Pediatr Radiol (1988) 18: 45-50

Pediatric Radiology

Dominant and recessive polycystic kidney disease in children: classification by intravenous pyelography, ultrasound, and computed tomography

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Abstract. Both dominant and recessive polycystic kidney disease appear in childhood. We have analyzed findings of intravenous pyelography, ultrasound and computed tomography in genetically classified cases of dominant (13 children) and recessive polycystic kidney disease (5 children) and thus defined criteria by which sporadic cases of childhood polycystic kidney disease can be classified to dominant or recessive polycystic kidney disease.

Polycystic kidney disease consists of two main entities: the autosomal dominant or adult polycystic kidney disease (DPKD) and the autosomal recessive or infantile polycystic kidney disease (RPKD).

RPKD manifests in infancy or childhood; most cases are of the neonatally lethal type. Also DPKD may manifest during childhood, even in a newborn baby [1].

DPKD and RPKD can usually be differentiated from each other by family history, histologic findings of kidney and liver or by radiologic and sonographic studies. If the case is sporadic and if histologic studies have not been performed imaging studies remain the only way to reach the differential diagnosis.

In intravenous pyelography (IVP) enlarged kidneys with accumulation of contrast material in dilated collecting tubules [2, 3], and in ultrasound (US) diffusely increased echogenicity [3] and poor definition of renal borders [4] have been considered typical of RPKD.

Several "macroscopic" cysts seen in IVP, US, or computed tomography (CT) have been regarded as typical of DPKD [2, 5]. Yet larger cysts can develop also in the kidneys of children with RPKD when they grow older [6] and the IVP and US findings in RPKD and neonatal DPKD may resemble each other [7]. Thus the distinction between DPKD and RPKD by imaging studies only is sometimes difficult. Precise etiologic diagnosis, however, is necessary for evaluating the prognosis and for genetic counselling.

The purpose of this study was to define radiologic and sonographic criteria for differentiating these two types of polycystic kidney disease from each other. The final aim of our studies now proceeding is to find a selection of clinical, histological and imaging criteria by which any sporadic case could be reliably classified.

Patients and methods

All children under 16 years of age treated for polycystic kidney disease in Finland in 1974-83 were sought using death certificates and diagnosis lists of the university hospitals and of the Department of Medical Genetics in Väestöliitto. Of the 82 children thus found, 31 had survived the neonatal period (28 days) and at least some imaging studies had been performed to each of them. They came from 30 families. The family histories were taken and the parents and siblings were studied by US or IVP. If one of the parents of the proband was affected, the disease was considered to be DPKD (11 families). If there were at least two affected siblings and the parents were unaffected the disease was considered to be RPKD (3 families). In 16 families the proband was the only affected person; they are called here "sporadic". The sources and criteria used, the pedigrees of the familial cases as well as details of the family studies will be published elsewhere [8].

The original films of all the imaging studies performed for these 31 children and their 3 affected siblings, who were under 16 years at the time of the study, were collected. Altogether 52 IVP, 53 US and 22 CT examinations were analyzed. Most of the US examinations had been performed by one of us (JJ) using a real-time sector scanner with 3.5, 5 or 7.5 MHz transducers. CT examinations were performed with a Siemens Somatom DR 2 (slice thickness 8 mm, incrementation 8 mm, scanning time 2-3 s) doing sequential scanning immediately after intravenous injec-

tion of Omnipaque. The details of the imaging studies of the children with DPKD were compared with those of the children with RPKD. The findings which always or nearly always differed between these two groups of patients were used as criteria for classifying the sporadic cases.

Results

The various details that were recorded from the IVP, US, and CT examinations of the 13 children with DPKD and the five children with RPKD are presented in Table 1. The findings that seemed to differentiate most reliably between DPKD and RPKD are as follows:

In IVP, the pattern of enlarged collecting tubules was always seen in RPKD (5/5 patients examined) but never in DPKD (0/10). Slow excretion was more common in RPKD (3/5) than in DPKD (2/10).

In US, "macroscopic" cysts were seen in DPKD (12/13) but not in RPKD. In DPKD the echogenicity of the liver was greater (7/13) or equal (6/13) to that of the kidneys but in RPKD the echogenicity of the kidneys was increased (2/2). The contours of the kidneys were obscure in RPKD (2/2) and in all those cases of DPKD (5/5) that had manifested in infancy. Generally increased echogenicity of the liver with a more marked increase adjacent to the portal veins was seen in RPKD (2/2) but only exceptionally in DPKD (1/13). This pattern was thought to represent the US picture of the morphologic finding of periportal fibrosis.

