Long term results of heart transplantation in patients with amyloid heart disease

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Abstract

Objective—To determine the outcome of heart transplantation for end stage amyloid heart disease in patients treated at a single centre.

Design—Records of all patients with amyloid heart disease who underwent heart transplantation were examined to determine survival, graft involvement by amyloid, the course of systemic amyloidosis, and the cause of death.

Patients—10 patients, mean (SD) age 54 (8) years, received transplants in the 13 year period 1984 to 1997.

Results—Two patients, both with AL amyloid (primary systemic amyloidosis), died perioperatively. Mean follow up in the remaining eight patients was 49.9 (39.5) months (range 3–116 months). