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## Rapidly progressive nephromegaly in a neonate with autosomal recessive poly cystic kidney disease

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### ABSTRACT

**Background:** Autosomal recessive polycystic kidney disease (ARPKD) associates with significant renal and liver-related morbidity and mortality in children. Rarely severe enlargement of kidneys necessitates nephrectomy and initiating dialysis.

**Case Presentation:** A 5-day-old newborn boy with prenatal ultrasonography suggestive of ARPKD admitted in the hospital due to anuria from first day of life. One week after admission, left nephrectomy was conducted because of severe enlargement of kidneys accompanied by respiratory distress and repeated vomiting. Patient was placed on peritoneal dialysis. Pathology of kidney revealed cystic lesions consisted of dilated collecting duct, with lack of involvement of glomeruli and other parts of the nephrons. Patient died at age 17 days with respiratory hemorrhage.

**Conclusions:** Our case is interesting because of progressive increase in kidney sizes requiring nephrectomy. Such huge nephromegaly in ARPKD has not been reported yet.

### *Implication for health policy/practice/research/medical education:*

The course of the disease in our case emphasizes on respiratory problems as the main medical concerns in neonatal onset ARPKD, even if the patients have no respiratory symptoms at birth.

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### 1. Introduction

Autosomal recessive polycystic kidney disease (ARPKD) belongs to a group of congenital hepatorenal fibrocystic syndromes which result in significant renal and liver-related morbidity and mortality in children. In the majority of cases, the disease presents as bilateral enlarged kidneys in neonatal period. Renal involvement is characterized by nephromegaly, hypertension, and varying degrees of renal dysfunction. Within the first decade of life, the disease progresses to end-stage renal disease (ESRD) in >50% of affected cases. Approximately 30% of cases die within the first year of life from respiratory insufficiency due to pulmonary hypoplasia or superimposed pulmonary infections (1).

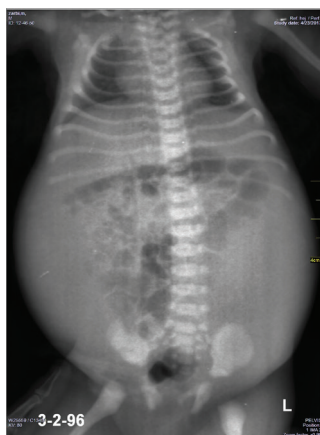
### 2. Case Presentation

A 5-day-old newborn boy was admitted in hospital because

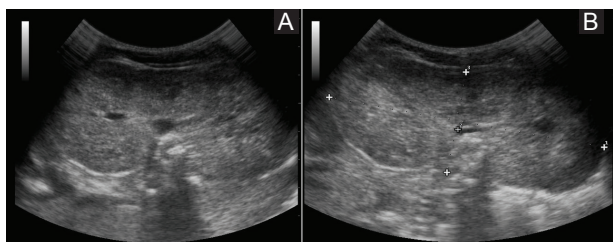
of anuria from first day of life. An obstetrical ultrasound (US) was performed in last month of gestation and has been reported bilateral hyper-echogenic enlarged kidneys and decreased amniotic fluid volume. According to the abnormal US findings, the patient was admitted in a local hospital for more evaluation. He was borne by normal vaginal delivery and no respiratory distress. In fifth day of birth, the patient was discharged from local hospital and transferred to our center because of persistent anuria. Parents presented a history of death in one of their sons in neonatal period with diagnosis of polycystic kidney disease. At the time of admission, the mother complained on poor feeding of the neonate, however, the neonatal reflexes were intact. In physical examination, systolic blood pressure (BP) was 80 mm Hg with no measurable diastolic BP. Pulse and respiratory rates were 110/min and 35/min respectively and temperature was

