Syndactyly in Maturity-onset Diabetes of the Young Type 5 (MODY 5): Expanding the Clinical Phenotype - A Case Report

Mustafa Unubol[1]*, Ayse Iyiyapici Unubol[2], Omer Komac[3], Deniz Cetin[3], Gokay Bozkurt[4], Engin Guney[3]

[1]Private Clinic of Endocrinology, Turkey

[2]Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Aydın Adnan Menderes University, Turkey

[3]Division of Endocrinology and Metabolism, Department of Internal Medicine, Faculty of Medicine, Aydın Adnan Menderes University, Turkey

[4]Department of Medical Genetics, Faculty of Medicine, Aydın Adnan Menderes University, Turkey

***Corresponding author:**

Mustafa Unubol, MD,

Private Clinic of Endocrinology, Aydın, Turkey, Phone: +90 552 660 3096, E-mail: drmunubol@yahoo.com.tr

Received : January 07, 2026
Published **:** February 24, 2026

ABSTRACT

Maturity-onset diabetes of the young type 5 (MODY 5) is a rare monogenic form of diabetes caused by mutations in the HNF1B gene and is characterized by a multisystem phenotype. Skeletal anomalies are not classically associated with MODY 5. We report a 21-year-old woman with newly diagnosed diabetes initially misclassified as type 1 diabetes who was found to have congenital simple syndactyly of the left hand. She had a strong family history of early-onset diabetes, negative pancreatic autoantibodies, preserved C-peptide levels, and no ketosis at diagnosis. Imaging demonstrated dorsal pancreatic hypoplasia and unilateral renal hypoplasia, and laboratory tests showed hypomagnesemia and hyperuricemia. Genetic analysis identified a heterozygous pathogenic HNF1B variant, confirming the diagnosis of MODY 5. This case suggests a possible and previously unreported association between MODY 5 and syndactyly.

Keywords: MODY 5, HNF1B Mutation, Syndactyly, Monogenic Diabetes, Pancreatic Hypoplasia

INTRODUCTION

Maturity-onset diabetes of the young (MODY) represents a diverse group of monogenic diabetes conditions that usually manifest early in life, show autosomal dominant inheritance, and are characterized by partial preservation of endogenous insulin secretion [1]. In a study conducted among individuals with diabetes diagnosed before the age of 20 years, the prevalence of MODY was reported to be at least 1.2% [2]. The most common subtypes are GCK-MODY, HNF1A-MODY, and HNF4A-MODY, which together account for more than 90% of cases [1].

DOI : https://doi.org/10.35702/cases.10025

MODY 5 is a rare subtype with a distinct multisystem phenotype, most commonly caused by mutations in the HNF1B gene and, less frequently, in PPARG (3). In contrast to other forms of MODY, HNF1B-related disease is frequently associated with extrapancreatic manifestations, including renal, pancreatic, and genitourinary abnormalities [4].

A substantial proportion of patients with MODY is initially misdiagnosed as having type 1 or type 2 diabetes, which may result in delayed diagnosis and underrecognition of associated systemic features [2]. Here, we present a young patient initially diagnosed with type 1 diabetes in whom the presence of congenital syndactyly prompted further evaluation and ultimately led to the diagnosis of MODY 5. This case aims to highlight the importance of considering monogenic diabetes in young patients with atypical phenotypic features.

CASE REPORT

A 21-year-old woman presented with a one-month history of polyuria, polydipsia, dry mouth, and approximately 3 kg of weight loss. At presentation, fasting plasma glucose was 245 mg/dL, 2-hour postprandial glucose was 356 mg/dL, and HbA1c was 10.2%. Her body weight was 47 kg, height 148 cm, and body mass index 21.46 kg/m^2. She was initially diagnosed with type 1 diabetes and started on intensive insulin therapy.

Three months later, she was referred to our clinic. Glycemic control was achieved with a basal-bolus insulin regimen (insulin aspart 8-10-6 units and insulin glargine 16 units daily). Physical examination revealed congenital simple syndactyly between the first and second digits of the left hand. There was no family history of limb anomalies, and no history of maternal medication use, radiation exposure, or infection during pregnancy. Hand radiography showed no bony fusion, consistent with soft tissue syndactyly.

The patient had completed only primary school education but was able to perform daily activities independently. She did not smoke or consume alcohol. Family history was notable for early-onset diabetes in her mother, sister, two maternal aunts, and maternal grandmother, all diagnosed before the age of 40 years and treated with insulin.

Autoimmune markers including anti–glutamic acid decarboxylase (anti-GAD) antibodies, islet cell antibodies, and insulin autoantibodies were negative. Postprandial C-peptide level was 2 ng/mL, and urinary ketones were absent. There were no clinical features suggestive of insulin resistance. Given the presence of a skeletal anomaly, reduced academic performance, a strong family history of early-onset diabetes, and clinical features not typical of type 1 or type 2 diabetes, the possibility of monogenic diabetes (MODY) was considered. The Exeter MODY Risk Calculator estimated a probability of 8.2% [5].

