TYPE 1 DIABETES MELLITUS: FEATURES OF DIFFERENTIAL DIAGNOSIS

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Type 1 diabetes mellitus is a condition caused by autoimmune damage to insulin—producing beta cells of the pancreatic islets, leading to endogenous insulin deficiency. Despite the sufficient knowledge of the disease and the availability of clinical recommendations for substitution therapy, the number of patients with this pathology is growing worldwide. At the same time, their cohort is very heterogeneous, including amid different etiology, concomitant genetic background, variations in the manifestation of the disease and severity. In this regard, traditional ideas about type 1 diabetes mellitus are being questioned, which requires special attention when managing patients with a clinical picture of the disease that differs from the traditional one. The article presents a clinical case of type 1 diabetes mellitus in a young patient, which demonstrates the importance of a personalized approach to the diagnosis and treatment of diabetic patients with a "non-classical" history.

Keywords: type 1 diabetes mellitus, latent autoimmune diabetes in adults, differential diagnosis, diabetic neuropathy

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Compliance with ethical standards: the patient signed a voluntary informed consent to the publication of personal medical information in an anonymized form.

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САХАРНЫЙ ДИАБЕТ 1-ГО ТИПА: ОСОБЕННОСТИ ДИФФЕРЕНЦИАЛЬНОЙ ДИАГНОСТИКИ

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Диабет 1-го типа — это состояние, вызванное аутоиммунным повреждением инсулин-продуцирующих β-клеток островков поджелудочной железы, приводящее к эндогенному дефициту инсулина. Несмотря на достаточную изученность заболевания и наличие клинических рекомендаций по проведению заместительной терапии, количество больных с данной патологией растет по всему миру. При этом их когорта очень неоднородна, в том числе ввиду различной этиологии, сопутствующего генетического фона, вариаций манифестации заболевания и степени тяжести. В связи с этим, традиционные представления о сахарном диабете 1-го типа ставятся под сомнение, что требует особого внимания при ведении пациентов с клинической картиной заболевания, отличающейся от традиционной. В статье представлен клинический случай течения сахарного диабета 1-го типа у молодого пациента, который демонстрирует важность персонифицированного подхода к диагностике и лечению больных сахарным диабетом с «неклассическим» анамнезом.

Ключевые слова: сахарный диабет 1-го типа, аутоиммунный диабет взрослых, дифференциальная диагностика, диабетическая нейропатия

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Type 1 diabetes mellitus (DM1) continues to be one of the global medical and social problems due to its widespread prevalence, polymorphism, the development of severe sequelae and the irreversibility of changes. The number of patients in the Russian Federation with DM1 at the beginning of 2023 was 277,092 [1].

Despite the high degree of coverage of DM1 and the existing traditional paradigms of diagnosis and treatment approaches, it is not always possible to correctly diagnose this type of DM, which is associated with a variable onset and course, the presence of "non-classical" manifestations, as well as the existence of intermediate forms of the disease that combine the clinical signs of DM1 and type 2 DM (DM2), for example, such as latent autoimmune diabetes in adults (LADA) [2]. These factors also cause disadvantages in treatment, because the majority of people suffering from DM1 do not have an optimized glycemic profile [3].

In the clinical observation presented by us, the clinical picture of the course of DM1 with a "non-classical" history is shown and attention is focused on the need for diagnostic search and an individual approach to patient management.

Clinical case description

Primary hospitalization

Patient H. 26 years old, on 12.08.2022 entered the emergency department of the emergency hospital with complaints of general weakness, dry mouth, thirst, fatigue. During the initial examination, the following were revealed: hyperglycemia — 17 mmol/L, glucosuria, ketonuria. The patient was admitted to the therapeutic department of the hospital with a preliminary diagnosis of type 1 diabetes mellitus for the purpose of additional examination and selection of glucose-lowering therapy.