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37°C. Physical examination of abdomen revealed severe abdominal distension due to bilateral nephromegaly. The majority of the abdominal cavity was occupied by enlarged kidneys (Figure 1). Urinary catheterization was unsuccessful. The patient received two doses of normal saline (40 cc/each dose) and then intravenous furosemide 1 mg/kg. Few hours after administering normal saline and diuretic, urine output established (35 cc in the first day of admission). Abdominal US showed normal liver and spleen with enlarged kidneys. Lengths of right and left kidneys were reported 97 and 100 mm. Increased parenchymal echogenicity and abundant microcysts were other findings (Figures 2A-B). Again, in third day of admission, the patient had no urination. Abdominal distension rapidly increased and edema in lower extremities was detected. In fifth day, frequent vomiting, decreased BP (systolic BP = 60 mm Hg) and increased in respiratory rates added to previous findings. Infusion of dopamine, 50 mg in 24 hours was started and the patient received fresh frozen plasma (FFP) 40 cc for inducing volume expansion and correcting abnormal



**Figure 1.** Thoracic and abdominal X- ray of the patient. It shows no abnormal finding in lungs fields, bone and soft tissues of the chest. Abdominal cavity is severely distended and shadows soft tissues in flanks observes that pushes the bowels to the middle of abdominal cavity.



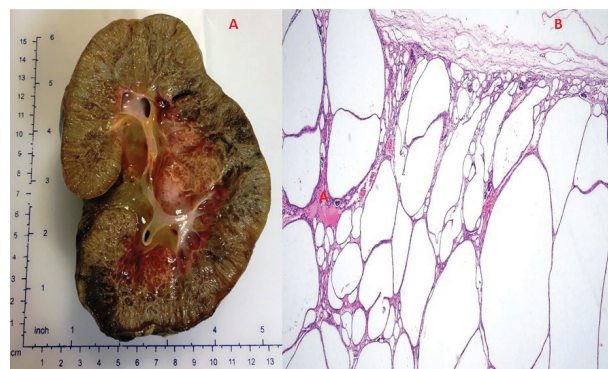
**Figure 2.** Ultrasound images of kidneys; a longitudinal low-frequency ultrasound image shows a markedly enlarged (longitudinal diameter; 97 mm) echogenic kidney with loss of corticomedullary differentiation (A). The linear high-frequency transverse image reveals numerous tiny cystic structures and relatively hypochoic peripheral cortex (B).

prothrombin time (PT) and partial thromboplastin time (PTT). Birth weight was 3.6 kg which reached to 4.2 kg on the fifth day of admission (age of 10 days). According to severe abdominal distension and severe nephromegaly, which resulted to compressive effects on stomach and diaphragm, a unilateral nephrectomy and insertion of peritoneal dialysis catheter was conducted and then the patient transferred to pediatric ICU. Figures 3A-B presents the macroscopic and microscopic details of kidney tissue.

Two days after nephrectomy acute peritoneal dialysis was started to control severe hypertension (BP of 150/110 mm Hg) which continued despite stopping dopamine administration. Hypertension was controlled by administering intravenous labetalol, high doses of furosemide and acute peritoneal dialysis. Despite respiratory support and acute dialysis, on 12th day of admission, the patient died following tracheal hemorrhage, severe hypoxemia and hypotension. Table 1 shows the laboratory tests and their changes during different days of admission. Kidney US was requested for parents, but unfortunately it did not perform due to lack of cooperation.

### 2.1. A summary history of other affected son of the family

He was admitted in our center in first day of life with generalized edema, severe abdominal distension due to kidneys enlargement and oliguria. Prenatal US was not performed and post-natal US revealed hyper-echogenic kidneys with increased sizes (length of each kidney was 106 mm) with multiple microcysts, and normal liver sonography. The case was hypoxemic; the respiratory



**Figures 3.** Left nephrectomy consisting of enlarged Reni form shaped kidney with persistent fetal lobation, measuring  $14 \times 9 \times 6$  cm and weighing 513 g, its attached proximal ureter measuring  $6.5 \times 0.2$  cm. On the cut surface, sponge-like renal parenchyma with radially oriented and fusiform cysts in cortex and more rounded cysts in medulla. The normal pattern of cortex and medulla is replaced by innumerable, radially arranged cysts. The calyces, ureter and pelvis are unremarkable (A). Sections of kidney show elongated, variable cystic collecting ducts, normal glomeruli and tubules seen between cysts (B) (H&E  $\times 40$ ).

