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Improved growth velocity with intensive dialysis. Consequence or coincidence?

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Abstract Growth failure in children with end-stage renal disease remains a difficult problem. A 2.5-month-old baby in renal failure due to primary hyperoxaluria type I received intensive dialysis aimed at decreasing oxalate tissue accretion. Over 5.5 months, while awaiting transplantation, his growth velocity was 29 cm/year compared with an average 4 cm/year in infants on hemodialysis and 22 cm/year in normal infants of this age. This remarkable growth rate, which could have represented catch-up growth, is hypothesized to be related to the delivered dialysis dose. It is suggested that this relationship be evaluated in a prospective randomized trial.

Key words Dialysis adequacy · Infant growth

Introduction

Growth retardation is a common feature of infants and children with end-stage renal disease (ESRD). Malnutrition, acidosis, renal osteodystrophy, and abnormalities in the growth hormone (GH) axis may be factors in the stunted growth of these children [1]. Correction of the metabolic and nutritional abnormalities does not usually result in normal growth velocity. Recombinant human GH (rhGH) has a positive short-term effect on the growth pattern of children with ESRD, and may even induce catch-up growth, but it remains to be seen whether GH-treated patients will achieve normal adult height [2, 3].

This report describes unusually rapid growth in a 2.5-month-old infant with hyperoxaluria type I (PHO I) who received 5.5 months of intensive dialysis therapy with the goal of reducing tissue oxalate accretion. We hypothesize that this improved growth rate may have been the consequence of this increased dialysis dose.

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Case report

A 2.5-month-old male infant was referred to the University of Minnesota Hospital for a combined liver kidney transplantation (LKT). He had previously presented to his local hospital at the age of 1.5 months, following a brief gastrointestinal illness, in oliguric renal failure. Diagnosis of PHO I was based upon renal ultrasound findings of nephrocalcinosis, open kidney biopsy findings of diffuse oxalate deposits, and evidence for oxalate deposition in the retina, long bones, and bone marrow. Elevated urinary oxalate excretion, documented 1 month following LKT transplantation [1.03 mmol (94 mg)/24 h per 1.73 m^2], subsequently confirmed the diagnosis [4].

Shortly after presentation, he became anuric and was started on continuous ambulatory peritoneal dialysis (CAPD) by the local pediatric nephrologist. He was also treated with Bicitra, phosphate binders, erythropoietin (rhEPO), pyridoxine, and multivitamins. His diet provided 115 calories/kg per day and 2.2 g/kg per day of protein. On transfer to the University of Minnesota Hospital, thrice weekly hemodialysis (HD) sessions were added in order to enhance the CAPD oxalate removal. One month later, due to peritonitis and leakage of PD fluid, his PD catheter was removed and his dialysis regimen was modified to six HD sessions per week. HD was performed using a single-lumen Hickman catheter terminating in the right atrium, infant dialysis lines, and a Lundia minor plate dialyzer (Gambro, Lund, Sweden). Blood flow was 43 ml/min, providing 3 ml/kg per min urea clearance. Each session was 4 h long, resulting in a weekly urea clearance of 72 ml/kg per min. This intensive HD regimen was maintained for 4.5 months when, at the age of 8 months, a suitable donor became available and a LKT was performed.

During this period his height increased from 60 cm (50th percentile for age) to 73 cm (>75th percentile for age) and his weight from 5.5 kg (50th percentile) to 10.0 kg (90th percentile) (Fig. 1). These changes correspond to an increase in standard deviation

