CASE REPORT

Early bilateral nephrectomy in infantile autosomal recessive polycystic kidney disease

Tamara Mary Mallett,^{1,2} Emma O'Hagan,^{1,3} Karl Gerard McKeever¹

¹Department of Paediatric Nephrology, Royal Belfast Hospital for Sick Children, Belfast, UK

²Department of Paediatric Nephrology, Royal Bristol Hospital for Children, Bristol, UK

³Department of Paediatric Nephrology, Royal Manchester Children's Hospital, Manchester, UK

Correspondence to

Dr Tamara Mary Mallett, tamaramallett82@doctors.org.uk

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SUMMARY

The management of neonatal autosomal recessive polycystic kidney disease (ARPKD) complicated by severe pulmonary insufficiency presents complex clinical challenges. Where massive nephromegaly exists, early bilateral nephrectomy, supportive peritoneal dialysis and early aggressive nutrition can minimise infant mortality. Consensus, however, is lacking on the role and optimal timing of nephrectomy, with decision-making driven by the patient's clinical condition and the expertise of the centre. We report on our experience of an infant with ARPKD requiring neonatal renal replacement therapy and survival at 14 months following early bilateral nephrectomy.

BACKGROUND

Autosomal recessive polycystic kidney disease (ARPKD) is one of the most common paediatric renal cystic diseases, with an estimated incidence of 1 in 20 000 live births.¹ The phenotype is very variable with a broad spectrum of clinical disease.²

The management of neonatal ARPKD complicated by severe pulmonary insufficiency is particularly challenging. Currently, there is a lack of reliable clinical prognostic markers to assist with decision-making in this population. Oligohydramnios is neither a sensitive nor specific predictor of non-survival,³ thereby making neonatal counselling difficult. In the neonatal ARPKD population with massive polycystic kidneys, there is a high early infant mortality rate associated with respiratory compromise.⁴ Where massive nephromegaly exists, early bilateral nephrectomy, supportive peritoneal dialysis (PD) and early aggressive nutrition can reduce infant mortality.⁴ Consensus, however, is lacking on the optimal timing and role of nephrectomy, with decision-making driven by the patient's clinical condition and the expertise of the centre.

We report on our experience of an infant with ARPKD requiring neonatal renal replacement therapy and survival at 14 months following early bilateral nephrectomy.

CASE PRESENTATION

A male infant diagnosed antenatally with ARPKD and third trimester oligohydramnios was born at 38 weeks gestation weighing 3330 g. He displayed significant respiratory distress, with gross abdominal distension and bilateral palpable massive nephromegaly. Day 1 abdominal ultrasound revealed massive bilateral cystic nephromegaly with

right kidney measuring 10.8 cm and left kidney 10.7 cm (figure 1).

High-pressure ventilation was required from birth to compensate for pulmonary hypoplasia and diaphragmatic splinting from massive nephromegaly. Progressive diaphragmatic splinting from accelerated renal growth resulted in the requirement for high-frequency oscillatory ventilation (HFOV).

Renal function was severely impaired (estimates of glomerular filtration rate 7 mL/min/1.73 m²) and the patient remained oligoanuric from birth with maximum urine output 0.7 mL/kg/day. He developed severe hypertension with maximum systolic blood pressure 136 mm Hg (mean arterial pressure 102 mm Hg, >95th centile) requiring maximum dosage of four antihypertensive agents—intravenous labetalol 4 mg/kg/h, intravenous hydralazine 5 µg/kg/min, oral amlodipine 0.6 mg/kg/day and oral minoxidil 0.4 mg/kg/day—to effectively achieve blood pressure control (mean arterial pressure 50 mm Hg). Echocardiogram confirmed dilated right ventricle with mild reduced left and right ventricular functions, and right ventricular systolic pressure 50 mm Hg. Severe hypervolaemia developed despite fluid restriction to 40 mL/kg/day and therefore calorie delivery was compromised. The need for dialysis to overcome these clinical

Figure 1 Abdominal ultrasound on day 1, of right cystic nephromegaly measuring 10.8 cm.

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challenges presented an ethical dilemma. The infant's parents were fully counselled regarding the options of dialysis or supportive palliation. The prognosis of infant dialysis, including lifetime dependency on renal replacement therapy and risks of congenital hepatic fibrosis, were explained.

Extensive regional multidisciplinary and multiprofessional discussions were underway in our unit, with additional advice sought from national and international centres of expertise regarding the clinical and ethical challenges presented. With support from parents and professionals for active management, a decision was made to start PD.