In CT, the overall distribution of the contrast material was normal in children with DPKD (6/6) but in RPKD (1/1) the initially high concentration of contrast in the cortex remained for longer than normally. Macroscopic cysts without any contrast enhancement were seen both in the cortex and medulla in DPKD but in RPKD only lace-like cysts of less than 0.5 cm in diameter were seen in the medulla.

Those findings in IVP, US and CT that seemed to differentiate most reliably between DPKD and RPKD were recorded in the 16 sporadic patients and are presented in Table 2. One patient (29 A) had all the findings typical of DPKD. In five patients (27 A, 30 A, 34 A, 37 A and 38 A) all the findings were typical of RPKD but one of them had

Table 1. Findings in IVP, US and CT examinations of 13 children with DPKD (families 1–11) and 5 children with RPKD (families 12–14)[a]. Only one examination of each type in case of each child is presented in the table; differing findings in other examinations are mentioned as footnotes

Family	1	2	2	2	3	4	5	6	7	8	9	10	11	12	13	13	14	14
Patient	D	A	B	C	A	A	A	B	A	A	A	B	A	B	A	B	A	B
IVP																		
Age (years)			6	0.2	13	13	15	11	13	1	9	15		2	New-born	2	0.2	12
Kidney size (right/left, +SD)			1/2[b]	3/3	0/1	2/3	1/5	4/4	3/3	1/1[b]	0/0	1/2		5/5	5/5	5/5	0/0	0/0
Deformed contour			−	−	+	−	−	−	+	−	−	−		−	−	−	−	−
Dilated collecting tubules			−	−	−	−	−	−	−	−	−	−		+	+	+	+[c]	+[c]
Radiolucent areas			−	?	−	−	−	+[d]	−	−	+	+		−	−	−	−	−
Deformed pelves/calyces			+[d]	?	+	+	−	+[d]	+	−	−	+		−	+	+[d]	+	−
Prolonged excretion			+	+	−	−	−	−	−	−	−	−		+	+	+	−	−
US of the kidneys																		
Age (years)	0.3	8	6	Newborn	13	13	19	11	26	1	9	15	11	1		7		
Obscure contour	+	−	+	+	−	−	−	+	−	+	−	−	−	+		+		
Increased echogenicity	+	−	+	+	+	+	+	+	+	+	+	−	+	+		+		
Echogenicity of																		
the kidneys > the liver	−[e]	−	−	−	−	−	−	−	−	−	−	−	−	+		+		
the kidneys = the liver	+	−	+	+	+	−	−	+	−	+	−	−	−	−		−		
the kidneys < the liver	−	+	−	−	−	+	+	−	+	−	+	+	+	−		−		
Cysts over 1.0 cm	−	+	+	+	+	+	+	+	+	+	+	+	+	−		−		
US of the liver																		
Cysts over 1.0 cm	−	−	−		−	−	−	−	+	−	−	−	−	−		−		
"Periportal fibrosis"	−	−	+		−	−	−	−	−	−	−	−	−	+		+		
CT																		
Age (years)			8	2	13	13		11				15				7		
Cysts over 1.0 cm			+	+	+	+		+				+				−		
Cortical accentuation of contrast medium			−	−	−	−		−				−				+		

[a] The numbering of the families is the same as in the pedigrees published elsewhere [8]. The affected siblings in each sibship are indicated by capital letters in alphabetical order starting from the eldest. [b] The kidneys were larger in standard deviations as a newborn. [c] Resembles medullary sponge kidney. [d] This finding was missing as a newborn. [e] The echogenicity of the kidneys was greater than that of the liver as a newborn

been studied by CT only and another by US only. In eight patients (26 A, 31 A, 33 A, 35 A, 36 A, 39 A, 40 A and 41 A) most findings suggested RPKD.

Controversial findings were found in two patients (28 A and 32 A).

From these results it was concluded that of the sporadic patients one had DPKD, 13 had RPKD, and the differential diagnosis could not be established in two patients.

Typical examples of IVP, US, and CT pictures in DPKD (Fig. 1) and RPKD (Fig. 2) are presented.

Discussion

The 13 children with DPKD in this series represented a wide spectrum of severity of childhood DPKD and thus their imaging findings can be considered representative of DPKD in children. As there were only five children with genetically evident RPKD, the general representativeness of their findings is less certain. However, kidney and/or liver histology had been studied in seven of the sporadic children classified in this study as RPKD by imaging findings (patients 30 A, 33 A, 34 A, 36 A, 37 A, 39 A and 40 A) and in each case also the histologic findings were typical of RPKD [1].

