SIUDEK, Bartosz, DRÓŻDŻ, Olgierd, BIŃCZYK, Wiktoria, LISSAK, Karina, NOWIŃSKA, Bianka, BRZOZOWSKA, Patrycja and WIŚNIEWSKA, Anna. Re-diagnosis of diabetes mellitus type 1 to maturity-onset diabetes of the young type 2 (MODY 2) in a 26-year-old male: a case report. Quality in Sport. 2024;18:53394. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.18.53394
https://apcz.umk.pl/QS/article/view/53394

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 11.07.2024. Revised: 22.07.2024. Accepted: 31.07.2024. Published: 07.08.2024.

RE-DIAGNOSIS OF DIABETES MELLITUS TYPE 1 TO MATURITY-ONSET DIABETES OF THE YOUNG TYPE 2 (MODY 2) IN A 26-YEAR-OLD MALE: A CASE REPORT

1. Bartosz Siudek, MD

A. Falkiewicz Specialist Hospital, 52-114 Wrocław, Poland

https://orcid.org/0009-0002-4053-9724, bartosz.siudek98@gmail.com

2. Olgierd Dróżdż, MD

Wroclaw Medical University, Faculty of Medicine, Clinical Department of Diabetology and Internal Diseases, Borowska Str. 213, 50-556 Wrocław

https://orcid.org/0009-0006-6134-9101, olgierd.drozdz@gmail.com

3. Wiktoria Bińczyk, MD

Wroclaw Medical University, Faculty of Medicine, Clinical Department of Diabetology and Internal Diseases, Borowska Str. 213, 50-556 Wrocław

https://orcid.org/0009-0004-6600-9259, wiktoria.binczyk98@gmail.com

4. Karina Lissak, MD

Lower Silesian Oncology Center in Wrocław, Hirszfelda Square 12 53-413 Wrocław,

https://orcid.org/0009-0000-9084-4060, karina.lis2323@gmail.com

5. Bianka Nowińska, MD

4. Military Clinical Hospital SP ZOZ, Weigla 5, 53-114 Wrocław, Poland,

https://orcid.org/0000-0003-2335-3207; bianovinska@gmail.com

6. Patrycja Brzozowska, MD

Jan Mikulicz-Radecki University Clinical Hospital, Borowska 213, 50-556 Wrocław, Poland,

https://orcid.org/0000-0002-6630-4539; patrycja.brzozowska@hotmail.com

7. Anna Wiśniewska, MD

A. Falkiewicz Specialist Hospital, 52-114 Wrocław, Poland

https://orcid.org/0009-0000-6001-2167, awis.contact@gmail.com

Corresponding author: Olgierd Dróżdż, MD, Olgierd.drozdz@gmail.com

Abstract

Diabetes mellitus (DM) encompasses a spectrum of metabolic disorders characterized by hyperglycemia due to defects in insulin secretion, action, or both. Type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) are the most prevalent forms, whereas Maturity-Onset Diabetes of the Young (MODY) represents a monogenic subtype, often misdiagnosed due to its phenotypic overlap. This case study highlights a 26-year-old male initially diagnosed with T1DM at age 12, managed with insulin therapy. Upon admission, despite stable glycemic control and preserved C-peptide secretion, genetic testing revealed MODY 2 due to a variant in the GCK gene. Unlike T1DM and T2DM, MODY 2 is characterized by mild, persistent hyperglycemia with a low risk of complications, emphasizing the importance of genetic diagnosis for tailored management and family counseling. This case underscores the critical role of genetic evaluation in accurately diagnosing and managing atypical diabetes presentations.

Keywords: diabetes mellitus, MODY, insulin, genetic testing

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder that is characterized by hyperglycemia, which results from defects in insulin secretion, insulin action, or both. The global prevalence of diabetes has been rising steadily, with an estimated 537 million adults living with the condition as of 2021 [1]. Type 1 diabetes mellitus (T1DM), typically diagnosed in childhood or adolescence, constitutes approximately 5-10% of all diabetes cases. It is an autoimmune disorder in which the immune system attacks and destroys the beta cells in the pancreas that produce insulin, necessitating lifelong insulin therapy [2].

