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Management of Finnish congenital nephrotic syndrome by unilateral nephrectomy

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Abstract. Finnish congenital nephrotic syndrome is fatal unless managed aggressively; treatment in hospital with albumin infusions and subsequent bilateral nephrectomy allows survival. However, it consistently results in protein malnutrition which may lead to serious infections and severe physical and developmental retardation, as well as the subsequent burden of dialysing an anephric child. We treated a boy by unilateral nephrectomy at 3 months. The reduced protein loss allowed home management with albumin infusions and resulted in a substantial rise in his plasma IgG levels. The glomerular filtration rate declined fairly rapidly after unilateral nephrectomy, so he needed peritoneal dialysis by 16 months, which was straightforward as he still maintained a good urine output. Management by unilateral nephrectomy has allowed this boy to grow and develop normally. The time spent in hospital was minimal and the very high cost of providing albumin preparations was reduced considerably.

Key words: Congenital nephrotic syndrome – Finnish – Unilateral nephrectomy

Introduction

Infants with congenital nephrotic syndrome of the Finnish type (CNF) have extremely heavy proteinuria from birth which is refractory to steroid treatment. The placenta is large and symptoms begin soon after birth. Without aggressive treatment most children die under a year, and all die under the age of 3 years [1, 2]. Their problems are related to the degree of protein loss rather than to renal impairment; they are grossly malnourished, which results in severe infections and marked physical and developmental retardation. Venous thromboses are common and may be fatal. Uraemia is seldom present and is never severe enough to cause death.

Aggressive treatment with intravenous albumin infusions and eventual bilateral nephrectomy followed by dialysis and transplantation allows survival [2, 3]. The results of treatment are, however, far from ideal. Before nephrectomy the protein losses cannot be adequately matched by intravenous replacement, and up to a quarter still die [2, 3]. The survivors spend many months in hospital, serious infections remain a major problem, and hypotonia and gross physical and developmental delay are virtually universal. Although renal transplantation is associated with some developmental catch-up, this is far from guaranteed; about one-third may remain severely educationally subnormal, and about one-fifth may have other neurological sequelae [2].

Faced with a boy with CNF we performed a unilateral nephrectomy at 3 months in the hope that the reduction in protein loss would ease the burden of his early management, and that the reduction in renal mass would accelerate his course towards renal failure and so enable us to dialyse him while he still had a urine output. We report on the results of this treatment.

Case report

A woman had very high plasma and amniotic fluid alphafetoprotein concentrations at 16 weeks of pregnancy, but repeated foetal ultrasound scans were normal and the possibility of it being due to nephrotic syndrome was not considered. She had a normal delivery at 36 weeks of a 2.73 kg boy whose placenta was about twice its expected weight at 1.27 kg. The boy devel-

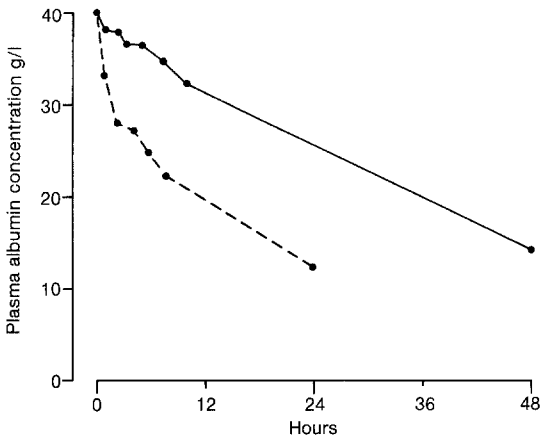

Fig. 1. The rate of the plasma albumin concentration after stopping an intravenous infusion; before nephrectomy (● -- ●), and after nephrectomy (●———●)

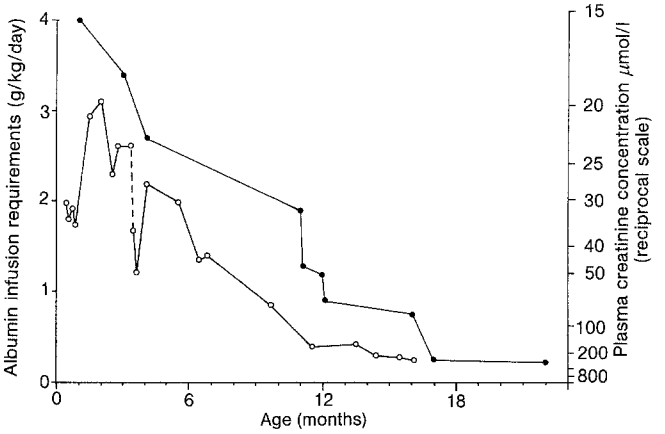

Fig. 2. The plasma creatinine concentrations (–○– plotted on a reciprocal scale) and albumin infusion requirements (●) of a boy with Finnish Congenital nephrotic syndrome. The timing of the unilateral nephrectomy is indicated by the *dashed line* in the creatinine graph

oped obvious oedema at 6 days of age and he was referred for further management with a diagnosis of congenital nephrotic syndrome at 11 days. On arrival he had gross pitting oedema, very heavy proteinuria, a plasma creatinine concentration of 31 μmol/l, and a plasma albumin of 12 g/l.

