Challenges of neonatal-onset kidney replacement therapy: a case report

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RESUMEN

La insuficiencia renal terminal (IRT) es una enfermedad poco frecuente durante el periodo neonatal, pero su manejo durante los primeros meses de vida es particularmente difícil, especialmente en lo que respecta a la nutrición, el equilibrio de líquidos, el acceso dialítico y la elección de la modalidad. La monitorización del crecimiento y la optimización de la nutrición son de vital importancia, al igual que lo es el manejo del mayor riesgo de infección y otras comorbilidades frecuentemente asociadas.

Presentamos un caso de IRT de inicio neonatal, en programa dialítico desde el sexto día de vida, con varias comorbilidades asociadas. Se mantuvo en diálisis peritoneal (DP) hasta los 20 meses, cuando, tras complicaciones infecciosas recurrentes, fue transferido a un programa de hemodiálisis (HD). Tras el inicio de la HD, se observó una mejoría del trastorno óseo mineral y del estado nutricional, con un aumento del índice de masa corporal y de los niveles de albúmina.

Este caso refleja la dificultad de tratar la afectación multiorgánica asociada a la IRT de inicio neonatal, especialmente en presencia de comorbilidades que también repercuten en el crecimiento y el desarrollo, como las afecciones cardiovasculares, pulmonares y endocrinas. La mejor eficiencia dialítica de la HD mostró un impacto positivo, lo cual evidencia las ventajas de esta técnica en determinados contextos.

Palabras clave:
Insuficiencia renal terminal neonatal, nutrición, enfermedad renal crónica-trastorno mineral y óseo.

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INTRODUCTION

The incidence of neonatal end-stage renal disease (ESRD) is about 7.1 per million age-related population[1]. Congenital anomalies of the kidney and urinary tract are the most frequent aetiology[1,2]. The management of chronic kidney disease (CKD) during this period is particularly challenging, and poses several difficulties related to nutrition and fluid balance, dialytic access availability, increased risk of infection and the presence of comorbid conditions[2,3].

Peritoneal dialysis (PD) is frequently the first option as kidney replacement therapy in infants, among whom vascular access is difficult to obtain. However, a less efficient ultrafiltration and rate of solute clearance, when compared to haemodialysis (HD), can result in inadequately controlled fluid and salt homeostasis, and worsening bone disease[4,5]. A loss of obligate protein in the dialysate also contributes to malnutrition and impaired growth, which might lead to considering a technique shift[6]. There is also a potential for infection at the exit site and subcutaneous tunnel of the catheter[7]. The use of HD in the first months of life, besides being dependent on the establishment of central vascular access, with its known inherent risks (such as infections), is additionally limited by technical issues, with a paucity of machines with circuits adapted to these cases[2]. Recently, novel machines designed for neonates and small children have emerged and are being used in reference centres[8,9].

Poor nutrition is one of the best-described causes of impaired growth in CKD. The fluid restriction needed in ESRD patients requires optimization of caloric intake to meet the nutritional requirements without augmenting fluid intake since milk is the main dietary source of infants[10-12].

In the spectrum of CKD, abnormalities in mineral bone metabolism occur early and universally, with

the development of CKD-mineral and bone disorder (CKD-MBD), and consequent changes in bone turnover, mineralization and architecture. In infants with neonatal-onset CKD, the potential for linear growth impairment, bone deformities, fractures and extra-skeletal calcification is very high and special efforts to adequately manage CKD-MBD should be pursued[4,13,14].

Globally, these difficulties justify the higher rates of complications and mortality among infants on dialysis, making the choice and guidance of dialysis strategy particularly demanding in the first months of life.

CASE REPORT

We present the case of a 3-year-old Caucasian boy with ESRD secondary to prenatally diagnosed bilateral multicystic dysplastic kidneys.

He was born prematurely at 31 weeks, with adequate anthropometry for his gestational age. He developed oligoanuria and suffered a progressive worsening of azotemia, hyponatraemia, and hyperkalaemia, which led to manual initiation of PD on the 6th day of life. The PD prescription was gradually adjusted to reach an optimized stable prescription with five dialysate exchanges per day, of alternated 1.36%/2.27% glucose concentration solutions and a long night dwell with an icodextrin solution.

