Case Report

A Diabetic Imposter: A Case Report on MODY 13 Coexisting with Charcot-Marie-Tooth IJ Syndrome

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Maturity-onset diabetes of the young (MODY) is a rare, inherited form of diabetes caused by a single gene defect affecting insulin secretion. It typically presents at a young age, runs in families, and differs from common types of diabetes by preserving endogenous insulin production, often allowing treatment with oral agents instead of insulin. However, it is frequently misdiagnosed. We describe an unusual case of MODY 13 due to a KCNJ11 mutation in a young adult initially treated as type 1 diabetes, who demonstrated a significant response to sulfonylurea therapy. The case is further distinguished by advanced multisystem complications and a rare coexisting genetic variant, highlighting the diagnostic challenges and clinical significance of recognizing this uncommon entity.

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Introduction

Maturity-onset diabetes of the young (MODY) is a distinct form of monogenic diabetes resulting from single-gene defects that impair pancreatic β-cell function. It typically presents in adolescence or early adulthood as nonketotic diabetes mellitus and follows an autosomal dominant pattern of inheritance, often affecting multiple members across successive generations.[1] Despite accounting for approximately 1 to 2% of all diabetes cases, MODY remains underdiagnosed in clinical practice due to its phenotypic overlap with type 1 and type 2 diabetes.[2] Patients are frequently misclassified and inappropriately managed, underscoring the need for greater clinical awareness.[3,4]

MODY comprises several genetic subtypes, each associated with mutations affecting insulin secretion pathways. Among these, mutations in the KCNJ11 gene represent a rare entity (MODY 13).[5,6] This gene encodes the Kir6.2 subunit of the ATP-sensitive potassium (KATP) channel, which plays a critical role in insulin secretion.[6] Although KCNJ11 mutations are more commonly implicated in neonatal diabetes, their occurrence in MODY is uncommon and has been reported in only a limited number of cases globally.[7]

Previously reported cases have demonstrated significant phenotypic variability, ranging from mild asymptomatic hyperglycaemia to early-onset diabetes with marked glycaemic instability.[8,9] Features such as early age of onset, absence of ketosis, preserved endogenous insulin secretion, and negative autoimmune markers may help distinguish it from other forms of diabetes.[1,2] Importantly, accurate identification has therapeutic implications, as several MODY subtypes respond well to oral hypoglycaemic agents, particularly sulfonylureas.[10]

Documenting such cases improves recognition of atypical diabetes presentations and helps prevent misdiagnosis. We report a case of a 26-year-old male initially diagnosed with type 1 diabetes mellitus, who presented with suboptimal glycaemic control despite insulin therapy and absence of ketoacidosis, and was subsequently found to have a heterozygous KCNJ11 mutation consistent with MODY 13.

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Case Presentation

A 26-year-old male patient, a known case of Diabetes Mellitus type 1 for 2 months treated with human insulin, presented to the outpatient department with complaints of bilateral blurring of vision for 1 year, breathlessness on exertion for 1 year, numbness of both lower limbs for 6 months, musculoskeletal fatigue for 3 months, increased urinary frequency for 1 month, and erectile dysfunction for 1 month. Family history revealed a maternal uncle and a maternal grandmother with Diabetes.

On examination, the patient is thin built and is of short stature with a recorded capillary blood glucose level of 482 mg/dL. Neurological examination revealed decreased visual acuity with impaired colour vision on both eyes. Muscle wasting is noted on the right supraclavicular region, right supraspinatus and infraspinatus, and bilateral thigh adductors and flexors. There is reduced tone and power with absent reflexes on the lower limbs of both sides. Somatosensorial deficit is seen on both lower limbs. In addition, he shows orthostatic tachycardia and hypotension. With further probing, conditions suggestive of autoimmune disease or obesity were ruled out. The remainder of the general physical and systemic examination was unremarkable.

A glucose panel revealed remarkably high HbA1c levels (Table 1). Skeletal muscle wasting was confirmed with an elevated CK/CK-MB finding. Urine routine showed presence of albumin and glucose loss (Table 1) confirming diabetic nephropathy, making it part of the provisional diagnosis. An electrolyte panel disclosed severe hypokalaemia, which was corrected later.