In contrast, type 2 diabetes mellitus (T2DM), which accounts for 90-95% of diabetes cases, typically manifests in adults and is associated with insulin resistance and relative insulin deficiency [3]. Both forms of diabetes are associated with a considerable increase in morbidity and mortality due to complications such as cardiovascular disease, neuropathy, retinopathy, and nephropathy [4].

Maturity-Onset Diabetes of the Young (MODY) is a monogenic form of diabetes that presents in adolescence or early adulthood and presents with clinical features that are similar to those of Type 1 or Type 2 diabetes. MODY accounts for approximately 1-2% of all diabetes cases and is frequently misdiagnosed due to its phenotypic overlap with other forms of diabetes [5]. It is inherited in an autosomal dominant pattern and is characterized by non-insulin-dependent diabetes with a significant family history of the disease. There are several subtypes of MODY, each caused by mutations in different genes affecting pancreatic beta-cell function. MODY 2, caused by mutations in the glucokinase (GCK) gene, results in mild, stable fasting hyperglycemia due to a higher glucose threshold for insulin secretion.

This case study presents the case of a young male who was initially diagnosed with T1DM at age 12. In accordance with the established diagnostic protocols for T1DM, the patient was initiated on an insulin therapy regimen, which he has continued for 14 years. Despite consistent adherence to the insulin regimen, glycemic control remained stable with relatively modest insulin requirements, and there were no episodes of diabetic ketoacidosis, indicating that the insulin regimen was effective.

Case description

A 26-year-old man was admitted to the Clinic of Diabetology and Internal Diseases for the diagnosis and modification of diabetes treatment. In his history, he had type 1 diabetes for 12 years, but he did not have documentation from the time of diagnosis. Additionally, the C-peptide level was unknown, and there were no tests for the autoimmune background of diabetes. The patient was treated with prandial insulin but did not count carbohydrate exchanges and only measured glucose levels using a glucometer.

The patient's family history was burdened with diabetes—his father and sister were diagnosed with diabetes of an unknown type. According to the patient, his sister was diagnosed a year ago and is treated with insulin.
Upon admission, the patient was in good general condition. The physical examination revealed a slight increase in blood pressure. In the laboratory tests [see Table 1.], random blood glucose was 137 mg/dl, lipid metabolism was well-controlled, C-peptide secretion was preserved, and the glycated hemoglobin percentage was 6%.
The mild, long-term course of diabetes, fasting glucose levels up to 130 mg/dl despite the absence of basal insulin use, preserved endogenous insulin secretion after 14 years of the disease, and positive family history led to the re-diagnosis of previously diagnosed insulin-dependent diabetes. MODY diabetes was suspected, and material was collected for the determination of HNF4 + GCK + CEL + INS genes. Insulin therapy was maintained until the diagnosis was verified. After three months, results confirmed the molecular diagnosis of MODY diabetes—variant c.214G>C in one allele of the GCK gene.

Parameter	Reference	Admission
Glucose (mg/dl)	70-99	137
HbA1c (%)	4-6	6
EGFR (ml/min/1.73m2)	>90	112
Sodium (mmol/L)	136-145	139
Potassium (mmol/L)	3.4-4.5	4.4
C-peptide (ng/ml)	0.78-5.19	1.32
Creatinine (mg/dl)	0.73-1.18	0,87
Total cholesterol (mg/dl)	130-200	156
HDL cholesterol (mg/dl)	>40	79
LDL cholesterol (mg/dl)	0-135	57
Triglycerides (mg/dl)	0-150	99

Table 1. Initial laboratory investigations

Discussion

Maturity-onset diabetes of the young (MODY) is a form of monogenic diabetes characterized by an autosomal dominant inheritance pattern and typically presents before the age of 25. Unlike the more common types of diabetes (type 1 and type 2), MODY results from mutations in a single gene that affects insulin production [6]. It is often misdiagnosed as either type 1 or type 2 diabetes, leading to inappropriate treatment strategies, as seen in the patient described.

