Is cholesterol embolic disease an unrecognized cause of renal graft dysfunction?


Key words: cholesterol emboli; renal transplant

Introduction

There is a considerable literature on cholesterol emboli as a cause of renal dysfunction and poor patient prognosis [1-6]. In one series of native renal biopsies of patients over the age of 65 years it was found in 10% of cases presenting with subacute renal failure [7]. When clinically apparent it has been noted to be associated with a marked decline in native renal function [5], but it has also been found asymptptomatically at post-mortem [1,2]. Lye et al. [4] have reviewed a large series of published cases of native renal cholesterol embolic disease and found a death rate of 64% and an incidence of dialysis-dependent renal failure of 40%. In those patients in whom dialysis-dependent renal failure occurred only 21% had a recovery of renal function sufficient to stop dialysis.

Isolated case reports of cholesterol emboli in renal allografts have been reported [8-12]. At present it is not recognized as an important cause of renal graft dysfunction. We report four further cases of renal graft cholesterol emboli and compare these with the previously reported six cases.

Case Reports

Case 1. A 58-year-old caucasian male with non-insulin-dependent diabetes mellitus and hypertension for 10 years received a renal transplant prior to dialysis. At operation no obvious recipient iliac atheroma was seen. Neither donor nor recipient atherosclerotic vasculopathy was noted at retrieval or transplantation. One year prior to transplantation the patient had suffered a left hemiparesis from which he had made a full recovery. Due to initial non-function the patient was biopsied until function was established. The initial biopsy after vascularization and one subsequent biopsy showed cholesterol emboli. Cellular rejection was also found on one biopsy (Figure 1), and standard treatment given. Renal function gradually improved and the creatinine settled at a level of 280 μmol/l.

Case 2. A 50-year-old caucasian female with adult polycystic kidney disease was transplanted from haemodialysis. Neither donor nor recipient atherosclerotic vasculopathy was noted at retrieval or transplantation. A biopsy for initial non-function was performed.

Fig. 1. Renal transplant biopsy of patient 1 showing in different fields of the same biopsy section a, Lymphocytic tubulitis in acute cellular rejection (Picro-Mallory Trichome stain × 320), b, Cholesterol embolization in a small-calibre artery (H&E × 400).
which showed a combination of necrotic kidney and multiple cholesterol emboli. The histology from the transplant nephrectomy showed a combination of necrosis and cholesterol emboli especially in the arcuate arteries.

Case 3. A 48-year-old male caucasian developed renal failure secondary to severe trauma complicated by bacterial endocarditis and aortic valve replacement necessitating warfarin treatment. He received a renal transplant with good initial function and was maintained on the warfarin. Nine years after transplantation his creatinine rose from 150 to 230 μmol/l. A biopsy was performed which showed chronic rejection and cholesterol emboli. Graft function stabilized but did not return to baseline.

Case 4. A 45-year-old caucasian male with glomerulonephritis received a renal transplant from haemodialysis. Immediately after transplantation he developed bilateral buttock claudication, and angiography revealed bilateral common iliac artery stenosis. Fifteen years after transplantation he suffered a myocardial infarction and was treated with streptokinase. In the weeks following this his creatinine rose from a baseline level of around 120 to 170 μmol/l. A renal angiogram showed no evidence of renal artery stenosis, but his creatinine rose to 330 μmol/l. A biopsy showed the presence of cholesterol emboli. Subsequently his creatinine has settled to 200 μmol/l.

**Discussion**

These are the four cases we could identify over a 10-year period 1985–1995 in this unit, where cholesterol emboli were reported in the renal transplant biopsy. We feel that this probably underestimates the size of the problem for two reasons. Firstly it is not a diagnosis we have sought as a cause for graft dysfunction and it is a diagnosis that can be missed due to sampling error as previously discussed [10]. Secondly if the cholesterol deposition is predominantly in the arcuate vessels, as in one of these cases, then the biopsy changes will only be those of non-specific glomerular ischaemia unless the arcuate artery is biopsied.

