Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Neonatal Onset of Autosomal Recessive Polycystic Kidney Disease Mimicking Bartter Syndrome: A Case Report

Dr. Punith MS[1], Dr. Santosh B Kurbet[2], Dr. Mahantesh V Patil[3], Dr. Roopa M Bellad[4], Dr. Vineetha Gautam[5]

[1]Junior resident-II MBBS, M.D paediatrics, Department of paediatrics, JNMC, Belagavi

[2]Professor and HOD, M.S., M. Ch (paediatric surgery), DNB, Department of paediatric surgery, JNMC, Belagavi

[3]Professor M.D Paediatrics, Paediatric Nephrologist, JNMC, Belagavi

[4]Professor D.C.H., M.D Paediatrics, Department of paediatrics, JNMC, Belagavi

[5]Senior resident, D.C.H., D.N.B Paediatrics, Department of paediatrics, JNMC, Belagavi

Cite this paper as: Dr. Punith MS, Dr. Santosh B Kurbet, Dr. Mahantesh V Patil, Dr. Roopa M Bellad, Dr. Vineetha Gautam, (2025) Neonatal Onset of Autosomal Recessive Polycystic Kidney Disease Mimicking Bartter Syndrome': A Case Report, *Journal of Neonatal Surgery*, 14 (32s), 714-720

ABSTRACT

Autosomal recessive polycystic kidney disease is an uncommon genetic disorder characterized by cystic enlargement of the renal collecting ducts along with varying degrees of congenital hepatic fibrosis. Neonatal presentation can mimic other tubulopathies like Bartter syndrome due to overlapping biochemical abnormalities. We present a case of a late preterm male neonate, born to consanguineous parents, who exhibited lethargy, dehydration, and significant weight loss by day 8 of life. Clinical evaluation and investigations revealed features of salt-wasting tubulopathy with metabolic alkalosis. Imaging showed enlarged, cystic kidneys, and genetic testing confirmed a homozygous mutation in the PKHD1 gene, consistent with ARPKD. Supportive therapy, including fluid and electrolyte correction and indomethacin, led to clinical improvement. This case underlines the importance of considering ARPKD in neonates with electrolyte imbalance and renomegaly and demonstrates the diagnostic utility of early genetic analysis.

1. INTRODUCTION

Autosomal recessive polycystic kidney disease' is a rare hereditary disorder that primarily affects the kidneys and hepatobiliary system.[1] It follows an autosomal recessive pattern of inheritance and has an estimated incidence of about 1 in 20,000 live births. [2] The disease is caused by mutations in the PKHD1 gene located on chromosome 6p12, which encodes fibrocystin—a protein that plays a vital role in maintaining the structure and function of renal collecting ducts and biliary epithelial cells.[3] Disruption of fibrocystin function leads to cystic dilatation of collecting ducts and varying degrees of congenital hepatic fibrosis.[4]

The clinical spectrum of ARPKD is broad. In severe cases, it may be identified during the antenatal period via ultrasound findings such as oligohydramnios and bilateral renomegaly, and may result in neonatal mortality due to pulmonary hypoplasia.[5] Less severe presentations may arise during infancy or childhood with signs of renal dysfunction, systemic hypertension, and hepatic manifestations such as portal hypertension or hepatosplenomegaly.[6] Neonatal imaging typically shows bilaterally enlarged, echogenic kidneys with poor corticomedullary differentiation.[7]

In rare cases, neonates with ARPKD may present with electrolyte imbalances—including hyponatremia, hypokalemia, and metabolic alkalosis—mimicking Bartter syndrome, a tubulopathy affecting Na and Cl reabsorption in the Loop of Henle.[8] This phenotypic overlap may obscure the diagnosis unless supported by imaging or genetic analysis.[9] Therefore, ARPKD should be considered in any neonate with salt-wasting features and renomegaly.

Advances in molecular diagnostics have made genetic testing central to confirming ARPKD, especially in ambiguous or overlapping clinical scenarios. Early identification of PKHD1 mutations aids in diagnostic clarity and allows for appropriate family counselling, particularly in consanguineous families at increased genetic risk.[10]

Case Report

A late preterm male neonate was born to a 25-year-old mother, a G3P2L0D1A1, at 35 weeks and 3 days of gestation via emergency lower segment cesarean section in view of polyhydramnios. The baby cried immediately after birth and weighed 2.8 kg. The infant was the third order child of the mother with bad obstetric history, born to a second-degree consanguineous couple. There was no significant maternal history of infections, hypertension, or diabetes during pregnancy.