MODY diabetes currently includes 14 subtypes, each caused by mutations in different genes. The most commonly reported MODY subtypes, HNF1A-(MODY3), GCK-(MODY2), HNF4A-(MODY3), and HNF1B-(MODY5), together account for over 80% of all MODY cases, while other subtypes (7-14) include mutations in various genes such as KLF11, CEL, PAX4, INS, BLK, ABCC8, KCNJ11, and APPL1 and are extremely rare.

MODY 2, caused by mutations in the glucokinase (GCK) gene, is the second most common subtype and is recognized as the cause of 30% to 60% of disease cases [7,8].

MODY 2 results from mutations in the GCK gene, which encodes glucokinase, an enzyme that acts as a glucose sensor in pancreatic β-cells. Glucokinase catalyzes the first step in glucose metabolism, which affects insulin secretion. Mutations lead to a higher glucose threshold for insulin release, resulting in mild, persistent hyperglycemia. This pathophysiology explains the typically mild clinical presentation of MODY 2, with stable blood glucose levels and a low risk of complications [9,10]. It also explains the good general condition, relatively low glycated hemoglobin percentage (indicating good glycemic control) and preserved C-peptide secretion in the described patient.

Because MODY diabetes, especially MODY 2, is a distinct clinical entity with unique genetic and pathophysiologic features, proper diagnosis and differentiation from type 1 and type 2 diabetes are critical for optimal management and family counseling. Differentiation can be based on clinical symptoms, blood glucose levels, HbA1c, and the presence of characteristic autoantibodies and low C-peptide levels (T1DM) or the presence of insulin resistance markers (T2DM). In terms of clinical presentation, T1DM is characterized by autoimmune destruction of pancreatic β-cells resulting in absolute insulin deficiency. It typically presents with acute symptoms of polyuria, polydipsia and weight loss, often in children and adolescents. TD2M is characterized by insulin resistance and relative insulin deficiency. It is more common in adults, often associated with obesity, and develops gradually. In contrast, MODY 2 diabetes usually presents with mild, asymptomatic hyperglycemia detectable from birth. Patients often have stable blood glucose levels without the risk of acute metabolic decompensation [11]. Another clue to consider MODY 2 as a potential diagnosis is a strong family history of diabetes, especially if diagnosed before the age of 25 [12].

The diagnosis of MODY involves a detailed clinical evaluation followed by genetic testing. First, the patient's family history and clinical features are evaluated to distinguish MODY from T1- and T2DM, as described above. Genetic testing is then performed to identify specific mutations in MODY-related genes. For MODY 2, sequencing of the GCK gene is performed. Commonly used methods include polymerase chain reaction (PCR) and Sanger sequencing. Next-generation sequencing (NGS) provides a more comprehensive analysis by sequencing the entire coding region of the GCK gene. In addition, multiplex ligation-dependent probe amplification (MLPA) has the ability to detect large deletions or duplications that may go undetected by other methods [7,12,13]. In the case of the described patients, the NGS method was used, which revealed the variant c.214G>C in one allele of the GCK gene (heterozygous state). This genetic confirmation is crucial as it not only solidifies the diagnosis, but also informs clinical management and allows screening of at-risk family members.

In summary, MODY 2 is a unique and distinct form of diabetes with specific genetic and clinical characteristics. Understanding these differences is essential for accurate diagnosis and management to ensure that patients receive appropriate care and genetic counseling. The patient's story and the initial misdiagnosis illustrate the importance of considering MODY 2 as a potential diagnosis in patients with hyperglycemia.