**Table 1.** Laboratory findings in the patient before and after initiating dialysis and before death

Laboratory parameters	First day	7th day (before initiating dialysis)	9th day of admission (starting dialysis)	12th day
Serum urea (mg/dL)	64	70	66	47
Serum creatinine (mg/dL)	1.2	2.1	2.3	1.7
Serum sodium (meq/L)	141	132	135	131
Serum potassium (meq/L)	5.2	2.4 <sup>a</sup>	3.4 <sup>b</sup>	2.6 <sup>c</sup>
Serum calcium (mg/dL)		8.5	9	8.6
Serum phosphorus (mg/dL)		5.1	3.7	3.1
Serum glutamic oxaloacetic transaminase (SGOT), U/L	34			
Serum glutamate pyruvate transaminase (SGPT), U/L	10			
Serum albumin (g/dL)	3.2	2.3	2.9	2.6
Serum prothrombin time (PT; second)	>40 (control =12)	24 <sup>d</sup>	25 <sup>e</sup>	22 <sup>e</sup>
Serum partial thromboplastin time (PTT; second)	46 (control = 30)	58 <sup>d</sup>	58 <sup>e</sup>	50 <sup>e</sup>
Hematocrit (%)	50.2	25.8 <sup>f</sup>	36.6	34.9
Serum hemoglobin (g/dL)	17.8	8.6 <sup>f</sup>	12.3	12.3
Platelet count (cell/ $\mu$ L)	163000	151000	77000	53000
Blood culture	Negative	Negative	--	--
Urine culture	Negative	Negative	--	--

<sup>a</sup> The dose of furosemide reduced; <sup>b</sup> potassium chloride was added to dialysis solution (3 meq/L) and furosemide was discontinued; <sup>c</sup> Potassium chloride was added to dialysis solution (4 meq/L) and also potassium chloride was added to serum (20 meq/L); <sup>d</sup> Patient received FFP and intravenous vitamin K. There were no apparent hemorrhage; <sup>e</sup> Patient received FFP. There were no apparent hemorrhage; <sup>f</sup> Patient received packed cells.

rate at admission was 54/min and blood pressure was within normal ranges. Serum creatinine and sodium levels were 1.3 mg/dL and 133 meq/L in the first day of admission respectively which reached to 1.5 and 133 in the fifth day of hospitalization. The chest X-ray was normal. The parents did not consent for more evaluation and treatment of their boy and discharged the patient. Few days later he died in a local hospital probably due to respiratory failure.

### 3. Discussion

ARPKD is a rare (1/20 000 live birth) hepatorenal fibrocystic disease commonly diagnosed in uterus or at birth. Enlarged echogenic kidneys with loss of cortico-medullary differentiation due to fusiform dilatation of the collecting ducts are the typical findings on kidney US. Clinical findings in the proband and the absence of renal disease in the proband's biological parents are the main basic findings needed for suspecting to ARPKD. However establishing the diagnosis needs to identify biallelic pathogenic variants in *PKHD1* in the affected individuals (1). A detailed history, complete physical examination, imaging, and rarely genetic testing or biopsy are usually sufficient to distinguish ARPKD from neonatal onset ADPKD. In macroscopy, the cut surface of kidneys reveals a radial pattern of the spindle-shaped collecting duct cysts that extended into the renal cortex. The glomeruli and other tubular segments appears to be decreased in proportion due to collecting duct ectasia and interstitial changes that squeeze and atrophy of renal

parenchyma (2-4). Symptomatic hepatic involvement is present in only 40%-50% of neonates with ARPKD (1). Distinguishing autosomal dominant polycystic kidney disease (ADPKD) from ARPKD by US is very difficult or impossible. The classic US appearance in ARPKD is enlarged kidneys with increased echogenicity of the renal parenchyma. Cysts are rarely seen. The renal borders are usually poorly defined. In ADPKD renal cysts may or may not be present initially, but the cysts usually increase in size and proportion with increasing age. One or more renal cysts within enlarged kidneys are typical US appearance of ADPKD in children. Kidney cysts form in glomeruli and in all tubular segments (5). Slow but progressive enlargement of the kidneys with renal failure occurring between 5 to 6 decades of life is characteristic of ADPKD. The disease presents with hypertension, flank pain, hematuria, and renal cysts infection in adults. However ARPKD typically presents in younger patients, and is characterized by cystic dilation of the collecting ducts of the kidneys, along with dysgenesis of the biliary ductal plate, resulting in congenital hepatic fibrosis and often death in the perinatal period due to respiratory failure. Despite different and variable clinical presentations, a single gene, *PKHD1* is responsible for the disease. The diagnosis of ARPKD typically is based on clinical findings alone, with liver and kidney biopsies needed only in rare instances (6).

