Case Report

Recurrence of lecithin cholesterol acyltransferase deficiency after kidney transplantation

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Introduction

Some metabolic diseases lead to the accumulation of lipids in renal tissue, which then affects the kidney structure and function [1]. One of them is a primary lipidosis familial lack of lecithin cholesterol acyltransferase (LCAT). This is a rare autosomal recessive disease [2] which may lead to corneal opacification, anaemia, and moderate haemolysis. Atherosclerosis may develop early and tendon and planar xanthomas have also been reported. However, it is the renal manifestations of the disorder that make it life-threatening [3]. Proteinuria usually occurs early in life and remains moderate for many years, but renal failure and hypertension may develop rapidly. There are foam cells in the bone marrow, and the glomeruli and erythrocytes contain abnormally large amounts of unesterified cholesterol and phospholipids. Diagnosis is confirmed by the absence of LCAT activity and free cholesterol esterification, increased free plasma cholesterol and LDL cholesterol and a low HDL cholesterol. Patients with LCAT deficiency and end-stage renal failure have made excellent long-term recoveries after renal transplantation [4], but the disease may recur because of persistence of metabolic disturbances [5,6]. This report describes a case of recurrent disease in which the early reappearance of lipid deposits was detected by ultrastructural study in an asymptomatic patient.

Case report

A 29-year-old man was found to have proteinuria during a check-up by a company doctor in 1981. He was lost to further follow-up until 1985, when he was hospitalized for persistent proteinuria. The clinical examination was normal apart from bilateral gọngoxon. His blood pressure was 140/80 mmHg and his haemoglobin was 8 g/dl; bone marrow studies showed foam cells. His serum creatinine was normal (90 μmol/l), but analysis of his plasma showed multiple lipoprotein abnormalities (Table 1). Serum complement was normal. Urinalysis showed 3 g/24 h proteinuria and microhaematuria. A percutaneous kidney biopsy was performed. The sample included material from the renal cortex and medulla. It contained 11 glomeruli, of which four were sclerotic. The mesangium of the other glomeruli was enlarged by the presence of many lipid-containing vacuoles, some of which had fused. The walls of the glomerular capillaries were irregularly thickened and there was an interstitial fibrosis with atrophic tubules. The interlobular arteries had severe arteriosclerotic lesions. LCAT deficiency was suspected and a total absence of LCAT activity was demonstrated. His mother and three children had normal activity and no specific lipoprotein abnormalities (Table 1).

He complained of chest pain in 1988 and a coronarography was performed. This revealed normal coronary vasculartization. At this time his serum creatinine was 110 μmol/l. He suffered from uncontrolled hyperten-

Table 1. Lipoprotein abnormalities in the patient, his mother and children

<table>
<thead>
<tr>
<th></th>
<th>TC</th>
<th>EC/TC</th>
<th>TG</th>
<th>PH</th>
<th>HDL C</th>
<th>LDL C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>5.43</td>
<td>0.22</td>
<td>4.91</td>
<td>10.2</td>
<td>0.07</td>
<td>5.07</td>
</tr>
<tr>
<td>Mother</td>
<td>5.56</td>
<td>0.74</td>
<td>6.2</td>
<td>6.7</td>
<td>0.59</td>
<td>3.77</td>
</tr>
<tr>
<td>Child 1</td>
<td>2.58</td>
<td>0.74</td>
<td>1.29</td>
<td>3.75</td>
<td>0.72</td>
<td>1.83</td>
</tr>
<tr>
<td>Child 2</td>
<td>2.71</td>
<td>0.73</td>
<td>0.9</td>
<td>3.68</td>
<td>0.82</td>
<td>1.81</td>
</tr>
<tr>
<td>Child 3</td>
<td>2.58</td>
<td>0.71</td>
<td>1.29</td>
<td>3.23</td>
<td>0.62</td>
<td>1.78</td>
</tr>
</tbody>
</table>

TC, total cholesterol (N, 4.10–6.20 mmol/l); EC, esterified cholesterol; HDL C, high-density lipoprotein (N, 0.9–2 mmol/l); LDL C, low-density lipoprotein (N, 2–4.86 mmol/l); PH, phospholipid (N, 2–3.20 mmol/l); TG, triglycerides (N, 0.4–1.40 mmol/l); EC/TC, (N, 0.7–0.9).

