AACE Clinical Case Rep. 10 (2024) 75–76

Clinical Case Reports™
www.aaceclinicalcasereports.com

Visual Vignette

Cystic and Atrophic Kidneys, Atrophic Pancreas, Arcuate Uterus, and Diabetes Mellitus Associated With Deletion of *HNF1β* Gene

Rachel L. Usala, MS, MD [1,*], Alberto Sobrero, BSc [2], Amy Riek, MD [1], Janet McGill, MD [1], Fumihiko Urano, MD, PhD [1]

[1] *Division of Endocrinology, Metabolism, and Lipid Research, Department of Medicine, Washington University in St. Louis, St. Louis, Missouri*
[2] *Washington University School of Medicine in St. Louis, St. Louis, Missouri*

ARTICLE INFO

Article history:
Received 12 June 2023
Accepted 22 June 2023
Available online 6 September 2023

Case Presentation

The patient is a 33-year-old female with end-stage kidney disease who was referred for diabetes management. She developed diabetes at the age of 30 years, 3 years prior to the referral, presenting with an A1C of 9.1% (76 mmol/mol), and a body mass index of 31 kg/m^2. Notably, glucose levels were normal for 4 to 5 years after her kidney transplant at the age of 25 years, increasing moderately in the year prior to referral. Diabetes testing revealed negative anti-GAD65 and antipancreatic islet cell antibodies. C-peptide was 2.9 ng/mL on fasting and 5.2 ng/mL on a random check. She denied any family history of diabetes or renal disease. Glucose control improved rapidly with diet, exercise, administration of glucagon-like peptide-1 agonist, and low doses of insulin. The patient's kidney disease history includes progressive loss of kidney function as an adolescent and young adult, with pretransplant imaging at the age of 25 years showing bilateral renal cysts and markedly atrophic left kidney (Fig. 1). Imaging at the age of 31 years showed scarred native kidneys and atrophy of the body and tail of the pancreas. Serial sweeping transvaginal ultrasound (Fig. 2) showed a normal uterine body (Fig. 2*A*) with uninterrupted endometrial stripe (Fig. 2*B*), but also an abnormal fundal arcuate contour (Fig. 2*C*) as evidenced by interrupted endometrial stripe (Fig. 2*D*).

What is the diagnosis?

Answer

HNF1β-associated disease, also known as maturity-onset diabetes of the young (MODY) type 5 and Renal Cysts and Diabetes Syndrome. Genetic testing revealed complete deletion of the entire coding sequence of gene *HNF1β*. *HNF1β*-associated disease has variable penetrance and unknown prevalence. De novo mutations account for approximately 50% of cases, and phenotypic presentation is variable.[1] Common clinical findings include congenital kidney disease with hyperechoic and/or cystic kidneys, onset of diabetes mellitus in adolescence or young adulthood with pancreatic hypoplasia or atrophy, genital tract malformations, abnormal liver function tests, hypomagnesemia, hyperuricemia, and early onset gout. Secondary hyperparathyroidism and neurologic features have also been described.[2] *HNF1β* is predominantly expressed in the kidneys and likely plays a role in tubular development. It also has an important role in urogenital and pancreas development.[2]

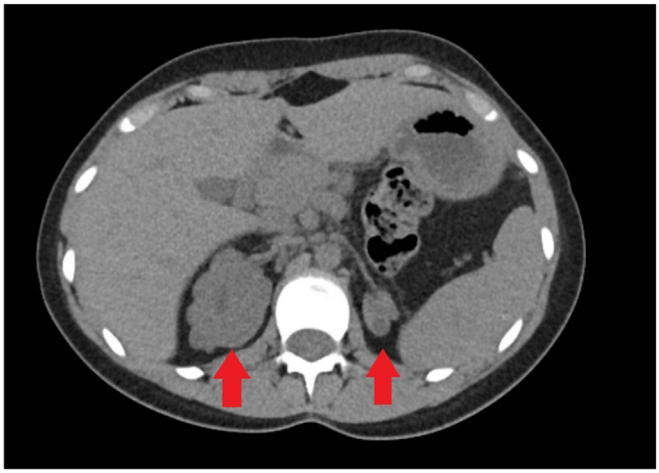

Fig 1.

Editor's Note: Submissions to "Visual Vignettes" are welcomed. Please submit online via the Journal's Editorial Manager site.