Findings in IVP

The kidneys were usually enlarged in both forms of the disease but more markedly in RPKD. Normal kidney size did not exclude either of the forms.

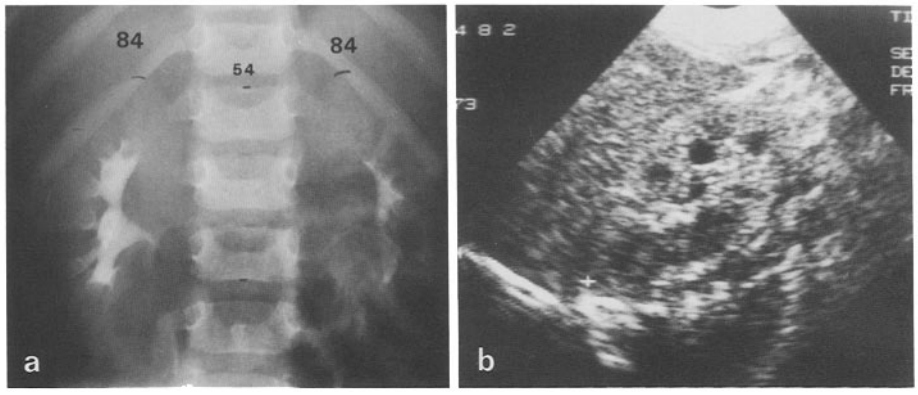
The findings typical of RPKD both in our patients and in the earlier reports [2] have been striated accumulation of contrast material in the enlarged collecting tubules and slow excretion. The tubular enlargement resembled the finding called medullary sponge kidney in the siblings 14 A and 14 B. The autopsy of 14 A at 9 months showed RPKD with mild renal and more pronounced hepatic involvement; this type has been called juvenile polycystic kidney disease [9]. IVP findings in this form of RPKD have resembled medullary sponge kidney also in some previously reported patients [10].

Accumulation of contrast material suggesting tubular enlargement has also been seen in some neonates with DPKD [11–14], giving sometimes a "mottled" or "puddled" rather than streaky appearance [15]. The distinction between these two patterns

Table 2. The findings in IVP, US and CT of 16 sporadic children with polycystic kidney disease that were used in differential diagnosis between DPKD and RPKD. Only one examination of each type in case of each child is presented in the table; differing findings in other examinations are mentioned as footnotes

Family	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	Typical findings in	
Patient	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	DPKD	RPKD
IVP																		
Age (years)	12		2	8	6	4	3	6	Newborn	0.1	1.5		Newborn	Newborn	5	10		
Dilated collecting tubules	+		+[a]	−	+	+	+	+[b]	+	+	+		+	+	+	+	−	+
Prolonged excretion	−		−	−	−[c]	−[c]	−	−	+	+	−		+	+	+	−	+or−	+
US of the kidneys																		
Age (years)	20		1	14	6	8	3	12	2	12	4	Newborn	5	1	16	11		
Obscure contour	+		+	−	+	+	−	−	+	+	+	+	+	+	+	+	+or−	+
Echogenicity of the kidneys > the liver	−		−	−	+	+	−	−	−[c]	+	+[d]	+	+	−	−	+	−	+
the kidneys = the liver	+		+	−	−	−	−	+	+	−	−	−	−	+	−	−	+or−	−
the kidneys < the liver	−		−	+	−	−	+	−	−	−	−	−	−	−	+	−	+or−	−
Cysts over 1.0 cm	−		−	+	−	+[e]	−	−	−	−	−	−	−	−	−	+[e]	+	−
US of the liver																		
"Periportal fibrosis"	−		+	−	+	−	−	+	+	−	−	−	+	+	+	+	−	+
CT																		
Age (years)		Newborn	3	14	6	9				13	Newborn		5	3	16	11		
Cysts over 1.0 cm		−	−	+	−	+[e]				−	+[e]		−	−	−	−	+	−
Cortical accentuation of contrast medium		+	−	−	+	+				+	+		+	+	+	+	−	+

[a] Resembles the finding called the medullary sponge kidney. [b] This could not be seen any more at 13 years. [c] This finding was + as a newborn. [d] Patches of strongly echogenic areas that had increased by age. [e] One or two small cysts