Table 1. Assessment of the level of glycemia (mmol/L) by a glucometer at using of insulin therapy (soluble insulin + insulin-isophane) in the period from 13.08.2022 to 22.08.2022

Date	Before breakfast	2 h after eating	Before lunch	2 h after eating	Before dinner	2 h after eating	At night
13.08.2022	15.7	16.1	12.5	13.6	11.0	13.2	12.1
14.08.2022	12.0	13.2	11.9	14.5	9.8	14.0	11.2
15.08.2022	10.9	11.8	10.5	9.3	10.0	10.9	9.1
16.08.2022	8.9	10.5	9.2	8.9	10.0	11.4	10.2
17.08.2022	11.3	10.5	9.3	9.8	10.1	11.3	9.2
18.08.2022	10.8	11.0	8.7	9.5	9.1	10.0	8.1
19.08.2022	8.8	9.1	7.3	8.8	7.9	9.1	8.5
20.08.2022	7.9	8.0	7.1	8.1	5.8	7.5	5.6
21.08.2022	7.7	8.3	6.0	7.2	5.8	6.3	5.3
22.08.2022	6.3	7.1	5.8	6.8	9.1	6.3	5.5

According to the patient, episodes of hyperglycemia up to 8–9 mmol/L were detected earlier during medical preventive examinations for two years, but he did not attach any importance to this, referring to violations of the rules for testing. In addition, for two months before going to the hospital, the patient had noted increased thirst and weight loss of 5 kg. He did not seek medical help.

It is known from the life history that the patient developed according to gender and age, has no bad habits. There are no chronic diseases and a burdened hereditary history, endocrinopathy included.

Objective findings: height — 190 cm, weight — 84 kg. The body mass index (BMI) is 23.3 kg/m^2. The skin and visible mucous linings are of the usual color and moisture content, skin tightness is retained. The thyroid gland is not palpable. There is no peripheral swelling. The heart tones are clear, rhythmic. Heart rate (HR) — 65 beats/min, blood pressure (BP) — 120/80 mm Hg. Breathing is auscultatory vesicular on both sides. Percussion — clear pulmonary sound. Respiratory rate (RR) is 16 per minute. The abdomen is of the correct shape, participates in the act of breathing, with palpation — soft, painless. The stool is formed, without any pathological admixtures. The urination is unimpeded, painless. The kidneys are not palpable. Pounding symptome (Pasternatsky's symptome) is negative on both sides.

1. Full blood count (FBC) from 12.08.2022: without pathological findings.

2. Urine analysis (UA) from 12.08.2022: glucosuria (+++), ketonuria (+), hypersthenuria (1,028 g/L).

3. Biochemical blood test: hyperglycemia: 12.08.2022 — 17.5 mmol/L, 19.08.2022 — 18.3 mmol/L, 20.08.2022 — 7.7 mmol/L, 23.08.2022 — 6.8 mmol/L. Glycated hemoglobin (HbA1c) — 10.5%. Indicators of protein metabolism, bilirubin fractions, iron, alanine aminotransferase (AlAT), aspartate aminotransferase (AsAT), gamma-glutamyl transferase (GGT), alkaline phosphatase, creatinine, urea, uric acid, C-reactive protein, Na^+, K^+, Ca^{2+}, Mg^{2+} ions are within normal limits.

4. Lipid profile: total cholesterol — 4.9 mmol/L, triglycerides (TG) — 1.8 mmol/L, high density lipoproteins (HDL) — 1.40 mmol/L, low density lipoproteins (LDL) — 3.1 mmol/L, very low-density lipoproteins (VLDL) — 0.8 mmol/L, atherogenicity index — 2.5.

5. Coagulation profile indicators are within the normal range.

6. The analysis of acid-alkali balance showed no abnormal changes.

7. The glomerular filtration rate (GFR) was calculated: 123.81 ml/min/1.73 m^2.

The patient was treated in the medical ward from 12.08.2022 to 24.08.2022.

The patient was treated in the form of basal bolus insulin therapy: soluble insulin and insulin-isophane.

