Asymptomatic proteinuria, renal cysts and dorsal pancreas agenesis

Cynthia C. Lim¹, Angeline H.M. Lai² and Jason C.J. Choo¹

¹Department of Renal Medicine, Singapore General Hospital, Singapore and ²Department of Pediatrics, KK Women’s and Children’s Hospital, Singapore

Correspondence and offprint requests to: Cynthia Lim; E-mail: cynthia.lim.c.w@sgh.com.sg

Keywords: Hepatocyte Nuclear factor 1-beta; kidney cysts; diabetes mellitus; type 2

The case

A 28-year-old woman was referred to our institution for evaluation of asymptomatic proteinuria. She had no significant past medical history and no family history of diabetes mellitus or kidney disease. Physical examination was unremarkable: blood pressure was 108/70 mmHg and she had no edema. Laboratory investigations found serum creatinine 74 µmol/L and normal electrolyte levels. Serum albumin was 38 g/L and liver enzymes were normal. Fasting glucose was 5.7 mmol/L. Serum complements were normal. Anti-nuclear antibody and anti-double-stranded deoxyribonucleic acid antibody were negative. Urine protein-creatinine ratio was 0.51 g/g. Urine examination under high-power field microscopy found three white blood cells and no red cells. Kidney ultrasonography found normal sized kidneys with simple subcentimeter subcortical cysts bilaterally. A computer tomography urogram found mild cortical scarring in the upper pole of the right kidney but no hydronephrosis. The urinary bladder was unremarkable. The uterus and endometrial cavity appeared to diverge at the fundus, suggesting an arcuate uterus.

What is the diagnosis?

The diagnosis

The clinical findings of renal cysts, dorsal pancreas agenesis and genital tract malformation suggested a hepatocyte nuclear factor-1 beta (HNF1B) transcription factor gene mutation. Genetic testing by Sanger sequencing of all coding regions and exon/intron boundaries of the HNF1B gene and dosage analysis by multiplex ligation-dependent probe amplification (MLPA) confirmed that the patient had a heterozygous whole gene deletion of HNF1B. HNF1B is a transcription factor that is expressed in the liver, pancreas, gut, genitourinary tract and lung. The HNF1B gene is located on chromosome 17q12, and several different mutations have been described, including deletion, missense and frameshift mutations [1]. The majority of these mutations were familial but spontaneous mutations have occurred [2]. These mutations may manifest in a myriad of clinical conditions, including asymptomatic liver enzyme elevation, renal cysts or kidney malformation, pancreatic agenesis or atrophy, maturity-onset diabetes mellitus of the young (MODY) and genital tract abnormalities [1, 2]. In a large case series, Edghill et al. [3] evaluated 160 Caucasians with renal disease of unknown etiology and found 23 subjects with heterozygous HNF1B gene mutations. Renal cysts and diabetes mellitus (DM) were common, occurring in 19 and 11 patients, respectively. In contrast, genital tract malformations were present in only two patients. The study did not identify any genotype-phenotype correlation.

Three years after initial presentation, our patient remained normoglycemic. Serum creatinine was 80 µmol/L and urine protein-creatinine ratio 0.69 g/g. Several case reports have described impaired renal function at presentation but longitudinal studies of non-diabetic patients with kidney cysts and HNF1B whole-gene deletion are not available, and the renal prognosis is generally unknown. She will thus require annual surveillance for DM and progressive CKD.
Conflict of interest statement. None declared.

References

Received for publication: 27.5.14; Accepted in revised form: 1.6.14