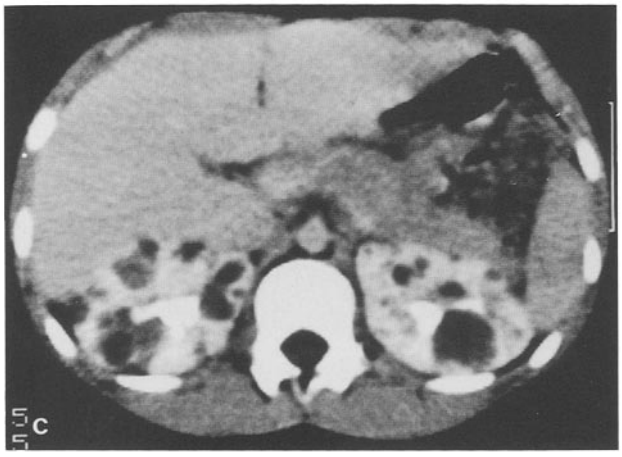


Fig. 1a–c. Children with DPKD. **a** IVP of patient 8 A at 1 year of age is normal. **b** US of the same patient at the same age shows slightly increased echogenicity, unsharp contour and cysts of about 1.0 cm in diameter. **c** CT of patient 6 B at 11 years shows cortical and medullary cysts and evenly distributed contrast medium

does not seem to be clear-cut. In our series no signs of dilated collecting tubules were seen in neonates with DPKD.

It has been suggested that if gross renal enlargement and homogenously striated and prolonged nephrogram is seen in a newborn with RPKD, short-time survival can be expected [16]. In our material from which neonatally lethal cases had been excluded this appearance did not correlate with very poor prognosis.

Expansions in the contours, radiolucencies, and distortion of pelves and calyces, which are the typical IVP findings in adults with DPKD [2], were more often absent than present in these children with DPKD. Thus in childhood, it is usually not possible to confirm nor to exclude the diagnosis of DPKD by IVP only.

Findings in US

In our patients as well as in earlier reports [7] the existence of macroscopic kidney cysts usually differentiated DPKD from RPKD. Yet roundish larger cysts may develop in patients with RPKD [6] and infants with DPKD may lack macroscopic cysts [13], as did our patient 1 D. Thus, the presence of macroscopic cysts is not an absolute criterion for DPKD. The fact that cysts in the liver were not seen in children with DPKD was not surprising as they are known to develop later in life and to be rare even in young adults with DPKD [17].

The relatively greater echogenicity of the kidneys versus the liver should be used as criterion for RPKD with caution because hepatic fibrosis increases with age [6] and thus the situation may be reversed when the patient grows older (see patient 40 A). The value of obscure contours of the kidneys as criterion for RPKD is also limited because early manifestation in DPKD may show the same findings.

Findings in CT

CT was performed to only one child with genetically evident RPKD but also to five sporadic children who had histologic verification of RPKD. All these six examinations were similar with each other and totally different from DPKD. In RPKD the contrast appeared to concentrate in the cortex but evidently it was diluted in the medulla. Two sporadic patients with CT findings otherwise typical of RPKD had one or two macroscopic cysts among the small lace-like ones in the medulla (patients 31 A and 36 A). As the findings in one sporadic patient (28 A) did not suggest any cystic disease it must be questioned whether she has polycystic kidney disease at all.

Comparison of the criteria defined by this genetic approach with the earlier ones shows that the IVP findings are in accordance with earlier reports [2, 3], but, in our material, IVP in RPKD did not have much prognostic value. Also US criteria were, as a rule, parallel with earlier reports [3, 4] but we would not use obscure contours of the kidneys as criterion against DPKD. The clearly different appearance of DPKD from RPKD seen in CT has not been stressed earlier.