During the entire treatment period, blood glucose was monitored (Table 1). The patient was discharged with a diagnosis of type 1 diabetes mellitus, first identified, the goal of HbA1c < 6.5%. It was recommended to continue treatment with insulin aspart subcutaneously (s/c) for 10–12 units before meals and insulin glargine s/c for 30 units in the evening once under the control of glycemia levels with possible dose adjustment, as well as to keep a diary of self-monitoring of blood glucose levels and adhere to a diet with a restriction of easily digestible carbohydrates. Preventive counseling on treatment issues was carried out, but group counseling at the Diabetes School was not practiced.

A few days after discharge, the patient began to present with thirst, dry mouth, frequent urination, and a feeling of crawling goosebumps in the area of the feet. Within a week, the glucose level began to rise again and was in the range of 10–13 mmol/L.

Repeated hospitalization

The patient was admitted on 30.08.2022 to the medical ward in a day hospital, taking into account clinical and laboratory decompensation of DM.

Upon admission: height — 190 cm, weight — 82 kg, BMI — 22.7 kg/m^2. Blood pressure — 115/68 mm Hg, heart rate — 71 beats/min, RR — 17 in min. There were no other changes in the objective status of the patient compared to the examination on 12.08.22. FBC, UA, lipid profile, coagulogram — within the normal range. The biochemical analysis revealed glucosuria — 13.9 mmol/L, the remaining parameters are without pathological findings. The HbA1c level from 30.08.2022 is 10.5%. Glycemic profile from 30.08.2022 (venous blood): 13.49 mmol/L (on an empty stomach); 17.4 mmol/L — 2 hours after meals, 4 hours — 16.6 mmol/L.

Ultrasonography of the abdominal organs from 31.08.2022 revealed no pathology.

Due to the presence of complaints about the feeling of "crawling goosebumps" in the area of the feet, a neurologist was consulted with. A symmetrical decrease in biceps reflexes, carporadial, hock reflex, a significant decrease in the Achilles reflex, impaired surface sensitivity of the polyneuritic type (according to the type of "stockings" from the lower tertile level of the shin) was revealed. When evaluated on the Neuropathy Symptom Scale (NSS), the total score was 4, which corresponds to moderate neuropathy [4]. Conclusion:

Table 2. Assessment of the level of glycemia (mmol/L) by a glucometer at using of insulin therapy (glulisin + degludec) in the period from 31.08.2022 to 09.09.2022

Date	Before breakfast	2 h after eating	Before lunch	2 h after eating	Before dinner	2 h after eating	At night
31.08.2022	10.1	12.5	8.3	13.0	10.0	10.8	7.9
01.09.2022	8.8	15.6	12.0	13.2	9.8	10.2	9.3
02.09.2022	7.9	10.2	9.8	9.5	7.6	8.1	7.8
03.09.2022	7.1	9.2	7.9	8.1	6.9	7.1	6.1
04.09.2022	6.3	7.5	5.9	7.1	5.6	7.8	5.6
05.09.2022	5.3	6.8	5.5	7.5	6.3	7.0	5.5
06.09.2022	5.6	7.0	6.0	6.9	5.8	7.1	5.8
07.09.2022	5.3	5.9	6.3	6.9	5.3	6.2	4.9
08.09.2022	5.6	6.9	5.0	5.2	5.3	6.2	5.4
09.09.2022	5.4	6.5	4.8	–	–	–	–

diabetic distal polyneuropathy, sensory form, moderate manifestations.

During the entire time of the patient's stay in the hospital, carbohydrate metabolism was monitored (Table 2).

The patient was treated with insulin degludec 25 units at 22.00, insulin glulisin at the rate of 1 bread unit (BU)): 2 units before meals to eliminate persistent postprandial hyperglycemia.

Starting from 05.09.2022, the glucose level began to gradually approach the goal, on 09.09.2022, reaching 5.4 mmol/L on an empty stomach and 6.5 mmol/L 2 hours after eating.

In order to verify the diagnosis, the patient was recommended to perform a study for the presence of autoantibodies to glutamic acid decarboxylase (GAD) and islet cells (ICA). The result from 09.09.2022: GADA — more than 1000 ME/ml; ICA — 256 U/ml.

