Remission of a refractory nephrotic syndrome after low-density lipoprotein apheresis based on dextran sulphate adsorption

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Case report

A 43 year-old-man presented in August 1992 with nephrotic syndrome. For the previous 3 months he had been treated for ankylosing spondylitis with sulphasalazine 2 g per day. Percutaneous renal biopsy showed normal glomeruli without mesangial hypercellularity. The nephrotic syndrome was steroid-dependent with a high threshold (40 mg prednisone per day). Between 1992 and 1995 the patient experienced severe relapses despite continuous steroid treatment (with serum albumin falling to 12 g/l). A second renal biopsy performed in September 1993 showed minimal-change disease. Successive concurrent therapy with cyclosporin A, chlorambucil, and quinolones failed to improve the condition.

In April 1995, a massive relapse of the nephrotic syndrome was associated with deterioration of renal function (plasma creatinine 180 μmol/l). A third renal biopsy was performed and showed minimal changes with global sclerosis of 3/9 glomeruli. Segmental glomerular hyalinosis was not observed. There were some focal areas of fibrosis with tubular atrophy, but no cellular infiltration. Clinical deterioration and progression of biochemical changes occurred despite a new therapeutic regimen: two pulses of 500 mg methylprednisolone followed by prednisone 50 mg per day, and then polyvalent immunoglobulins. The patient suffered from nausea and malnutrition and clinical examination showed oedema (weight gain 15 kg), ascites, and pleural effusion. Prednisone was then progressively reduced and symptomatic treatment reinforced (frusemide 500 mg per day; nadroparine 0.6 ml b.i.d.). Biochemical findings are shown in Table 1. Under treatment with simvastatin, cholesterol and triglyceride concentrations remained dramatically high (28 mmol/l and 20 mmol/l respectively). Simvastatin was therefore stopped. The severity of the nephrotic syndrome and the renal insufficiency made the use of fibric acid derivatives unsafe. The use of other lipid-lowering drugs was not considered because of their modest efficacy in such severe dyslipidaemia. Subsequently we performed 10 LDL-A sessions to lower cholesterol concentration [1], whilst tapering the prednisone dose from 15 mg to 9 mg per day. The other drugs prescribed were sulphasalazine 2 g/day until July 1995, and frusemide, which was given at a dose of 500 mg/day until September 1995; this treatment was then progressively reduced and stopped; omeprazole 20 mg/day, cizapride 20 mg/day, nadroparine 0.6 ml b.i.d. and fenofibrate 67 mg/day from October 1995.

LDL apheresis [1] was performed using haemofilter Sorin BT 900 with a surface of 1.10 m² as the plasma separator and a dextran sulphate cellulose column (Liposorber LA-40, Kaneka, Japan) as the LDL absorber. A double-lumen central vascular access was used and 55 ml/kg of plasma processed at each session. The duration of each procedure was about 2 h. We performed 10 LDL-A in a period of 9 weeks. During the LDL-A period, serum cholesterol decreased from 28 mmol/l to 9.5 mmol/l and serum triglycerides from 20 mmol/l to 3.5 mmol/l (Figure 1). Proteinuria decreased to 1.26 g/day after the last LDL-A session, in parallel with the reduction in serum cholesterol \( r = 0.9 \) (Figure 2). From session 4, serum albumin concentrations rose progressively to reach the normal range after session 6. Renal function improved progressively.

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<tr>
<th>April 95</th>
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<td>P. triglyceride (mmol/l)</td>
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<td>18.9</td>
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<td>P. creatinine (μmol/l)</td>
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<td>228</td>
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<td>Proteinuria (g/24 h)</td>
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Potential role of sulphasalazine in the nephrotic syndrome

The patient had been treated for ankylosing spondylitis since the age of 18. Sulphasalazine therapy was started 3 months before the onset of the nephrotic syndrome and stopped 2 months before signs of improvement were first seen. This chronology suggests a potential role of sulphasalazine in the development of the nephrotic syndrome. There have been few reports of nephrotoxicity associated with sulphasalazine in patients being treated for ulcerative colitis [2,3], and only one case of nephrotic syndrome has been reported [3].

In the patient reported here, three renal biopsies failed to demonstrate inflammatory interstitial lesions suggestive of drug-related nephrotic syndrome.

Potential beneficial effects of LDL-apheresis on the outcome of the nephrotic syndrome

We found a strong correlation ($r = 0.9$) between the decrease of serum cholesterol levels and the reduction of proteinuria during LDL-A. Renal function improved during the treatment period. Recent investigations have provided evidence for the adverse renal effects of hyperlipidemia [4,5]. Lipoproteins can bind to polyanionic glycosaminoglycans in the mesangial matrix and glomerular basement membrane and may alter the permeability of the latter by neutralizing fixed negative charges in the filtration barrier [6]. Correction of serum lipid levels may therefore have a beneficial effect on renal function. The benefits of LDL-A on renal function and proteinuria in this case are consistent with previous reports. Hattori et al. [7] reported the case of a 15-year-old boy with drug-resistant nephrotic syndrome due to focal segmental glomerulosclerosis. A slight improvement in renal function, hypercholesterolaemia, proteinuria and hypoalbuminaemia following treatment with pravastatin and LDL-A was observed. Muso et al. [8] performed LDL-A treatment in nine cases of steroid-resistant nephrotic syndrome and observed a 40–50% improvement in proteinuria and hypoalbuminaemia in five patients. However, six of the nine cases received concurrent steroid therapy or immunosuppressants and LDL-A.

The removal by dextran sulphate adsorption of a circulating factor responsible for the nephrotic syndrome is another hypothesis to explain the benefits of LDL-A. LDL-A removes not only LDL and VLDL but also immunoglobulins [9]. Cases of mild and transitory improvement have been reported after plasmapheresis or protein adsorption column [10,11]. However, there are no reports of complete remission after these treatments. These apheresis techniques do not use dextran sulphate adsorption. Further advantages of LDL-A over other apheresis techniques would be the absence of exposure to exogenous blood products and the hypolipidaemic effect of the procedure.

Discussion

Two factors could have favoured the remission of nephrotic syndrome in this patient: the withdrawal of sulphasalazine and the LDL-A treatment.

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Remission of nephrotic syndrome after LDL lipoprotein apheresis

References


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