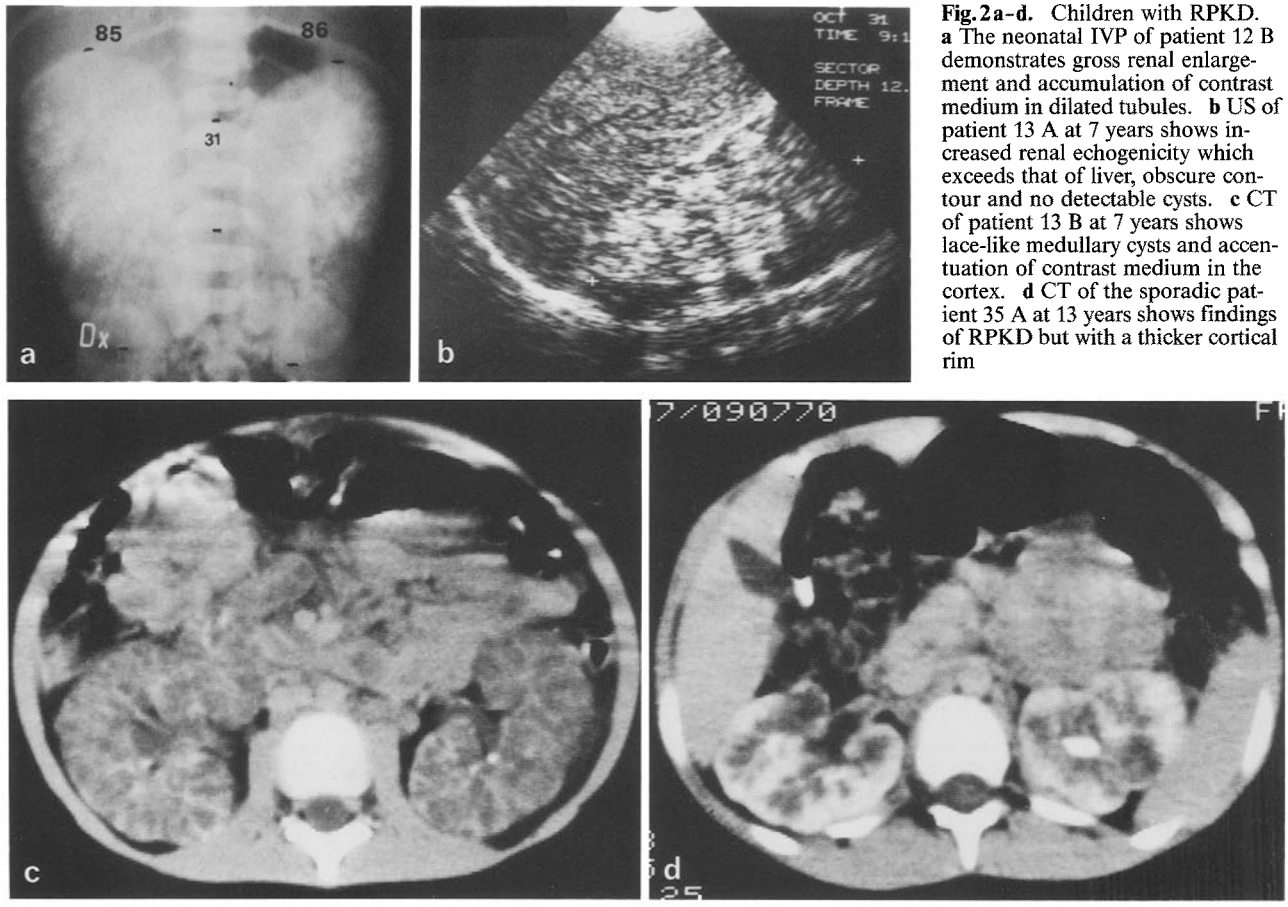


Fig. 2a–d. Children with RPKD. **a** The neonatal IVP of patient 12 B demonstrates gross renal enlargement and accumulation of contrast medium in dilated tubules. **b** US of patient 13 A at 7 years shows increased renal echogenicity which exceeds that of liver, obscure contour and no detectable cysts. **c** CT of patient 13 B at 7 years shows lace-like medullary cysts and accentuation of contrast medium in the cortex. **d** CT of the sporadic patient 35 A at 13 years shows findings of RPKD but with a thicker cortical rim

Conclusion

It is usually possible to determine whether a child with sporadic polycystic kidney disease has DPKD or RPKD if IVP, US, and CT examinations have been performed. A summary of the criteria is as follows:

The child has DPKD if there are macroscopic kidney cysts in US or CT, if contrast material is evenly distributed to renal cortex and medulla in CT, and if tubular enlargement is not seen in IVP. Normal excretion, and in US normal liver with the echogenicity of the kidneys equal or less than that of the liver support the diagnosis. In exceptional cases macroscopic cysts may be lacking.

The child has RPKD if a streaky pattern of enlarged collecting tubules is seen in IVP, if the echogenicity of the kidneys exceeds that of the liver in US, and if the contrast material remains in the renal cortex for longer than normally and lace-like cysts are seen in the medulla in CT. Slow excretion, absence of macroscopic cysts and in US obscure renal contours and liver texture suggests the histologic finding of periportal fibrosis support the diagnosis.

Acknowledgements. This work was supported by grants from three Finnish foundations: the Foundation for Pediatric Research, the Kidney Foundation and the Paulo Foundation.

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Received: 15 January 1987; accepted: 16 March 1987

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