Conclusions

This case serves to illustrate the pivotal role of genetic evaluation in young patients presenting with a diabetes phenotype that does not fully align with either Type 1 or Type 2 diabetes. This case study shows the

potential for prolonged misdiagnosis, which can have significant implications for treatment and the quality of life of the patient. A correct diagnosis of MODY 2 can lead to more appropriate management strategies, often reducing or eliminating the need for insulin therapy, thus improving patient outcomes.

Disclosure

Author's Contribution:

Conceptualization, OD, WB and BS; methodology, BN and PB; check, OD and KL; formal analysis, OD; resources, OD, WB and BS; data curation, PB; writing - rough preparation, OD, WB, KL, BS, BN, PB and AW; writing - review and editing, OD, WB, KL, BS, BN, PB and AW; visualization, OD; supervision, OD; project administration, OD; All authors have read and agreed with the published version of the manuscript.

Funding statement: Not applicable.

Acknowledgements: None

Informed Consent Statement: Written informed consent has been obtained from the patient to publish this paper.

Conflict of Interest Statement: The Authors declare that there are no competing interests.

References:

1. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119. https://doi.org/10.1016/j.diabres.2021.109119.
2. Atkinson MA, Eisenbarth GS, Michels AW. Type 1 diabetes. Lancet. 2014;383(9911):69-82. https://doi.org/10.1016/S0140-6736(13)60591-7.
3. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018;14(2):88-98. https://doi.org/10.1038/nrendo.2017.151.
4. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Diabetologia. 2019;62(1):3-16. https://doi.org/10.1007/s00125-018-4711-2.
5. Steele AM, Shields BM, Wensley KJ, Ellard S, Hattersley AT. Prevalence of vascular complications among patients with glucokinase mutations and prolonged, mild hyperglycemia. JAMA. 2014;311(3):279-286. https://doi.org/10.1001/jama.2013.283980.
6. Amed S, Oram R. Maturity-Onset Diabetes of the Young (MODY): Making the Right Diagnosis to Optimize Treatment. Can J Diabetes. 2016 Oct;40(5):449-454. https://doi.org/10.1016/j.jcjd.2016.03.002. Epub 2016 Apr 26.
7. Aarthy R, Aston-Mourney K, Mikocka-Walus A, Radha V, Amutha A, Anjana RM, Unnikrishnan R, Mohan V. Clinical features, complications and treatment of rarer forms of maturity-onset diabetes of the young (MODY) - A review. J Diabetes Complications. 2021 Jan;35(1):107640. https://doi.org/10.1016/j.jdiacomp.2020.107640.
8. Pacholczyk M, Krawczyk-Rusiecka K, Ferenc T. Diabetes of the young MODY - molecular background, clinical features and treatment. Advances in Cell Biology. 2022; 49(4): 267-307 https://doi.org/10.59674/pbk8.

9. Fajans SS, Bell GI, Polonsky KS. Molecular mechanisms and clinical pathophysiology of maturity-onset diabetes of the young. N Engl J Med. 2001 Sep 27;345(13):971-80. https://doi.org/10.1056/NEJMra002168.
10. Tsakiris D, Ioannou K. An underdiagnosed type of diabetes: the MODY syndromes. Pathophysiology, clinical presentation and renal disease progression. J Nephrol. 2004 Sep-Oct;17(5):637-41.
11. Urakami T. Maturity-onset diabetes of the young (MODY): current perspectives on diagnosis and treatment. Diabetes Metab Syndr Obes. 2019 Jul 8;12:1047-1056. https://doi.org/10.2147/DMSO.S179793.
12. Peixoto-Barbosa R, Reis AF, Giuffrida FMA. Update on clinical screening of maturity-onset diabetes of the young (MODY). Diabetol Metab Syndr. 2020 Jun 8;12:50. https://doi.org/10.1186/s13098-020-00557-9.
13. Delvecchio M, Pastore C, Giordano P. Treatment Options for MODY Patients: A Systematic Review of Literature. Diabetes Ther. 2020 Aug;11(8):1667-1685. https://doi.org/10.1007/s13300-020-00864-4.