After careful consideration it was decided to treat his condition aggressively with intravenous infusions of albumin through a surgically placed right atrial catheter. He needed a constant albumin infusion of 8 g/kg daily to maintain a stable plasma concentration of 40 g/l; in practice he was given 2 g/kg as a bolus from a syringe pump over 4 h twice a day and fed a protein supplemented milk formula, and only had minimal oedema. His IgG levels were extremely low at 0.3 g/l (normal range 3–12) and he had two very severe infective illnesses for which he was treated with broad spectrum antibiotics, continuous fresh frozen plasma and a 5% human immunoglobalin preparation. He received prophylactic penicillin-V. Clinically his thyroid status was normal; his T4 was very low at 27 nmol/l (normal 76–160) associated with a very low thyroid binding globulin, but his free T3 was normal at 1.7 nmol/l (normal 1.2–3.0). His central venous catheter was replaced after 2 months because the first thrombosed, and low-dose aspirin was given subsequently to prevent further thrombotic problems. His parents were only able to cope with him at home for 18 days in the first 3 months. During that time he grew satisfactorily, but the burden of treatment was large.

At 3 months we performed a left nephrectomy after confirming equal function on radionucleide scanning. The hope was that his albumin and IgG losses would be reduced sufficiently to ease the burden of management and to increase his resistance to infections. The histology was typical of CNF and only about 1% of the glomeruli showed sclerosis. The rate of fall of the plasma albumin concentration after an infusion was considerably slower following unilateral nephrectomy so that it took 35 h for the level to fall from 40 g/l to 20 g/l instead of 10 h as previously (Fig. 1). In practice it was possible to reduce the frequency of his infusions four-fold from twice daily to alternate days, which resulted in peaks and troughs of about 38 g/l and 16 g/l, and only minimal oedema on the 2nd day. His IgG concentrations rose to the lower normal range at 3.3 g/l, and he had no further serious infections. His parents managed him at home with ease. His height and weight both remained on the 50th centile before and after his nephrectomy, and he continued to develop normally.

The plasma creatinine concentration doubled immediately post-operatively, and then fell to about 30 μmol/l. It subsequently rose so that he needed peritoneal dialysis at 16 months of age (Fig. 2), by which time he weighed 9.8 kg and his plasma urea was 38.5 mmol/l. Dialysis was straightforward and helped by the fact that he still produced urine. Throughout this time his albumin requirements fell in parallel with his falling glomerular filtration rate (Fig. 2). By his second birthday he only needed one albumin infusion every 2 weeks. After developing end-stage renal failure he became relatively anorexic and required overnight supplemental nasogastric tube feeding, but still maintained normal growth. His head circumference has increased along the 75th centile and his development has been normal at all stages. A formal assessment at 21.5 months using the Griffiths Scales showed his developmental age to be equal to his chronological age.

Discussion

The fact that CNF is likely to cause a raised plasma and amniotic fluid alpha-fetoprotein concentration may not be widely appreciated in countries where the condition is rare; without this information parents are unable to consider the option of termination of pregnancy.

Aggressive treatment of CNF without unilateral nephrectomy produces a huge burden on parents, and children can seldom be managed outside of hospital. The frequency with which albumin infusions need to be given and the tendency to develop serious infections are major reasons for this. Unilateral nephrectomy in our patient resulted in a much more manageable infusion frequency, which these parents coped with easily at home, and eliminated serious infections, presumably because his immunoglobulin levels rose. Reports of aggressive treatment without nephrectomy emphasise the severe growth failure and developmental retardation seen [2, 3]. Presumably

these are the consequence of protein malnutrition, as they are also seen with severe congenital nephrotic syndrome other than the Finnish type [4]. Our patient's normal growth and development probably reflect the fact that it was possible to keep up much better with his reduced protein losses using albumin infusions and an oral protein supplement.

Although some decline in glomerular filtration may be seen during the 2nd year of life in CNF without unilateral nephrectomy, it is unusual and is seldom severe [1–3]. In our patient end-stage renal failure necessitated dialysis early in the 2nd year of life. The typical histological appearance of CNF and lack of glomerulosclerosis seen in the nephrectomy specimen at 3 months makes it likely that he would have had a typical time-course to renal failure without a nephrectomy, and that the reduction in renal mass may have accelerated glomerulosclerosis in the remaining kidney.

Human albumin for infusion is extremely expensive. This boy's treatment cost £19,500 in albumin alone up to the age of 2 years. We anticipate being able to stop it shortly. If he had continued to lose protein at the pre-nephrectomy rate (but failed to thrive as other aggressively managed children have), we estimate the cost would have been £36,800. These costs are very high compared with the cost of peritoneal dialysis.

Unilateral nephrectomy allowed our patient to be managed at home and to grow and develop normally. It probably caused end-stage renal failure to develop sooner, resulting in large financial savings, and meant that we did not have the added difficulties of dialysing an anephric child. These conclusions are based on observations from a single patient; their validation must await confirmation from a group of children with CNF.

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