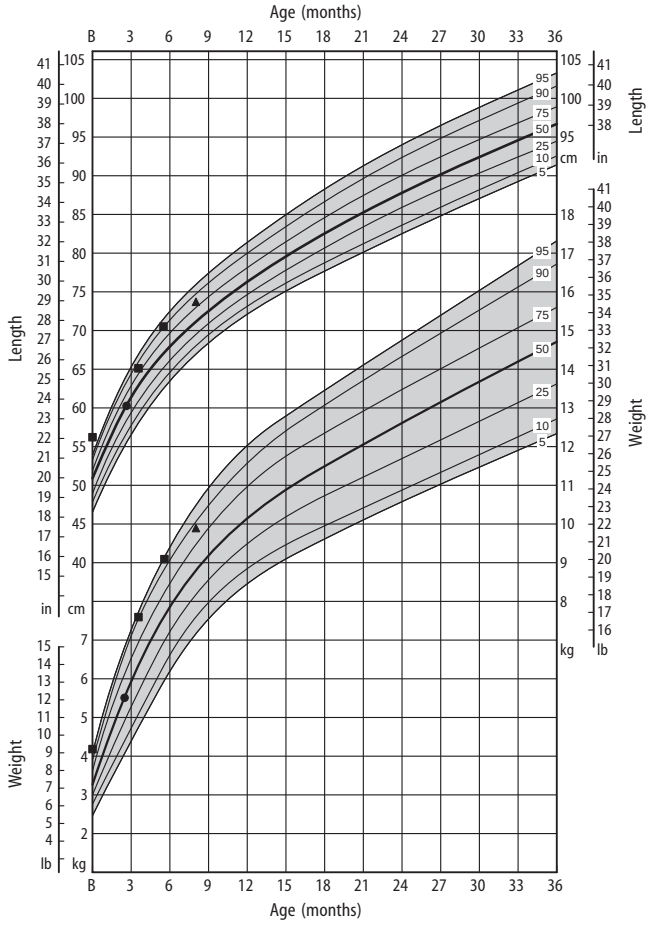

Fig. 1 Representative growth data showing growth failure occurring in the first months of life, followed by improved growth velocity in conjunction with the initiation of the intensive dialysis regimen (● admission to the University of Minnesota, ▲ combined liver kidney transplantation)

score (SDS) of +0.8 and +1.28 for height and weight, respectively. His head circumference at this time was 45 cm (>50th percentile). There was no significant change in medications and dietary intake during this time. An improvement in serum phosphorus (8.0 to 3.6 mg/dl), bicarbonate (22 to 25 mEq/l), and albumin (2.3 to 3.4 g/dl) occurred in the 1st month while under CAPD supplemented with thrice weekly HD. Those levels remained unchanged for the rest of the 5.5 months of intensive HD treatment. There was no significant change in hemoglobin (averaging 9.2 g/dl) over this time.

Discussion

Growth retardation is a manifestation of uremia in infants and children. It is thought to result from low caloric intake, acidosis, renal osteodystrophy, and resistance to the effects of GH. Providing a high calorie/protein intake, correction of acidosis, and the use of various vitamin D derivatives does not usually result in marked improvement in growth velocity. Moreover, such meticulous therapy is difficult to maintain over a long period. Failure to achieve satisfactory growth rates with the above strategy, together with the reduced potential for catch-up growth with increased age, has led some centers to suggest early kidney transplantation in order to circumvent this problem [5]. The use of rhGH has significantly improved height SDS, but it is still unclear whether its use will lead to attainment of full growth potential, especially in children on renal replacement therapy [2, 3]. In addition, rhGH use is associated with rare yet potentially harmful side-effects, including metabolic abnormalities [hyperinsulinemia, diabetes, and increased serum lipoprotein(a)], of which the long-term consequences are not fully understood [2, 3–6].

Management of this patient prior to his referral for LKT had been excellent. It included standard infant dialysis therapy with CAPD, adequate nutrition, good control of renal osteodystrophy and acidosis, and administration of rhEPO – the latter only with moderate success due to oxalate deposition in the bone marrow. The only significant change in his care, initiated after transfer to the University of Minnesota, was the increase in the delivered dialysis dose. This followed our guidelines for the pretransplantation management of PHO I patients [7]. The current case is unique in that the intensive HD was maintained for 4.5 months, whereas usually it had been performed only during the week prior to transplantation [7]. Post-dialysis blood urea nitrogen levels were not measured and thus delivered dialysis dose cannot be calculated. Discrepancies between the prescribed and delivered dose of dialysis could stem from inaccurate estimates of blood or dialysate flow, recirculation, suboptimal heparinization with intradialyzer clotting, and differences between effective and planned treatment times. However, since HD in this infant was uneventful, and the weekly dialysis time doubled, it is highly likely that the delivered weekly dose of dialysis was significantly increased.

Over a 5.5-month period, the patient increased in height from the 50th to the 75th percentile, representing a growth velocity of 29 cm/year, a rate slightly greater than that of healthy age-matched male infants (22 cm/year). This is an unusual growth pattern in our experience as well as in the medical literature, especially in infants and children with PHO I [8]. According to a recent United States Renal Data System report, growth velocity for age-matched infants on HD and PD is 4.5 and 6.2 cm/year, respectively [9]. The increase in head circumference is encouraging, since it may be related to improved cognitive abilities [10].

The landmark results of the National Cooperative Dialysis Study established a link between the fractional clearance of urea and morbidity in adult dialysis patients [11]. Since then, numerous studies in adult HD patients have reported that increasing the delivered dialysis dose results in improved patient survival, facilitates blood pressure control, and reduces the requirements for rhEPO and phosphate binders [12]. Parallel data regarding the association between dialysis dose and outcomes do not exist for children [13]. The recent National Kidney Foundation guidelines for HD adequacy suggest that a higher

urea clearance (Kt/V) may be beneficial for the growth and development of children [13]. Our observation of an association between improved growth and increased dialysis dose strongly supports the need for a long-term prospective randomized study to define optimal dialysis dose for optimal growth in children.

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