Table 1: Routine laboratory investigation findings

Variable	*Value*	*Reference range/ impression*
Random Blood Sugar (mg/dL)	516	<140 (Very High)
Fasting Blood Sugar (mg/dL)	227	70–90 (Very High)
Post Prandial Blood Sugar (mg/dL)	486	<140 (Very High)
HemoglobinA1c (HbA1c) (%)	12.1	4.0–5.6 (Very High)
Fasting C-peptide (ng/dL)	0.45	0.50–2.00 (Low)
Potassium (mEq/L)	1.9→3.8	3.5–5.0 (Corrected)
Creatine Kinase (IU/L)	2894	52–336 (Elevated)
Creatine Kinase-MB (IU/L)	45	<25 (Elevated
24-hour Urinary Potassium (mmol/day)	13.5	25.0–125.0 (Low)
Urine Routine	Albumin + Glucose 2+	Diabetic nephropathy

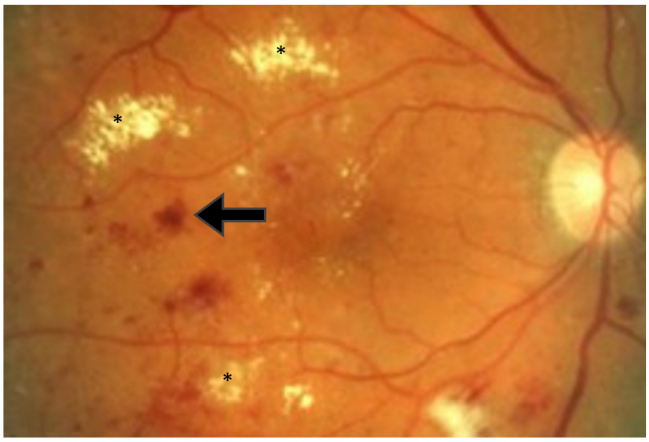

Figure 1: Fundoscopic examination showing clinically significant macular edema, characterized by multiple hard exudates (asterisk) and retinal haemorrhages (arrow)

The uncontrolled hyperglycaemia with no history of ketosis, family history of diabetes and a fasting C-peptide test in near normal range (Table 1) suggested diabetes of monogenic origin prompting specialized investigations.

Fundoscopic evaluation revealed features consistent with proliferative diabetic retinopathy with clinically significant macular oedema (Figure 1) Two-dimensional echocardiography demonstrated global hypokinesia of the left ventricle with a left ventricular ejection fraction of 46% and Grade III left ventricular diastolic dysfunction. Nerve conduction studies showed absent F-wave latency, compound muscle action potentials (CMAP), and sensory nerve action potentials (SNAP) in the lower limbs, suggestive of severe axonal neuropathy. Autoimmune evaluation, including anti-GAD65, anti-IA2, anti-insulin, and anti-ZnT8 antibodies, was negative.

Whole exome sequencing identified a heterozygous missense mutation in the KCNJ11 gene (c.1094G>A, chromosome 11) and an additional heterozygous missense mutation in the ITPR3 gene (c.2497A>G, chromosome 6).

With this, a conclusive diagnosis of MODY type 13 with Charcot–Marie–Tooth disease type 1J was established, along with proliferative diabetic retinopathy; distal large and small fibre neuropathy with autonomic involvement; diabetic amyotrophy; heart failure (ejection fraction 46%); nephropathy; and hypokalaemia of inconclusive etiology.

Hypokalaemia was promptly corrected, following which there was a notable improvement in proximal muscle weakness. The patient was initially managed with injectable human insulin to achieve adequate glycaemic control. Once stable glycaemic parameters were attained, therapy was transitioned to oral sulfonylurea (glimepiride

2 mg twice daily), to which the patient demonstrated a favourable response, evidenced by a reduction in insulin requirement.

There was a gradual improvement in neuropathic symptoms, with decreased numbness in the lower limbs and resolution of giddiness. In view of concomitant cardiac involvement, the patient was initiated on guideline-directed medical therapy for heart failure, including antiplatelet therapy (aspirin), statin, beta-blocker, enalapril, mineralocorticoid receptor antagonist, and an SGLT-2 inhibitor. Neuropathic symptoms were further managed with gabapentin. Given the presence of proliferative diabetic retinopathy, pan-retinal photocoagulation was advised. The patient was counselled regarding adherence to a diabetic diet and was started on oral potassium supplementation.

On follow-up at two weeks and one month, the patient maintained good glycaemic control, with sustained clinical improvement and no new complications.