The family history was notable for the loss of two previous children. The first child, a male fetus, was medically terminated at 22 weeks due to bilateral renal anomalies. The second child, a female, died at 7 months of age. She had no significant perinatal complications but was noted to have developmental delay and failure to thrive—achieving neck holding at 2 months but unable to sit at 7 months. Photographs taken shortly before her demise show a markedly undernourished appearance with dysmorphic facial features, which may retrospectively suggest underlying renal or syndromic pathology (Figure 1 and 2).

Figure 1: Image of the same sibling with distinctive facial features and hypotonia.

Figure 2: Image of the affected sibling at ~6 months, showing undernourishment and developmental delay.

On the second day of life, the neonate showed early signs of irritability, which was temporarily relieved by feeding. By day 5, the baby was noted to be excessively micturating (10–12 times a day), and by day 8, progressive weight loss (21% of birth weight) was noted. He was referred to "KLEs Dr. Prabhakar Kore Hospital and Medical Research center, Belagavi", for further management. Upon admission to our hospital on day 8 of life, the neonate presented with lethargy, poor feeding, and a decrease in activity level. Clinical examination revealed a pale, hypotonic, and sick appearance with a sunken anterior fontanelle and frog-leg posture. Abdomen was distended. Bilaterally enlarged kidneys were palpable with smooth surfaces. The baby had dysmorphic features including triangular facies, broad forehead, depressed nasal bridge, large eyes, and pseudo hypertelorism.

Initial laboratory investigations showed hypovolemic hyponatremic (127 mmol/L) hypokalemic (2.35 mmol/L) hypochloremic (66 mmol/L) metabolic alkalosis (31.5 mmol/L). Blood urea and serum creatinine progressively decreased with hydration, suggesting prerenal azotemia. Inflammatory markers were mildly raised initially (HsCRP 4.9 mg/L on 18/03). Liver function tests were within acceptable limits. Serum calcium, magnesium, and phosphate were within normal range. Urinalysis showed proteinuria (+1 to +2), and mildly elevated RBCs, with negative ketones, nitrites, and glucose. Urine osmolality remained low (255–267 mOsm/kg), and urinary electrolytes indicated increased urinary sodium and potassium losses (Na 26 mmol/L, K 27.3 mmol/L, Cl 41.8 mmol/L). Blood and urine cultures showed no growth. The infant was immediately started on intravenous fluids tailored to correct fluid and electrolyte deficits. Sodium and potassium supplementation was closely titrated based on serial monitoring.

Ultrasound of the abdomen revealed bilaterally bulky kidneys with increased medullary echogenicity and multiple cysts of varying sizes, the largest measuring 8.5 × 6.5 mm on the right and 1.1 × 0.9 cm on the left. The right and left kidney dimensions were 6.8 × 3.5 cm and 7.2 × 3.1 cm, respectively. Based on these findings, a provisional diagnosis of bilateral 'Autosomal recessive polycystic kidney disease' was made, which was later supported by pediatric surgical evaluation.

Given the suspicion of neonatal Bartter syndrome with a background of confirmed 'Autosomal recessive polycystic kidney disease', the baby was initiated on indomethacin at a dose of 1.6 mg/kg/day, later titrated down to 1 mg/kg/day depending on renal function and electrolyte status. Supportive medications included IV antibiotics (Cefotaxime), proton-pump inhibitors, calcium and vitamin D3 supplementation and oral potassium supplementation (Kesol).

The baby showed clinical improvement over the course of hospitalization. He was gradually transitioned to direct breastfeeding along with spoon feeds, tolerated feeds well, and demonstrated gradual weight gain. Renal function tests and electrolytes were closely monitored throughout the stay and remained stable on ongoing treatment. The baby's activity improved, and daily weight gain was observed. After stabilization and weight recovery, the baby was shifted to the mother's side for rooming-in and further care.

At discharge, the infant was clinically stable, feeding well, passing urine and stools adequately. Parents were counseled in detail and discharge advice included exclusive breastfeeding every two hours, regular burping after feeds, and the continuation of medications at home.

The baby was discharged in a clinically stable condition with adequate feeding and urine output. Parents were advised to continue exclusive breastfeeding every two hours, ensuring proper burping after each feed. They were instructed to maintain the baby in a warm, clean, and dry environment at all times. Oral potassium supplementation (Syrup Kesol) and calcium without phosphorus (Syrup Calcimax, 2 mL at 11 AM and 10 PM) were prescribed to support electrolyte balance and bone health.

Sodium supplementation was continued in the form of Tablet Sodium Ion, 1/4th tablet four times a day, calculated at 8 mEq/kg/day. Indomethacin sachets were advised at a dose of 1.5 mg twice daily at 7 AM and 7 PM, with Nexpro sachets (1/3rd sachet) to be administered 20 minutes prior to each indomethacin dose to prevent gastrointestinal side effects. Vitamin D3 supplementation was continued with Ultra D3 drops, 1 mL once daily at 4 PM. Parents were counseled in detail regarding medication timing, feeding practices, warning signs, and the importance of regular follow-up for monitoring growth and renal function.

