agents may contribute to the development of FT1DM.

In 2021, the Japanese Diabetes Society updated the diagnostic criteria for fulminant type 1 diabetes mellitus (FT1DM) [11]. A diagnosis of FT1DM can be established when all three of the following conditions are fulfilled: 1) ketosis or diabetic ketoacidosis develops within one week of the onset of diabetes symptoms; 2) plasma glucose levels are ≥ 16.0 mmol/L and glycated hemoglobin levels are < 8.7%; 3) fasting serum C-peptide levels are < 0.3 ng/mL and postprandial C-peptide levels are < 0.5 ng/mL. Furthermore, additional characteristics of FT1DM include: 1) islet-related autoantibodies are typically undetectable; 2) insulin therapy is generally required within 1 - 2 weeks of symptom onset; 3) elevated serum pancreatic enzyme levels are observed in 98% of patients; 4) approximately 70% of patients may exhibit flu-like or gastrointestinal symptoms prior to disease onset; 5) the condition may occur during pregnancy or immediately postpartum; 6) it is associated with the HLA DRB1*04:05-DQB1*04:01 haplotype. FT1DM constitutes 14.0% to 30.4% of adult cases of type 1 diabetes mellitus [12]. However, in recent years, there have been reports of fulminant type 1 diabetes occurring in the context of type 2 diabetes management. For such cases, clinicians should ensure accurate diagnosis and timely intervention.

This case report involves a 70-year-old diabetic patient who has been managed with oral hypoglycemic agents for two years. One month ago, during hospitalization at our institution, pancreatic function was assessed as acceptable, and pancreatic-related autoantibodies were negative. During the hospital stay and following discharge, intensive insulin therapy was administered, achieving stable glycemic control. Three days ago, there was a marked increase in blood glucose levels, with fasting blood glucose reaching 16 mmol/L. Re-examination revealed glycated hemoglobin (HbA1c) of 8.6%, which was lower than the level prior to admission. At that time, fasting C-peptide was 0.01 ng/mL, and 2-hour postprandial C-peptide was also 0.01 ng/mL. After two months of intensive insulin therapy, re-evaluation of the meal tolerance test showed both fasting C-peptide and 2-hour postprandial C-peptide levels were < 0.01 ng/mL, indicating complete loss of pancreatic β-cell function. The patient did not exhibit overt ketosis or diabetic ketoacidosis, likely due to the initiation of insulin therapy before the onset of symptoms. Although most patients with fulminant type 1 diabetes mellitus (FT1DM) present with flu-like or gastrointestinal symptoms prior to disease onset, it has been reported that many elderly patients with FT1DM do not display prominent infection-related symptoms [1]. This patient experienced mild upper respiratory tract infection symptoms before symptom onset, confirming that factors such as autoimmunity, viral infection, environmental triggers, and pregnancy can all contribute to the development of FT1DM [13,14]. Most patients with FT1DM exhibit elevated pancreatic enzyme levels. In this case, both serum and urinary amylase levels increased after symptom onset; however, abdominal CT did not reveal pancreatitis. Following hypoglycemic treatment, amylase levels normalized. Based on the diagnostic criteria and clinical characteristics of FT1DM, this case was diagnosed as type 2 diabetes mellitus complicated by FT1DM.

Therefore, FT1DM is not exclusively observed in non-elderly patients but can also manifest in elderly individuals with type 2 diabetes. It should be considered as part of the differential diagnosis for diabetic ketoacidosis in elderly patients with type 2 diabetes to facilitate early diagnosis and timely intervention.

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Declaration of Interest:
All authors declare that they have no competing interests.

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