Neonatal Polycystic Kidney Disease

Priya Verghese, MD, MPH[a,*], Yosuke Miyashita, MD, MPH[b]

KEYWORDS

• Polycystic kidney • ARPKD • ADPKD • Multicystic dysplastic kidney • Renal cyst

KEY POINTS

- Neonatal polycystic kidney disease (PKD) is most commonly due to autosomal recessive PKD (ARPKD), multicystic dysplastic kidney disease (MCDK), cystic dysplasia, or, rarely, autosomal dominant PKD (ADPKD).
- ARPKD and ADPKD are inherited disorders involving bilateral renal cysts *without* dysplasia, unlike MCDK, which is classically unilateral, nonhereditary, and associated with dysplasia of intervening tissue.
- Ultrasonography is the diagnostic test of choice for neonatal PKD. MCDK must be differentiated from severe ureteropelvic junction obstruction by a renogram, as emergent surgical therapy may be indicated in the latter to preserve any residual renal function.
- There is no medication to prevent cyst formation for any neonatal PKD, but the complications of ARPKD and ADPKD must be carefully managed (hypertension, chronic kidney disease, or congenital hepatic fibrosis).
- MCDK must be followed clinically to ensure involution with normal compensatory hypertrophy and functioning of contralateral kidney.

INTRODUCTION

Due to an evolving trend for increased imaging in gestational care, prenatal ultrasound has increased the detection rate of fetal genitourinary abnormalities.[1] Although renal cysts occur in a variety of diseases in children, neonatal polycystic kidney disease (PKD) is a unique entity with a wide differential diagnosis often requiring prompt diagnostic and therapeutic interventions. Therefore, it is important that practicing perinatologists have a comprehensive understanding of neonatal cystic kidney disease.

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[a] Division of Pediatric Nephrology, Department of Pediatrics, Amplatz Children's Hospital, University of Minnesota, 2450 Riverside Avenue, MB 682, Minneapolis, MN 55454, USA; [b] Division of Pediatric Nephrology, Department of Pediatrics, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh School of Medicine, 4401 Penn Avenue, Pittsburgh, PA 15224, USA
* Corresponding author.
E-mail address: pverghes@umn.edu

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Neonatal cysts can occur as an isolated finding or they may occur as a part of a syndrome. The cysts could be hereditary or nonhereditary fetal malformations. We aim to provide an up-to-date comprehensive review on this area with emphasis on the clinical manifestations, diagnostic techniques, and potential therapeutic approaches to neonatal PKD. Notably, cystic kidneys are a feature of numerous genetic syndromes not covered in this review, such as Bardet-Biedl, Beckwith-Wiedemann, Ivemark, Jeune, juvenile nephronophthisis, Von-Hippel-Lindau, Hajdu-Cheney, Meckel-Gruber, orofacial-digital syndrome type 1, or Zellweger cerebrohepatorenal syndrome.[2] However since the most common genetic syndromes associated with cystic kidney are ARPKD and ADPKD, these rare genetic syndromes have not been included in this review.

Hereditary PKD

Background

Although PKD is a pathologic description of a kidney with multiple cysts, the term is most often used to describe an inherited disorder involving bilateral renal cysts *without* dysplasia. PKD is broadly divided into 2 forms depending on its mode of inheritance and genetic mutation.

- Autosomal recessive PKD (ARPKD)
- Autosomal dominant PKD (ADPKD)

PKD begins with conception, and ARPKD and ADPKD can have renal cysts present at any time in a person's life, ranging as early as antenatally to adolescence or older. Most often, ARPKD presents in the neonatal period or childhood with rare reports of initial presentation in late adolescence and early adulthood.[3,4] ADPKD most often presents in adults aged 20 to 40 years, but increasingly there are reports of ADPKD presenting in childhood and even in utero.[5] Both forms of PKD affect all racial and ethnic groups and they affect male and female individuals equally.

ARPKD

ARPKD is a rare cilia-related disorder primarily affecting the kidneys and liver with less frequent extrarenal manifestations occurring at any age. It is classically characterized by cystic dilation of renal collecting ducts associated with hepatic abnormalities of varying degrees, including biliary dysgenesis and periportal fibrosis. In 1994, the ARPKD gene was localized to the short arm of chromosome 6 (*PKHD1*). Fibrocystin/polyductin, a protein that is encoded by this gene, is expressed on the cilia of renal and bile duct epithelial cells and is thought to be crucial in maintaining normal tubular architecture of renal tubules and bile ducts. Different combinations of mutations in *PKHD1* and its resulting changes in fibrocystin may partially explain the wide phenotypic variance in this disease. However, there is also wide intrafamilial clinical variability among affected siblings that cannot be explained by genotypic differences.[6]

ARPKD is characterized by nonobstructive, bilateral, symmetric dilation and elongation of 10% to 90% of the renal collecting ducts, accounting for a wide variability of renal dysfunction. With an increase in the number of ducts involved, the kidneys enlarge but the reniform shape is maintained, as the abnormality is in the collecting ducts and the cysts are usually minute (<3 mm). Gross examination of an autopsied kidney shows multiple minute cystic spaces throughout the capsular surfaces. Cut sections of the kidney show that these cystic structures are subcapsular extensions of radially oriented cylindrical or fusiform ectatic spaces with poor corticomedullary differentiation due to the extension of the elongated and dilated collecting ducts from the medulla to the cortex. In all patients with ARPKD, there is congenital hepatic