Additionally, he presented congenital hypothyroidism (on thyroid hormone replacement therapy), pulmonary valve dysplasia and stenosis, and bronchopulmonary dysplasia with pulmonary hypertension, which contributed to the increased duration of his initial hospitalization and several intercurrent respiratory infections with hypoxemia.

Aged 6 months, after his mother had undergone adequate training, he was discharged home on an automated PD programme, supported by 24h-assistance from nursing and medical staff.

Around 7 months of age, he underwent surgical repair of an inguinal hernia with hydrocele and abdominal eventration near the site of the catheter insertion, with a need for catheter replacement.

The first peritonitis (by *Staphylococcus epidermidis*) occurred at 19 months of age and was treated with a 14-day course of antibiotics. Ten days after antibiotic discontinuation, he presented another peritonitis with tunnel infection and isolation of three agents (*Staphylococcus epidermidis, Corynebacterium amycolatum and Kocuria kristinae*). It was decided to remove the PD catheter and place a temporary central catheter for HD. After three weeks of antibiotherapy, a new PD catheter was inserted, which started to produce a purulent exudate one week later. The identification of *Pseudomonas aeruginosa* precluded the use of this catheter. After a multidisciplinary discussion with the family, and considering maternal exhaustion, the patient was permanently transferred to a regular HD programme at 20 months of age (weight 7700 g). He is currently undergoing an intensified regimen with 3.5h sessions, five times per week, via tunnelled right internal jugular vein catheter.

Despite supplemental enteral nutrition, initially by nasogastric tube (with night enteral nutrition since 18 months of age), and later by percutaneous gastrostomy, it was difficult to manage the persistent failure to thrive (Figure I).

Establishing parenteral nutrition following HD initiation allowed a progressive weight gain. A significant

Figure I. Evolution of weight, height and body mass index during the follow-up period (from birth to 35 months of age), for PD and HD, respectively.

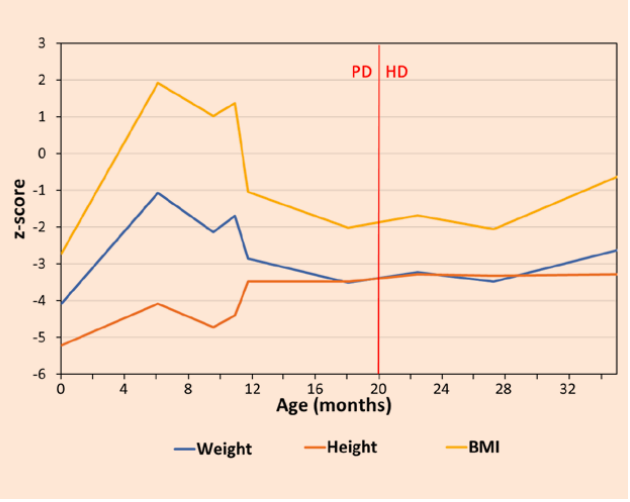
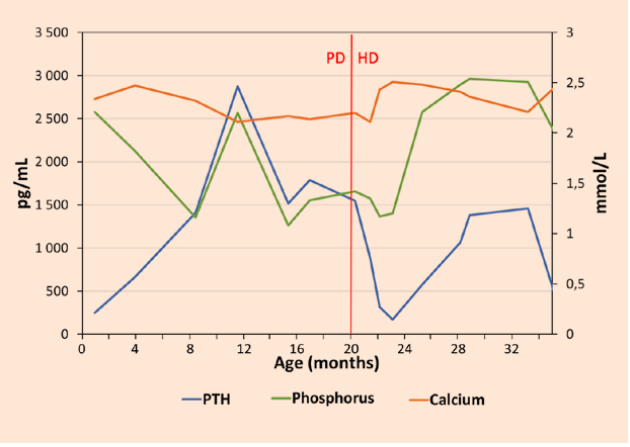


Figure II. Evolution of serum PTH, phosphorous and calcium levels during the follow-up period (from birth to 35 months of age), for PD and HD, respectively.



increase in appetite was also observed, along with increasing values of albumin (from a minimum of 2.0 to 4.0 g/dL) and body mass index (BMI SDS) (from -2.80 at HD initiation to a current -0.86 SDS) (Figure I).

