Low-density lipoprotein apheresis in a pediatric patient with refractory nephrotic syndrome due to focal segmental glomerulosclerosis

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Abstract
Focal segmental glomerulosclerosis (FSGS) often leads to refractory nephrotic syndrome (NS). A high level of low-density lipoprotein (LDL) is a risk factor for the progression of NS. An 8-year-old girl presented with severe proteinuria refractory to steroid therapy. She was diagnosed with non-IgA diffuse mesangial proliferative glomerulonephritis. Oral prednisolone, methylprednisolone (mPL) pulse therapy, and cyclosporine and cyclophosphamide therapy failed to achieve remission. Follow-up renal biopsy revealed FSGS. Her serum level of LDL was high, and LDL-apheresis (LDL-A) was performed five times, followed by mPL pulse therapy. Urinary protein decreased from 2–4 g·day\(^{-1}\) to 0.5–1.0 g·day\(^{-1}\). LDL-A may be beneficial in the treatment of multidrug-resistant FSGS.

Key words Low-density lipoprotein apheresis · Focal segmental glomerulosclerosis · Pediatric patient

Introduction
Focal segmental glomerulosclerosis (FSGS) often leads to severe nephrotic syndrome (NS), which is sometimes resistant to steroids or immunosuppressants and in which there is a rapid decline of renal function [1,2]. Although the pathogenesis of the disease has not been well elucidated, secondary hyperlipidemia plays a pivotal role in the progression of the renal injury [3]. Low-density lipoprotein apheresis (LDL-A) has been extended to the treatment of refractory NS due to steroid-resistant FSGS, minimal change nephropathy, or diabetic nephropathy [4–10]. LDL-A improved abnormal lipid metabolism and reduced urinary protein loss in adult NS [4–7]. However, there have been few reports on the efficacy of LDL-A for pediatric NS [8]. We here report a pediatric patient with NS due to FSGS successfully treated with LDL-A.

Case report
The patient was an 8-year-old girl who was 128 cm tall and weighed 29 kg. She had developed eyelid edema 3 months previously and proteinuria was noted at an annual school examination. Laboratory studies disclosed urinary protein excretion (Up) 656 mg·dl\(^{-1}\); urinary occult blood, 3+; serum total protein (TP), 5.1 g·dl\(^{-1}\); albumin (Alb), 2.5 g·dl\(^{-1}\); and total cholesterol (T-cho), 399 mg·dl\(^{-1}\). She was diagnosed with NS, and a kidney biopsy revealed non-IgA diffuse mesangial proliferative glomerulonephritis. She was treated with prednisolone (2 mg·kg\(^{-1}\)·day\(^{-1}\)) and methylprednisolone (mPL) 800 mg·day\(^{-1}\) for 3 consecutive days at 1, 2, 5, 7, and 9 weeks after admission. Cyclosporine (CyA; 80 mg·day\(^{-1}\)) was also administered at 2 weeks after admission, but failed to decrease the protein loss. We stopped CyA and it was replaced with cyclophosphamide (CPA; 50 mg·day\(^{-1}\)) and a cyclooxygenase II inhibitor (aluminum flufenamate, 250 mg·day\(^{-1}\)).
loss remained at 2–4 g·day⁻¹ and Up/Ucr continued to show a value of 5–11 (Fig. 1). In week 13, she was diagnosed with FSGS by a transdermal needle biopsy of the kidney (Fig. 2). In week 15, LDL-A was started with CyA administration. After transferring the patient to an intensive care unit (ICU), we performed LDL-A, using a polysulfone hollow-fiber filter (Sulflux FPO2; Kaneka, Osaka, Japan) as a plasma separator and a dextran sulfate cellulose column (Liposorber LA-15; Kaneka) as an LDL adsorber. The volume of the extracorporeal circulation approximately 351 ml, and the line was primed with 5% albumin solution. An 8-Fr double-lumen urokinase immobilized central venous catheter (Blood Access UK-Catheter Kit, Twinend; Unitika, Hyogo, Japan) was inserted into the femoral vein. LDL-A was repeated five times in 3 weeks. The amount of plasma exchange was set at 2000 ml per session. After the completion of the LDL-A therapy, mPL 800 mg·day⁻¹ was administered for 3 consecutive days. Urinary protein loss and Up/Ucr decreased to 0.5–1.0 g·day⁻¹ and 1.8–3.3, respectively (Fig. 1). We kept prednisolone at 5 mg·day⁻¹ and CyA at 65 mg·day⁻¹. She