Final diagnosis: type 1 diabetes mellitus, goal of HbA1c < 6.5%. Complications of the main diagnosis: diabetic distal polyneuropathy, sensory form, mild malfunctions.

The patient was discharged on 10.09.2022. To continue treatment, he was prescribed 25 units insulin degludec in the evening at 22.00, insulin glulisin at the rate of 1 BU: 2 units before meals.

Clinical case discussion

In this clinical case, the diagnosis of DM1 was more probable, since the patient's common complaints (weakness, dry mouth, thirst, fatigue), hyperglycemia, glucosuria, ketonuria, weight loss over the last 2 months, age < 30 years and BMI < 25 kg/m^2, absence of signs of metabolic syndrome indicate this pathological condition. However, the slow progression of DM, the absence of an acute onset, autoimmune diseases and predisposing factors are not quite definitive of the "classic" insulin-dependent diabetes. These characteristics are observed both with DM2, and, together with the onset at a young age and normal weight, with LADA [2, 5]. Due to the discrepancy of these signs, there is a need for an extended differential diagnosis.

For this purpose, an enzyme immunoassay was performed for the presence of antibodies to GAD and ICA. The positive result obtained disproves the presence of DM2, but does not exclude LADA. However, DM1 in young patients has a greater immunogenic load with faster damage to β-cells and a high need for insulin [2, 6–8], which was observed in the described clinical case. This fact can be confirmed by the determination of sharply decreased levels of C-peptide in DM1 than in LADA, in which this indicator decreases gradually [9, 10].

Anamnestic data indicate a similarity with LADA diabetes, however, a high concentration of autoantibodies, indicating a rapidly progressive decrease in the function of β-cells with the development of an acute hyperglycemic condition, comes more under the phenotype of DM1. There is also a classification that distinguishes stages in the development of DM1, including those with an asymptomatic onset [2, 11]. HLA genotyping can help in clarifying the diagnosis, since studies describe differences in the genetic profile of patients with LADA and DM1 in terms of the frequency of predisposing, protective genotypes and haplotypes [12, 13]. However, this method is not routine and it is not used for diagnosis in normal clinical practice, and therefore, the main role in such a diagnostic search will be played by the clinical picture.

One of the peculiarities of this case is the rapid development of complications of DM: diabetic distal neuropathy was diagnosed almost immediately after the diagnosis. Such rapid progression of complications is rare. Several cases of early onset of polyneuropathy have been described [14, 15]. It is possible that the symptoms of polyneuropathy occurred earlier, as well as episodes of hyperglycemia, but the patient did not complain before the induction of more serious malfunctions.

Defining the type of diabetes and taking into account the "non-classical" symptoms are necessary for the correct selection of insulin therapy, especially due to the fact that the patient had decompensation of diabetes mellitus, it was not immediately possible to achieve a stable tendency to decrease glycemia and there are complications already. Since the insufficiency of β-cell function is significant, insulin therapy is the right treatment tactic. However, repeated hospitalization with deterioration of health and persistent hyperglycemia may indicate both low patient adherence to treatment between admissions and inappropriate insulin dosages, in connection with which the drugs and therapy regimen were changed. The importance of differential diagnosis is confirmed in respect of the aspect of the fact that if this case is attributed to LADA diabetes, combination therapy with sugar-lowering oral drugs would be possible with a residual β-cell function, for the evaluation of which the laboratory workup of C-peptide is recommended.

CONCLUSION

Summarizing all available data, it can be claimed that in the described clinical case, the diagnosis of DM 1 is most likely. However, in our opinion, in such "non-classical" clinical setting, it is advisable to conduct the widest workup of DM: identification of the level of C-peptide for accurate diagnosis

verification, assessment of diabetes progression; performing electromyography to exclude other causes of neuropathic symptoms; consultation with an ophthalmologist to search for other possible microvascular complications. It is also important to monitor and maintain a sufficient level of patient compliance. The clinical observation presented by us indicates the importance of an individual approach to the management of patients with DM1, especially in the presence of similar signs with other types of DM, for timely therapy correction and prevention of progression, development of complications.

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