Figure II illustrates the evolution of parathyroid hormone (PTH), calcium and phosphorus levels. Despite therapy adjustments to the maximum tolerated doses of phosphorus binders (sevelamer and calcium carbonate) and vitamin D analogues (alfacalcidol and later paricalcitol), while under PD, secondary hyperparathyroidism was very difficult to control, with a progressive increase in PTH (which reached 2800 pg/mL at 11 months of age). At this point, calcimimetic cinacalcet was initiated off-label with positive results.

The patient presented delayed motor development and signs of rickets, hard swelling of the left wrist dorsum with exaggeration of the physiologic *varus* and metastatic calcifications (Figure III).

The greater dialysis efficiency of HD allowed better bone mineral homeostasis, and there was an improvement in the skeletal clinical signs of secondary hyperparathyroidism and a reduction of PTH, with stable maintenance of calcium values (Figure II). The patient underwent balloon valvuloplasty to correct his pulmonary stenosis at 33 months of age, and treatment with growth hormone is scheduled to initiate next month.

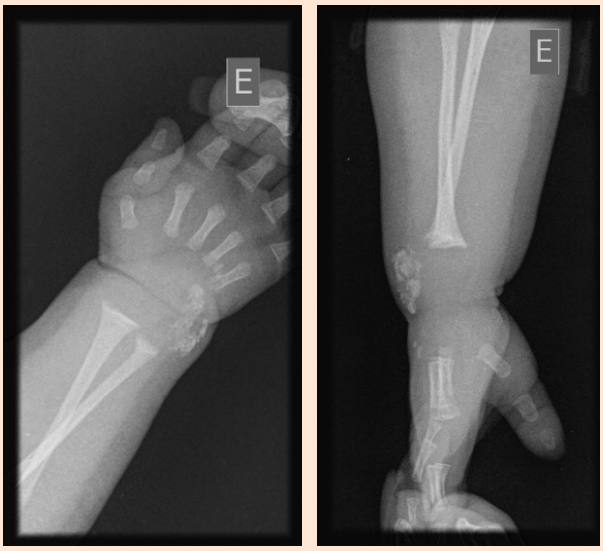
Following residual diuresis loss at 32 months of age, volume-dependent hypertension was evident and is currently under control with enalapril and amlodipine. Regarding CKD-related anaemia, he receives epoetin-β, with the occasional need for red blood cell transfusion.

DISCUSSION

Neonatal CKD, and particularly ESRD, is a rare and challenging condition, with high morbidity and mortality related to the disease and its treatment. Kidney replacement therapy in the neonatal period is technically complex, with all methods posing specific risks and ethical dilemmas that require consideration. Nutritional difficulties and the evolution of CKD-MBD may have serious consequences for growth if not properly tackled, with a major potential for compromised development in surviving infants[15].

This case reflects the difficulty of managing the multiorgan involvement associated with neonatal-onset ESRD, particularly with regard to nutrition and CKD-MBD, while aiming for both optimization of growth and prevention of vascular calcification and cardiovascular disease. In this patient, the coexistence of comorbidities that also impact on growth and development, such as congenital heart disease, bronchopulmonary dysplasia with pulmonary hypertension, and congenital hypothyroidism might help to frame the difficulties found. We wish to highlight the importance of these patients receiving follow-up at dedicated paediatric nephrology units, where different dialysis methods and specialized staff are available. Better dialytic efficiency of HD, especially in intensified regimens, showed a positive impact on the nutritional status and on renal osteodystrophy, which emphasizes the advantages of this technique in certain settings. It is expected that initiating growth hormone therapy will further contribute to sufficient weight gain to allow a kidney transplant in the near future.

Figure III. Radiography images of the left wrist, at 3 months of age.



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