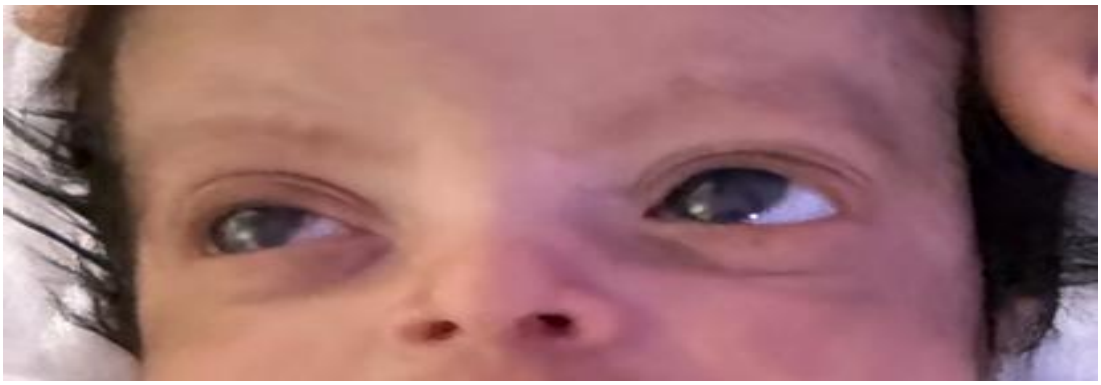

Figure 3 : Close-up facial image of the affected sibling showing dysmorphic features including frontal bossing, prominent eyes, and periorbital hollowing suggestive of syndromic phenotype.

Figure 4 : Clinical photograph of the neonate on day 8 of life showing abdominal distension with visible renomegaly and hypotonia.

Follow-Up

On the 29th day of life, a repeat abdominal ultrasound was performed to assess renal progression. Both kidneys appeared markedly enlarged with pronounced cortical thinning and increased medullary echogenicity. Multiple cysts of varying dimensions persisted, with the largest measuring 8.4 × 6.4 mm on the right and 1.0 × 0.8 cm on the left. The dimensions of the right and left kidneys were 8.5 × 3.3 cm and 8.4 × 3.3 cm, respectively. Hepatic morphology remained normal, with no ultrasonographic evidence of intrahepatic biliary dilatation or portal hypertension. The spleen appeared structurally intact and within normal limits. These imaging findings were consistent with 'Autosomal recessive polycystic kidney disease'.

Concurrent laboratory tests revealed anaemia with a Hb level of 8.9 g/dL, thrombocytosis (platelet count: 728,000/mm³), and a total leukocyte count of 10,600/mm³. A significant rise in inflammatory markers was noted, with a high-sensitivity C-reactive protein (CRP) value of 291 mg/L. Ongoing medical management had stabilized the patient's electrolytes—serum sodium measured 137 mmol/L, potassium 3.38 mmol/L, chloride 99 mmol/L, and bicarbonate 25.3 mmol/L. Serum calcium was 9.7 mg/dL and albumin 3 g/dL. Renal function parameters showed a blood urea level of 28 mg/dL, BUN of 13.08 mg/dL, and serum creatinine at 0.46 mg/dL.

Genetic evaluation confirmed a homozygous missense mutation in the PKHD1 gene, recorded as NM_138694.4:c.1838T>A (p.Leu613Gln), located on exon 20 of chromosome 6. This variant is associated with ARPKD, with or without hepatic involvement, and is currently classified as a Variant of Uncertain Significance (VUS), pending further evidence.

2. DISCUSSION

Prenatal indicators of ARPKD include findings such as oligohydramnios or polyhydramnios and increased echogenicity of the fetal kidneys with poor corticomedullary distinction. In this case, **excess liqour** and abnormal antenatal renal imaging prompted early clinical suspicion.[11] After birth, the child exhibited severe electrolyte abnormalities—namely hyponatremia, hypokalemia, and hypochloremia—alongside metabolic alkalosis. These findings mimicked neonatal Bartter syndrome, a less common early presentation described in the ARPKD spectrum. [12]

Phenotypic variability is frequently observed in ARPKD, even among affected siblings. In this family, two prior children had adverse outcomes—one with antenatally detected renal anomalies resulting in pregnancy termination, and another who succumbed in infancy with developmental delay and failure to thrive.[13] In contrast, the current neonate presented with early but treatable renal involvement and responded well to supportive therapy. This variability may reflect differences in the functional impact of the identified mutation on fibrocystin expression.[14]