* Address correspondence to Dr Rachel Usala, Washington University in St Louis, Diabetes Center, 4921 Parkview Place, 13th Floor, Suite B, St. Louis, MO 63110-1093.
E-mail address: usala@wustl.edu (R.L. Usala).

https://doi.org/10.1016/j.aace.2023.06.003

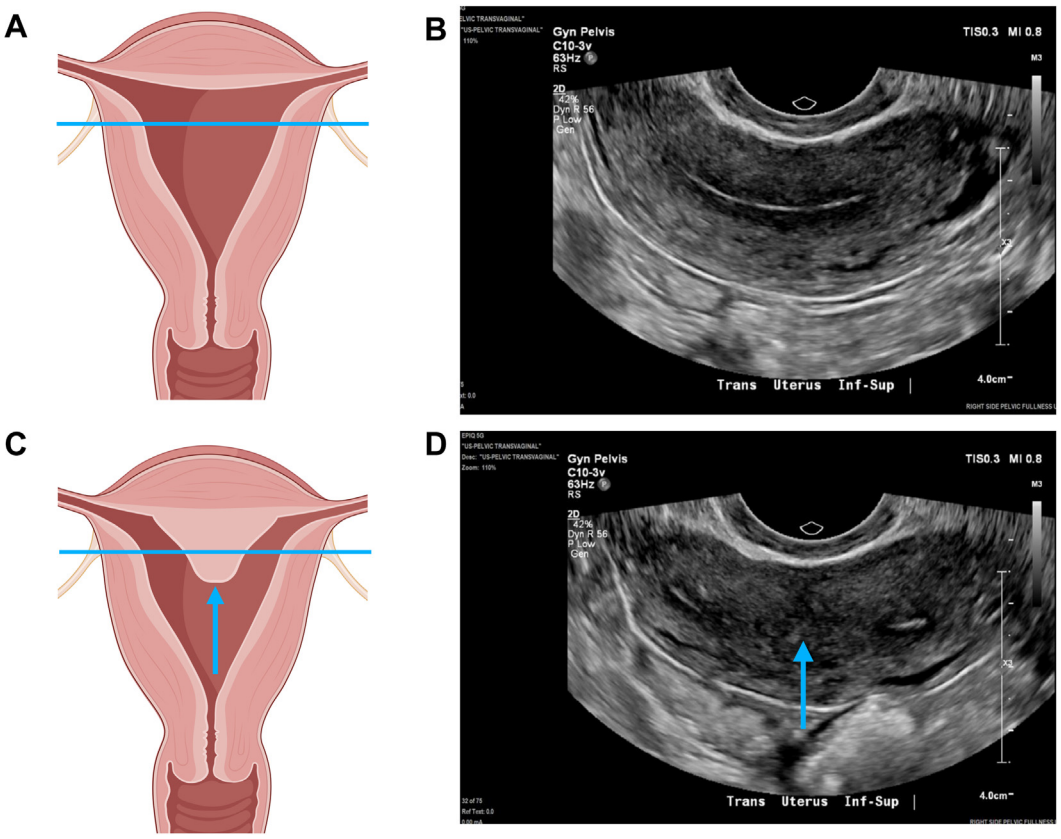

Fig 2.

This case highlights the importance of suspecting MODY, and specifically *HNF1β* defects, when patients present with this constellation of findings.[3] Diagnostic workup includes antibody and C-peptide testing, followed by molecular genetic testing. Establishing a MODY diagnosis is important as therapeutic strategies, transplant counseling, and routine health maintenance screenings vary by genetic mutation and mechanism of disease. Inheritance is generally autosomal dominant, which is important for genetic and reproductive counseling and may prompt genetic testing in family members.

Disclosure

The authors have no multiplicity of interest to disclose.

Acknowledgment

Patient consent for publication of clinical information and images were obtained. This work was supported by a grant from the National Institutes of Health, USA (NIH grant T32DK007120).

References

1. Faguer S, Decramer S, Chassaing N, et al. Diagnosis, management, and prognosis of HNF1B nephropathy in adulthood. *Kidney Int*. 2011;80(7):768–776.
2. Clissold RL, Hamilton AJ, Hattersley AT, Ellard S, Bingham C. HNF1B-associated renal and extra-renal disease-an expanding clinical spectrum. *Nat Rev Nephrol*. 2015;11(2):102–112.
3. Broome DT, Pantalone KM, Kashyap SR, Philipson LH. Approach to the patient with MODY-Monogenic Diabetes. *J Clin Endocrinol Metab*. 2021;106(1):237–250.