These cases illustrate many of the features in common with native cholesterol embolic disease, including the different precipitating factors which have been described, specifically anticoagulation and aortic instrumentation [6]. When compared with the other six reported cases in Table 1 two distinct clinical presentations are apparent. The first is early cholesterol emboli associated with initial non-function. The second is late cholesterol embolic disease which occurs in stable grafts often associated with known precipitating factors. The most striking feature of the first group was the poor prognosis of their grafts with three of the five being lost. This cholesterol deposition presumably represented cholesterol embolization prior to or during harvesting or during the anastomosis with atheromatous recipient vessels. The former appears more likely in that the average age of the recipients was 43 years but that of the donors was 58 years.

Embolization may have occurred to the donor kidneys prior to harvesting, as in native cholesterol embolic disease the majority of cases occurred spontaneously [4,13]. However, recipient aortic atheroma may not be apparent at surgery. With pressure for use of older donors the possibility of graft damage from donor cholesterol embolic disease could be an increasing problem in the future. The late cholesterol emboli

**Table 1. Details of patients with cholesterol embolic disease in their transplanted kidneys**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time of biopsy/histology</th>
<th>Biopsy indication</th>
<th>Age of recipient</th>
<th>Age of donor</th>
<th>Potential predisposing factor</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Early cholesterol emboli</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Bellamy et al., [11]</td>
<td>At transplant</td>
<td>Failure to perfuse at operation</td>
<td>38</td>
<td>59</td>
<td>Prior disease or harvesting</td>
<td>Nephrectomy</td>
</tr>
<tr>
<td>de Takats et al., patient 1</td>
<td>At transplant</td>
<td>Initial non-function</td>
<td>58</td>
<td>66</td>
<td>Prior disease or harvesting</td>
<td>Functioning graft</td>
</tr>
<tr>
<td>de Takats et al., patient 2</td>
<td>1 month</td>
<td>Initial non-function</td>
<td>50</td>
<td>55</td>
<td>Prior disease or harvesting</td>
<td>Nephrectomy</td>
</tr>
<tr>
<td>Aujla et al., [9], patient 2</td>
<td>1 week</td>
<td>Initial non-function</td>
<td>27</td>
<td>57</td>
<td>Prior disease or harvesting</td>
<td>Nephrectomy</td>
</tr>
<tr>
<td>Singh et al., [12]</td>
<td>1 week</td>
<td>Early deterioration in function</td>
<td>40</td>
<td>54</td>
<td>Prior disease or harvesting</td>
<td>Functioning graft</td>
</tr>
<tr>
<td><em>Late cholesterol emboli</em></td>
<td></td>
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<td></td>
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<tr>
<td>Aujla et al., [9], patient 1</td>
<td>2 years</td>
<td>Proteinuria</td>
<td></td>
<td></td>
<td>Recipient atherosclerotic disease</td>
<td>Functioning graft</td>
</tr>
<tr>
<td>Jennings et al., [10]</td>
<td>7 years</td>
<td>Graft dysfunction</td>
<td></td>
<td></td>
<td>Post fracture</td>
<td>Functioning graft</td>
</tr>
<tr>
<td>de Takats et al., patient 3</td>
<td>9 years</td>
<td>Graft dysfunction</td>
<td></td>
<td></td>
<td>Anticoagulation</td>
<td>Functioning graft</td>
</tr>
<tr>
<td>de Takats et al., patient 4</td>
<td>15 years</td>
<td>Graft dysfunction</td>
<td></td>
<td></td>
<td>Streptokinase</td>
<td>Functioning graft</td>
</tr>
<tr>
<td>Pirson et al., [8]</td>
<td>19 years</td>
<td>Graft dysfunction</td>
<td></td>
<td></td>
<td>Streptokinase</td>
<td>Functioning graft</td>
</tr>
</tbody>
</table>
group did relatively well when compared to those with primary non-function or those with native disease [4]. Many renal transplant recipients have atherosclerotic cardiac or peripheral vascular disease prior to transplantation. Those without significant atheromatous disease at the time of transplantation often develop it later. These patients may require interventional studies for their cardiac or peripheral vascular disease, which may lead to cholesterol emboli.

The finding of renal allograft dysfunction after angiography, thrombolysis, or anticoagulation in these patients must raise the possibility of cholesterol embolic disease. Cholesterol embolic disease has a relatively good prognosis when found in renal dysfunction in a stable graft.

We believe that cholesterol embolic disease is an important and under-reported cause of renal graft dysfunction with two distinct clinical presentations. Only with a prospective study will the exact incidence of this as a cause of graft dysfunction become clear.

References


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