The genetic analysis in this child revealed a homozygous missense mutation in exon 20 of PKHD1 (c.1838T>A; p.Leu613Gln), which is currently classified as a Variant of Uncertain Significance (VUS).[15] Although some mutations in PKHD1 are clearly pathogenic, missense variants such as this may display incomplete penetrance or variable expression, necessitating further investigation and family screening.[16]

Initial management focused on correcting fluid and electrolyte imbalances, minimizing polyuria, and ensuring adequate nutrition.[17] Indomethacin was used to reduce renal fluid loss, while ongoing monitoring of renal function helped prevent deterioration. Such supportive care is critical in delaying or preventing the progression to chronic kidney disease. In the long

term, patients with ARPKD may require blood pressure control, nutritional support, and potentially renal replacement therapy.[18]

Although hepatic complications were not prominent in this neonate, long-term follow-up remains essential. [19] Portal hypertension and hepatic fibrosis typically emerge later in life. Therefore, serial liver imaging and liver function testing are advisable.[20]

In summary, ARPKD presenting in the neonatal period can resemble other tubular disorders and may pose a diagnostic challenge. Early imaging and genetic testing are vital tools for diagnosis and long-term management. Genetic counseling is particularly important in consanguineous families to address recurrence risk and guide future pregnancies.

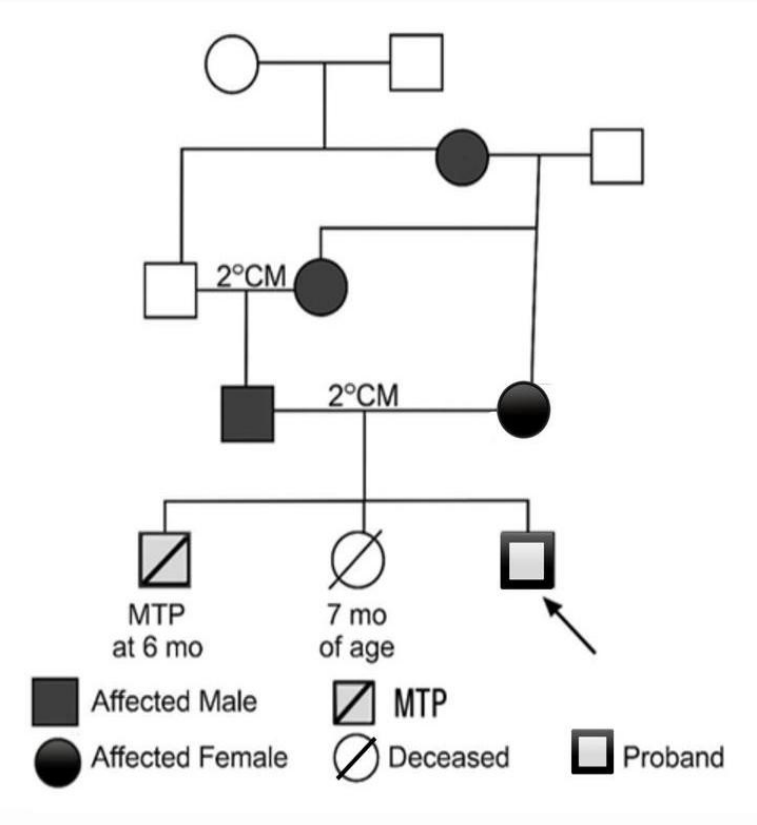

Figure 1: Pedigree Chart Illustrating Autosomal Recessive Inheritance with Second-Degree Consanguinity

■ = Affected Male
● = Affected Female
■ = MTP (Medical Termination of Pregnancy) at 6 months
⭕ (with a slash) = Deceased 7 months of age
□ / ○ = Unaffected
Horizontal lines = Marriages / Unions
Vertical lines = Offspring
Double horizontal lines = Consanguineous marriage
"2°CM" = Second-degree consanguinity marriage
Arrow → = Proband (index case)

3. CONCLUSION

This case emphasizes the importance of considering ARPKD in neonates presenting with biochemical features resembling Bartter syndrome, especially when accompanied by nephromegaly. Genetic analysis plays a pivotal role in distinguishing ARPKD from other mimicking conditions. Early recognition and appropriate management can stabilize renal function and improve survival outcomes.

Acknowledgment

We thank the Departments of Pediatrics and Radiodiagnosis at KLE's Dr. Prabhakar Kore Hospital for their support in the diagnosis and care of this case. We are especially grateful to the patient's family for their cooperation and consent in sharing this rare presentation. We also acknowledge the genetics team for their timely assistance with molecular testing

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