TREATMENT

A PD catheter was sited on day 12 and dialysis started (figure 2). PD proceeded without complication with good volume ultrafiltration between 300 and 400 mL on hourly cycles of physioneal 3.87%, with urine output 0.2–0.4 mL/kg/day. Hypertension gradually improved allowing control with single agent therapy (intravenous clonidine 7 µg four times a day). Despite fluid management and adequate ultrafiltration, the patient remained dependent on HFOV, with progressive cystic nephromegaly restricting ventilation. Serial ultrasound scans confirmed accelerated renal growth. At age 5 weeks the right kidney measured 13.1 cm and the left kidney 11.7 cm, a 2.3 and 1 cm increase, respectively, from birth. Establishing enteral feeding was also particularly challenging due to mass compression, with upper gastrointestinal contrast studies showing failure of small bowel passage with dilated bowel distally. Failure to establish feeds resulted in dependency on total parenteral nutrition (TPN).

As the patient remained ventilator and TPN dependent, it was decided to electively proceed with nephrectomy. Owing to the regional inexperience of, and potential perioperative need for, continuous veno-venous haemofiltration (CVVH), the infant was transferred for nephrectomy to the Royal Manchester Children's Hospital on day 41. On day 50, right open nephrectomy was performed via a retroperitoneal approach. There was no requirement for bridging CVVH, and PD proceeded without complication. In the early postoperative period, the patient was successfully extubated to nasal continuous positive airway pressure respiratory support and nasogastric feeding was started.

By postoperative day 11, increasing unilateral nephromegaly necessitated ventilatory support. Seventeen days after the initial nephrectomy, on day 70 of life, a left nephrectomy was performed via a retroperitoneal approach. Total combined kidney mass was 1.3 kg. Again, CVVH was not required and PD

proceeded without complication. Hypertension resolved post-operatively alongside early withdrawal of respiratory support and establishment of full enteral nutrition. The patient was transferred back to the regional unit for ongoing care on day 87 of life, and discharged home at age 10 months.

OUTCOME AND FOLLOW-UP

The patient is now 14 months old and on home nocturnal PD, complicated by a solitary episode of bacterial peritonitis. His current PD regime is 12 h cycles of 2.27% physioneal with fluid volume of 220 mL. He is normotensive with normal cardiac function. He has no chronic lung disease and has remained free from significant respiratory illness. Nutritional needs are met by nasogastric feeding. Weight at 8.5 kg is on the 2nd centile, with length on the 0.4th centile and head circumference growing steadily below the 0.4th centile. He developed seizure activity associated with electrolyte imbalance at age 6 months, controlled with single agent anticonvulsant. MRI of the brain and EEG are normal. His development is currently delayed by 7–8 months.

The patient has ultrasound evidence of hepatic fibrosis complicated by hypersplenism, thrombocytopaenia and oesophageal varices. He is being assessed for a combined liver–kidney transplant by Birmingham Children's Hospital and is due to be listed for cadaveric transplant.

DISCUSSION

ARPKD is a significant cause of morbidity and mortality in children.² The clinical course, similar to that of our reported case, is characterised by neonatal complications including renal and respiratory failure, hypertension and hepatogastrointestinal dysfunction.³ Renal failure is rarely a cause of neonatal death,⁵ although of those who survive the perinatal period, almost 50% progress to established renal failure within the first decade,⁶ and survival is associated with significant life-limiting comorbidities including systemic and portal hypertension.⁵

The phenotype is very variable,² with the most severely affected fetuses having enlarged echobright kidneys and oligohydramnios.¹ Oligohydramnios is neither a sensitive nor specific predictor of mortality in ARPKD, nor is it a predictor of life-limiting pulmonary hypoplasia,³ however, neonatal ventilation is a strong predictor of mortality.³ There is a lack of reliable clinical prognostic markers to assist with clinical decision-making in ARPKD, making antenatal and perinatal counselling difficult. Mutations at a single locus, PKHD1 (polycystic kidney and hepatic disease1) on chromosome 6p21, are responsible for all typical forms of ARPKD, with genotype–phenotype correlations identified for the type of PKHD1 mutation.⁷ Genetic testing was not performed on our patient, however, we are aware that two truncating mutations are associated with a severe phenotype with perinatal/neonatal demise, whereas survival beyond the neonatal period occurs in patients with at least one missense mutation.⁷

Despite recent advances in neonatal care and genetic knowledge, and excellent outcomes for paediatric transplant, the reported mortality at 1 year for the neonatal ARPKD population is still as high as 20%.⁸ Death from renal insufficiency is uncommon and is more often secondary to pulmonary hypoplasia. The management of the severely affected neonate therefore focuses on mechanical ventilation and, occasionally, on unilateral or bilateral nephrectomy,² however, the risk of accelerating renal function loss and the consequent need for renal replacement therapy early in life must be carefully weighed.⁹

Figure 2 Photograph on day 12, revealing gross abdominal distension with peritoneal dialysis catheter in situ.

