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CASE REPORT

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A Rare Case of HNF1B-Associated MODY (MODY 5) Presenting as Recurrent Diabetic Ketoacidosis with Urosepsis in an Adolescent: A Diagnosis More Often Missed Than Made

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ABSTRACT

Background: Maturity-onset diabetes of the young (MODY) is an uncommon genetic form of diabetes that arises from mutations in the HNF1B gene. Because it begins at a young age and typically requires insulin therapy, MODY is frequently mistaken for type 1 diabetes.
Case Presentation: We describe a 13-year-old Marwari boy with a history of type 1 diabetes, recurrent diabetic ketoacidosis DKA, and recurrent urosepsis post-pyeloplasty. Despite high-dose insulin therapy (>240 units/day), glycemic control was inadequate. Genetic analysis confirmed HNF1B-associated MODY (MODY 5).
Conclusion: In young individuals presenting with both diabetes and kidney abnormalities, MODY 5 should be considered as a possible diagnosis. Early recognition and precise diagnosis are crucial for guiding appropriate therapy and genetic counselling.

INTRODUCTION

Monogenic diabetes comprises 1–2% of all diabetes cases and is often under-recognised. MODY, first described in 1975 using Tattersall and Fajans criteria, has at least 15 subtypes; among these, MODY 5 (HNF1B-associated) accounts for less than 5% but is significant due to its multisystem involvement [1]. This case highlights the importance of considering MODY 5 in a typical presentation of diabetes with renal pathology.

CASE REPORT

A 13-year-old Marwari boy, who follows a vegetarian diet, was admitted with a three-day history of high-grade fever, abdominal discomfort, and continuous vomiting [2]. He had been diagnosed with type 1 diabetes two years prior (HbA1c 17.5%, negligible-peptide), treated with basal-bolus insulin, and had undergone left pyeloplasty with DJ stenting for congenital hydronephrosis [3] (Figure 1).

Investigations done at the First hospital dated 15/07/2023

1. **HBA1c 17.5%**
2. **Fasting C PEPTIDE : NEGLIGIBLE**

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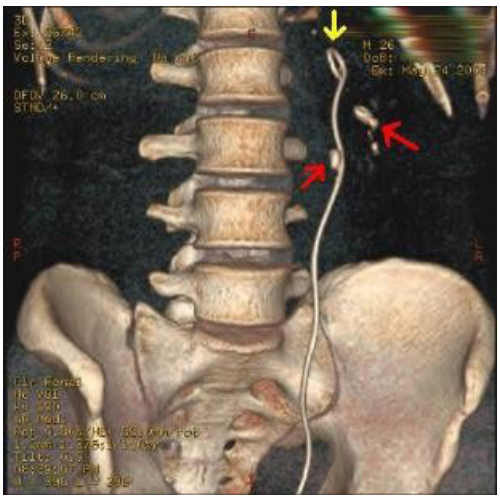

Figure 1. DJ stent left.

3. Post Prandial : 0.2 pmol/ml (N-1.5 – 4)

4. GAD-65 : 1.0 IU/ml
Negative GAD
(Between 0 to 17 IU is normal)

Diagnosis at the First Hospital

Diabetic Ketosis with Type 1 Diabetes.

Treatment given at the First Hospital

16/07/2023 - Basal Bolus Insulin	15-15-15 0–0–25
29/07/2023 - Basal Bolus Insulin	15-20-18 0–0–25

Then he underwent DJ stent with repair of the left hydronephrosis in a corporate hospital.

On current admission, he was febrile (103.2°F), dehydrated, hypotensive (BP 90/60), tachycardic (PR 132), and tachypneic (RR 30). BMI was <18, and severe left loin tenderness was noted [2]. Laboratory studies revealed severe hyperglycemia (RBS 620 mg/dL), HbA1c 16.8%, ketonuria, pyuria, elevated urea and creatinine, hyponatremia, hyperkalemia, and high CRP (>130 mg/L) [2]. Abdominal imaging showed residual hydronephrosis with perinephric fat stranding suggestive of acute pyelonephritis.

He required ICU care with IV insulin (up to 240 units/day), antibiotics (meropenem), and supportive measures [1]. Glycemic control remained challenging despite high insulin doses.

Suspecting an alternate diabetes etiology, further evaluation was done. GAD antibody testing returned negative (3.8 IU/ml) [4,5]. Both fasting and stimulated C-peptide levels were reduced at 0.6 ng/mL and 1.2 ng/mL, respectively. Given the presence of renal abnormalities and suboptimal response to insulin, MODY 5 was considered as a potential diagnosis [5].

Genetic analysis confirmed a heterozygous HNF1B mutation. Treatment was adjusted to include metformin, pioglitazone, and gliclazide, with reduced insulin (Tresiba 15 units HS) [4]. Over three months, the patient gained 10 kg weight, HbA1c improved to 6.8%, and no further.

DISCUSSION

First identified in 1997, MODY 5—also referred to as renal cysts and diabetes (RCAD) syndrome—is linked to mutations in the HNF1B gene on chromosome 17q. Although typically inherited in an autosomal dominant pattern, nearly half of the cases may occur as new (de novo) mutations [2].

The characteristic features include early-onset diabetes, renal anomalies (cysts, dysplasia, or hydronephrosis), and variable extrarenal manifestations (e.g., genital tract malformations, liver function [1].

MODY 5, also known as renal cysts and diabetes (RCAD) syndrome, was first described in 1997 [4]. This condition results from mutations in the HNF1B gene located on chromosome 17q and is typically passed down in an autosomal dominant manner, although nearly half of the cases may arise spontaneously without a family history [5].

The characteristic features include early-onset diabetes, renal anomalies (cysts, dysplasia, or hydronephrosis), and variable extrarenal manifestations (e.g., genital tract malformations, liver function abnormalities) [3]. Diabetes in MODY 5 is due to pancreatic hypoplasia and β-cell dysfunction, sometimes presenting with ketoacidosis mimicking type 1 diabetes [3].

Our case underscores the importance of suspecting MODY 5 in patients with early-onset diabetes and renal anomalies, especially when glycemic control remains despite high-dose insulin therapy [1]. Genetic confirmation is crucial, as treatment strategies differ and can include sulfonylureas, which may partially improve glycemic control [4].

Early diagnosis facilitates appropriate treatment, prevents unnecessary high insulin doses, reduces risk of recurrent infections and metabolic decompensation, and enables family genetic counselling [4].

CONCLUSION

This case illustrates a rare but important diagnosis of HNF1B-associated MODY (MODY 5), often missed and misclassified as type 1 diabetes [3]. Young diabetic patients with renal anomalies should prompt consideration of MODY 5. Precision diagnosis can significantly improve outcomes [3].

Author Contributions

Dr. S.S. Lakshmanan: Conceptualization, initial management, and case follow-up.

Dr. K.N.V. Adithya: Drafting manuscript, literature review, and critical revision.

Dinesh Noble B: Case discussion and manuscript editing.

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