Discussion

Maturity-onset diabetes of the young (MODY) represents a heterogeneous group of monogenic disorders characterized by primary β-cell dysfunction and early-onset hyperglycaemia.[1] Although traditionally considered rare, monogenic diabetes is now estimated to account for approximately 1–2% of all diabetes cases, with a significant proportion remaining misdiagnosed as type 1 or type 2 diabetes.[2,4] This under-recognition has important clinical implications, as failure to establish the correct diagnosis may result in inappropriate long-term management.

In the present case, a 26-year-old male initially diagnosed with type 1 diabetes mellitus was reassessed due to atypical clinical features. The absence of diabetic ketoacidosis, preserved endogenous insulin secretion (normal C-peptide), and negative pancreatic autoantibodies effectively argued against autoimmune diabetes. When combined with a positive family history suggestive of autosomal dominant inheritance, these findings raised strong suspicion for monogenic diabetes.[11] Definitive diagnosis was established through genetic testing, which identified a heterozygous mutation in the KCNJ11 gene, confirming MODY 13.

The significance of this diagnosis is most evident in its therapeutic implications. KCNJ11 encodes the Kir6.2 subunit of the ATP-sensitive potassium (KATP) channel, which plays a central role in insulin secretion.[12] Mutations in this gene impair β-cell depolarization and insulin release; however, this defect can be bypassed pharmacologically using sulfonylureas, which directly close KATP channels.[13] This forms the basis of precision treatment in monogenic diabetes. In this patient, transition from insulin to sulfonylurea therapy resulted in improved glycaemic control and reduced insulin requirement. Gonçalves *et al*. and Vedovato *et al*. describe similar therapeutic responses in KCNJ11-MODY cases, further supporting the role of sulfonylureas as targeted therapy.[14,15] This illustrates how accurate molecular diagnosis can prevent unnecessary lifelong insulin therapy and significantly improve quality of life.

Beyond treatment, establishing a diagnosis of MODY has important prognostic and clinical implications. Different MODY subtypes are associated with distinct risks of microvascular and macrovascular complications, and accurate classification allows for tailored monitoring and management strategies.[16] Furthermore, given the autosomal dominant inheritance pattern, identification of MODY facilitates cascade screening of family members, enabling early diagnosis and intervention.[17]

Bonnefond *et al*. first identified KCNJ11 as a causative gene for MODY in 2012.[12] It remains an exceptionally rare subtype of diabetes mellitus. While KCNJ11 mutations are more commonly implicated in neonatal diabetes, their role in MODY phenotypes is increasingly recognized. Current literature suggests that only a limited number of such cases, approximately 75 worldwide, have been reported to date, with several recent case reports further illustrating the expanding clinical spectrum of MODY 13.[8,9,14,18] This rarity contributes to diagnostic challenges and highlights the importance of considering monogenic diabetes in atypical presentations.

An additional notable feature in this case is the coexistence of a heterozygous ITPR3 mutation. Although its precise role in glucose homeostasis remains unclear, emerging evidence suggests that additional genetic variants may act as modifiers of disease phenotype, influencing severity and clinical presentation. [5] Furthermore, this case represents only the second documented association between Charcot–Marie–Tooth (CMT)–like neuropathy and MODY, first described by Wang *et al*.[19] This highlights a potentially novel clinical overlap that warrants further evaluation and contributes to a broader understanding of genetic interactions in monogenic diabetes.

The presence of advanced complications at presentation, including proliferative diabetic retinopathy, neuropathy, nephropathy, and cardiac dysfunction,

underscores the consequences of delayed diagnosis. A similar diagnostic challenge was reported by Fatani *et al*., who describe KCNJ11-associated MODY13 with coexisting autoimmunity.[20] Early recognition of MODY could facilitate timely initiation of appropriate therapy and potentially mitigate long-term complications.

Conclusion

Monogenic diabetes, though accounting for only 1–2% of all diabetes cases, remains significantly underrecognized in routine clinical practice. This case highlights the importance of considering monogenic etiologies in young individuals presenting with diabetes, particularly in the presence of a strong family history, preserved endogenous insulin secretion, and absence of autoimmune markers. Early identification is crucial, as it prevents misclassification as type 1 diabetes and enables a transition toward precision-based management.

The marked response to sulfonylurea therapy in this patient underscores the therapeutic value of an accurate genetic diagnosis, allowing avoidance of unnecessary lifelong insulin therapy while offering a more cost-effective alternative. Furthermore, precise classification aids in prognostication, individualized monitoring, and facilitates genetic counselling and screening of at-risk family members, ultimately advancing personalized and evidence-based care.

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