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sion and end-stage renal failure in September 1990, and peritoneal dialysis was started. The patient was given a cadaveric kidney transplant with one HLA A, B and DR compatibility in April 1993. A tendinous xanthoma was found on his right hand. The graft showed primary function, with a prompt fall in serum creatinine, which was 125 μmol/l at discharge 15 days after transplantation. Antithymocyte globulin induction therapy was used and long-term immunosuppression consisted of cyclosporin A plus a low dose of prednisone. His serum creatinine was stable (130 μmol/l) and urinalysis was normal 20 months after transplantation. A routine renal transplant biopsy was done (Figure 1a, b). The graft biopsy included tissue from the medulla and deep cortex. One of the 11 glomeruli in the biopsy was sclerotic, the others had a thickened mesangium, with occasional fibrosis, but no lipid vacuoles were evident. The walls of the glomerular capillaries were slightly thickened in places, but not double-layered (Figure 1a). Staining with Sudan red was negative. Immunofluorescence staining for C3 revealed C3 deposits within the membrane and along the walls of some glomeruli. There were foci of interstitial fibrosis with atrophic tubules. Arcuate arter-
ies showed moderate arteriosclerotic lesions. At electron-microscopy, deposits of heterogeneous electron-dense lipid material were located on the subendothelial side of the glomerulus basal membrane and in the mesangium (Figure 1b).

His serum creatinine was 130 μmol/l 47 months after transplantation; proteinuria was minimal, and blood pressure normal with nicardipine 100 mg/day. Immunosuppressive treatment consisted of cyclosporin A 3 mg/kg/day and prednisone 5 mg/day.

Discussion

A lack of LCAT activity results in changes in the serum concentrations of unesterified cholesterol and lecithin and abnormalities in the structure and composition of HDL and LDL particles. The HDL have a particular disk-shape with a large waist and contain no esterified cholesterol [2].

The pathogenesis of renal injury is still not totally understood and may be multifactorial. The relationship between the morphological changes in serum lipoprotein and renal damage has not yet been elucidated. It has been suggested that high-molecular-weight LDL particles became trapped in capillary loops and cause endothelial damage and vascular injury [2,7]. Electron-microscopy examination shows abnormal lipoproteins trapped in the glomeruli. While this does not exactly correspond to the ultrastructural appearance of the serum lipoproteins, they have many similarities [8,9]. Large LDL particles are also found that have a multilamellar structure or appear disk-shaped, and they often form stacks.

The subendothelial deposits of C3 may indicate that complement is involved in the pathogenesis of renal lesions. It could become activated at the site of glomerular lipid deposits, since there is no evidence of systemic activation [8]. This hypothesis is supported by experimental data showing that complement can be activated by liposomes via both the alternative and classical pathways by interaction with C-reactive protein. Complement activation may produce changes in the permeability of the basement membrane and allow the deposition of circulating particles.

The LCAT deficiency persists after renal transplantation and renal damage may reappear. Three cases of LCAT deficiency that have undergone renal transplantation have been reported. Graft biopsies were performed in all cases because of deterioration of renal function and all showed recurrent lipid deposits. Flatmark et al. [5] reported typical morphological changes due to LCAT deficiency in the kidney graft of two patients within a few months after transplantation. Horina et al. [6] detected histomorphological changes 42 months after transplantation in a patient who had increased serum creatinine. Our patient still has good graft function 4 years after transplantation, without any urinary abnormalities. The recurrence of the disease was demonstrated by electron-microscopy, the presence of C3 deposits and normal serum complement support the hypothesis of a local activation of complement.

Our case, like the three others, cannot be used to predict the frequency with which this rare disease recurs, but it suggests that lipid may be deposited soon after transplantation. Progression to end-stage renal failure is also unpredictable, but seems to be faster in renal grafts that in native kidneys, as in other recurrent renal diseases [10]. Nevertheless, LCAT deficiency is not a contraindication for renal transplantation provided there is no severe atheromatosis.

References


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