Abdominal magnetic resonance imaging demonstrated absence of the pancreatic tail with partial visualization of the pancreatic body and head, consistent with dorsal pancreatic hypoplasia/agenesis. The right kidney was hypoplastic, while the left kidney was compensatorily enlarged. Laboratory evaluation revealed hypomagnesemia (1.44 mg/dL; reference range 1.5–2.5 mg/dL) and hyperuricemia (8.2 mg/dL; reference range 2.5–6 mg/dL). Serum creatinine was 0.72 mg/dL, and other renal and liver function tests were normal.

Genetic testing, performed by PCR amplification followed by DNA sequence analysis, identified a heterozygous pathogenic variant in exon 4 of the HNF1B gene (p.His336Asp; c.1006C>G; HGMD: CM067046), confirming the diagnosis of MODY 5. The patient continued insulin therapy and was scheduled for regular follow-up for potential associated complications.

DISCUSSION

MODY is frequently misclassified as type 1 or type 2 diabetes, and clinical suspicion remains the most important factor for its recognition [2]. Due to its rarity and phenotypic heterogeneity, MODY 5 is often challenging to diagnose at an early stage, making it an important subject of ongoing research [3]. In our patient, the presence of congenital syndactyly, multisystem involvement, and a strong family history prompted further evaluation, leading to the diagnosis of MODY 5. This case highlights the clinical and laboratory characteristics of a rare MODY 5 patient initially misdiagnosed with type 1 diabetes, contributing to improved clinical recognition.

Prior investigations indicate that approximately one-third of patients with HNF4A- or HNF1B-associated MODY is initially classified as having type 1 or type 2 diabetes [6]. Similarly, our patient was initially diagnosed with type 1 diabetes.

MODY comprises a group of autosomal dominant monogenic diabetes disorders characterized by early onset, preserved endogenous insulin secretion, and absence of autoimmune destruction [7]. MODY 5 is characterized by a wide spectrum of clinical manifestations and may present from the neonatal period through adolescence with multisystem involvement, including renal, neurological, and growth-related abnormalities [3]. MODY 5 is particularly rare and accounts for

DOI : https://doi.org/10.35702/cases.10025

a small proportion of MODY cases [8]; in a pediatric cohort from Turkey, it represented only 3.1% of MODY patients [9]. Unlike other subtypes, MODY 5 is characterized by a heterogeneous and multisystem phenotype [8].

MODY 5 is most commonly caused by mutations in HNF1B, a transcription factor expressed during embryogenesis in the kidney, pancreas, genitourinary tract, liver, and lungs [10]. Consequently, HNF1B mutations are associated not only with diabetes but also with renal developmental anomalies, pancreatic hypoplasia, genitourinary malformations, hypomagnesemia, and hyperuricemia [3,11]. Approximately 40% of patients with HNF1B-MODY exhibit extrapancreatic manifestations [6]. Renal complications are frequently observed and often include structural abnormalities such as renal cysts. Our patient demonstrated several of these features, including dorsal pancreatic hypoplasia, unilateral renal hypoplasia, hypomagnesemia, and hyperuricemia. These observations reflect the diverse developmental consequences of the underlying genetic mutations and indicate that MODY 5 involves systemic organogenesis abnormalities beyond pancreatic beta-cell dysfunction [12]. Clinical manifestations may vary widely, ranging from hyperglycemia and recurrent urinary tract infections to structural renal abnormalities, unexplained growth impairment, and extrapancreatic anomalies. In the absence of distinctive clinical markers, such phenotypic variability may contribute to delays in timely diagnosis and accurate identification [13].

Syndactyly is one of the most common congenital hand anomalies, characterized by fusion of adjacent digits [14,15]. A review of the available literature did not identify previously reported cases describing an association between MODY 5 and syndactyly. Whether this finding represents a component of the MODY 5 phenotype or a coincidental association requires confirmation through larger clinical studies. Given the broad phenotypic spectrum observed in MODY 5, syndactyly is reported in this case as an atypical clinical feature that may serve as a potential diagnostic clue. This observation underscores the importance of considering early and atypical manifestations and of expanding diagnostic strategies beyond classical features when evaluating patients for MODY 5 [3].

There is increasing evidence that HNF1B abnormalities may also be associated with neurodevelopmental disorders [16]. Formal neuropsychological testing was not performed in our patient; however, it was noted that the patient discontinued schooling after primary education due to academic difficulties and did not pursue secondary education. Comorbid conditions associated with MODY 5 may worsen when opportunities for timely intervention are missed. Delayed or overlooked diagnoses may not only result in potentially preventable complications, such as advanced renal disease or irreversible organ damage, but may also lead to inappropriate management strategies, including unnecessary insulin dependence or treatments related to extrapancreatic manifestations [17]. For these reasons, this report draws attention to MODY 5 as a rare but clinically significant form of diabetes.

Management of MODY 5 typically involves insulin therapy and careful monitoring for associated complications, particularly progressive renal dysfunction. Long-term follow-up studies have demonstrated a gradual decline in renal function in patients with HNF1B-related nephropathy [18]. Our patient achieved good glycemic control and was scheduled for close follow-up, especially with regard to renal outcomes.