Consensual decision-making in neonatal ARPKD surrounding renal replacement therapy and the role and timing of nephrectomy is fraught with clinical challenges and ethical dilemmas requiring multidisciplinary input and parental counselling. Often, nephrology network support is required to aid decision-making, driven by the patient's clinical condition and the expertise of the centre.

Haemodialysis may be challenging due to low body weight and difficult vascular access, with PD limited by massive kidney enlargement and potential peritoneal damage post nephrectomy.¹⁰ In our reported case, PD was well tolerated despite limited abdominal space and sequential nephrectomies, with no requirement for bridging CVVH.

International consensus expert opinion states that there is no evidence that nephrectomy results in respiratory improvement, and no evidence to support nephrectomy for severe hypertension in early ARPKD.⁹ Nonetheless, there are several published reports describing unilateral nephrectomy^{11–13} or bilateral nephrectomy^{4 14–18} as rescue therapy for infants with severe perinatal ARPKD, with the latter being most successful. Beaunoyer *et al.*,⁴ in 2007, reported an aggressive approach in nine neonatal ARPKD patients with massive kidneys, which included early pre-emptive bilateral nephrectomy, supportive PD and aggressive enteral feeding to minimise early infant mortality, so that subsequent renal transplantation could be performed with excellent patient and graft survival. Historically sequential nephrectomy was the theoretically less aggressive option.^{11–13} Unilateral nephrectomy would aim to minimise the risks of peritoneal damage, anaesthesia and cardiovascular instability, with preservation of renal function and minimising the abdominal compartment syndrome mass effect, improving cardiorespiratory and gastrointestinal dysfunction.^{11–13} Improved homeostasis, nutrition and growth would facilitate delayed sequential nephrectomy, potentially at the time of kidney transplant. Although the benefit was evident in gastrointestinal function, the effect on respiratory failure and hypertension was limited.^{11–13} Bilateral nephrectomy and subsequent PD are now the preferred methods in most centres,^{4 14–18} despite the limitations of dependency on renal replacement therapy with its inherent risks, and the association with life-threatening persistent arterial hypotension due to renin deficiency.^{19 20} Our reported case evidences the failure of unilateral nephrectomy, with imminent sequential nephrectomy necessitated, increasing the patient's perioperative risk. The procedures were uncomplicated by failure of PD and persistent arterial hypotension.

We report on the survival of our patient at 14 months of age following early sequential nephrectomies with supportive PD in ventilator-dependent neonatal ARPKD. The patient's hypertension resolved completely following fluid removal on dialysis and sequential nephrectomies. The clinical course, challenges and ethical issues that arise from this patient's case illustrate some of the difficulties that exist when trying to achieve consensual decision making in neonatal ARPKD, and the benefits to be gained from nephrology network and family synergies. Our case supports early bilateral nephrectomy as the treatment modality of choice, in view of failure of unilateral nephrectomy alone. We stress the importance of nephrology network support to ensure the provision of equitable patient care.

This case adds to the body of literature for neonatal ARPKD supporting the role of early bilateral nephrectomy where progressive massive nephromegaly results in ventilator-dependent pulmonary insufficiency and failure to establish enteral nutrition. Such an aggressive surgical approach should be considered as potential rescue therapy in infants with severe ARPKD who

remain ventilator dependent with suboptimal nutritional support.

Learning points

- ▶ Neonatal autosomal recessive polycystic kidney disease (ARPKD) has a reported mortality rate at 1 year of up to 20%.
- ▶ The management of severe ventilator-dependent neonatal ARPKD presents complex clinical and ethical challenges, making consensual decision-making difficult.
- ▶ We support the role of early bilateral nephrectomy in severe ventilator-dependent neonatal ARPKD.

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Contributors All the authors contributed to the development of this case report by co-writing the report and editing it. KGM is the lead consultant primarily responsible for the care of the patient.

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