In 1%-2% of cases, ADPKD presents in newborns, often with signs and symptoms indistinguishable from ARPKD (7-9). Congenital hepatic fibrosis (CHF),

an invariable finding in ARPKD, is rarely observed in ADPKD (10). Pretorius et al (11) reported five cases of ADPKD diagnosed in the fetus by sonographic evaluation and a positive family history. In first case the left and right renal lengths at 8-day age were 8.1 cm and 6.2 cm respectively with a cyst in the left upper pole measured 3.3 cm in diameter, and no liver cysts. Case 2 was the sibling of case 1 who underwent therapeutic abortion at gestational age of 24 weeks because of US findings consistent with ADPKD. Case 3 had Potter's facies and moderate pulmonary hypoplasia and died few hours after birth with respiratory failure. The pathology of this case showed findings consistent with classic ADPKD such as enlarged kidneys with variable sized cysts involving all portions of the nephrons. Other case was a neonate with normal sized echogenic kidneys and no liver cyst in prenatal and neonatal US. Ultrasonography conducted at 25th day of age showed two cortical cysts. In case 5, the neonatal US showed enlarged, echogenic kidneys with several 2-3 mm cysts with no liver cyst. Severely progressive increase in kidney sizes immediately after birth which needed unilateral nephrectomy noted in our case were not reported in any of these cases.

In our patient, during a week (from age 5 to 12 days) the lengths of kidneys increased about 50 mm (5 cm) and resulted in respiratory problems and repeated vomiting and symptoms that seem partially related to compressive effects of enlarged kidneys. During delivery and also the first days of admission, our patient had no respiratory problem. In chest X-ray, the lungs' parenchyma were normal with no evidences of hypoplasia. Zerres et al (12) reviewed clinical courses of 66 boys and 49 girls with ARPKD over a mean period of 4.92 years. It was a selected group of children who mostly survived the neonatal period, presenting the largest group of case series of ARPKD that have not been reported yet. The age at diagnosis was prenatal period up to 14.5 years (median age of 29 days). Ten cases (8.7%) were prenatal forms. They found decreased glomerular filtration rate (GFR) in 72%, while 9.5% of cases developed end-stage renal disease. Kidneys lengths were above the 97th percentile in 68% of patients. Furthermore, none of their cases needed to nephrectomy due to massive nephromegaly. Clinical signs of hepatic fibrosis were detected in 46% of their patients. Thirteen patients (11%) died during the observation period. In our case, a history of PKD in proband with early neonatal presentation was existed. However we did not succeed to check parents for cystic lesions in kidney US. Early presentation of the disease in two members of a family, and laboratory evidence of hepatic dysfunction (abnormal PT and PTT tests) which were not corrected by several times infusion of fresh frozen plasma (FFP), all

were supportive findings for suspecting to ARPKD. We established the final diagnosis by pathology that showed cystic lesions consisted of dilated collecting ducts, lack of involvement of glomeruli and other parts of the nephrons, pathologic findings consistent with ARPKD. However hepatic US was normal with no evidence of periportal fibrosis, prolonged PT and PTT tests which did not improve by several times FFP infusion indicated hepatic dysfunction.

#### 4. Conclusions

Our case is interesting and also unique because of rapidly progressive enlargement of kidneys requiring nephrectomy to minimize compressive effects on diaphragm and abdominal viscerals. Such huge nephromaly in ARPKD has not been reported yet.

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#### Authors' contribution

All authors contributed to different stages of the preparation of the case report.

#### Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. Informed consent was obtained from the parents of patient for publication of this case report.

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