CONCLUSION

MODY 5 is a rare form of diabetes and should be considered in young patients who do not fit the classical features of type 1 or type 2 diabetes, particularly when autoimmune markers are negative and C-peptide levels are preserved. In this case, MODY 5 with a broad spectrum of clinical manifestations presented with syndactyly as an atypical clinical finding. Whether this association reflects an expansion of the phenotypic spectrum related to HNF1B mutations remains uncertain and warrants further investigation through clinical studies.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

FUNDING: This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ETHICS APPROVAL AND CONSENT: Ethical approval was waived as it is not required for single case reports. Written informed consent was obtained from the patient for publication of this case and accompanying data.

REFERENCES

1. Tosur M, Philipson LH (2022). Precision diabetes: lessons learned from maturity-onset diabetes of the young (MODY). J Diabetes Investig 13(9):1465-1471.

2. Pihoker C, Gilliam LK, Ellard S, Dabelea D, Davis C, Dolan LM, et al (2013). Prevalence, characteristics and clinical diagnosis of maturity onset diabetes of the young due to mutations in HNF1A, HNF4A, and glucokinase: results from the SEARCH for Diabetes in Youth. The Journal of Clinical Endocrinology and Metabolism. 98(10):4055-4062.

3. Nurkolis F, Syahputra RA, Nugrahanto AP, Taslim NA, Mustika A, Tjandrawinata RR, et al. (2025). Emerging phenotype: maturity-onset diabetes of the young type 5 (MODY-5)—mechanisms, clinical spectrum, and unmet needs. Diabetology & Metabolic Syndrome. 17(1):252.

4. Bellanné-Chantelot C, Chauveau D, Gautier JF, Dubois-Laforgue D, Clauin S, Beaufils S, et al (2004). Clinical spectrum associated with hepatocyte nuclear factor-1beta mutations. Annals of Internal Medicine. 140(7):510-517.

5. Shields BM, McDonald TJ, Ellard S, Campbell MJ, Hyde C, Hattersley AT. (2012). Development and validation of a clinical prediction model to determine the probability of MODY in patients with young-onset diabetes. Diabetologia. 55(5):1265-1272.

6. Warncke K, Kummer S, Raile K, Grulich-Henn J, Woelfle J, Steichen E, et al. (2019). Frequency and characteristics of MODY 1 and MODY 5. The Journal of Clinical Endocrinology and Metabolism. 104(3):845-855.

7. Hattersley AT, Greeley SAW, Polak M, Rubio-Cabezas O, Njølstad PR, Mlynarski W, et al. (2018). ISPAD clinical practice consensus guidelines. Pediatr Diabetes. 19(Suppl 27):47-63.

8. Balasubramanyam A (2021). Defining and classifying new subgroups of diabetes. Annual Review of Medicine. 72:63-74.

9. Özsu E, Çetinkaya S, Bolu S, Hatipoğlu N, Savaş Erdeve Ş, Evliyaoğlu O, et al. (2024). Clinical and laboratory characteristics of MODY cases. J Clin Res Pediatr Endocrinol.16(3):297-305.

10. Decramer S, Parant O, Beaufils S, Clauin S, Guillou C, Kessler S, et al. (2007). Anomalies of the TCF2 gene are the main cause of fetal bilateral hyperechogenic kidneys. Journal of the American Society of Nephrology : JASN. 18(3):923-933.

11. Gambella A, Kalantari S, Cadamuro M, Quaglia M, Delvecchio M, Fabris L, et al. (2023). The landscape of HNF1B deficiency. Cells. 12(2):307.

12. Clissold RL, Hamilton AJ, Hattersley AT, Ellard S, Bingham C. (2015). HNF1B-associated renal and extra-renal disease. Nature Reviews. Nephrology. 11:102-112.

13. Peixoto-Barbosa R, Reis AF, Giuffrida FMA (2020). Update on clinical screening of maturity-onset diabetes of the young (MODY). Diabetology & Metabolic Syndrome. 8;12:50.

14. Mahindroo S, Tabaie S. (2023). Syndactyly in the pediatric population. Cureus. 15(3):e36118.

15. Jordan D, Hindocha S, Dhital M, Saleh M, Khan W. (2012). Epidemiology, genetics and management of syndactyly. The Open Orthopaedics Journal.J. 6:14-27.

16. Moreno-De-Luca D, Mulle JG, Kaminsky EB, Sanders SJ, Myers SM, Adam MP, et al. (2010). Deletion 17q12 is a recurrent copy number variant that confers high risk of autism and schizophrenia. American Journal of Human Genetics. 87(5):618-630.

17. Unnikrishnan R, Shah VN, Mohan V (2016). Challenges in diagnosis and management of diabetes in the young. Clinical Diabetes and Endocrinology. 10;2:18.

18. Faguer S, Decramer S, Chassaing N, Bellanné-Chantelot C, Calvas P, Beaufils S, et al. (2011). Diagnosis, management, and prognosis of HNF1B nephropathy in adulthood. Kidney international. 80(7):768-776.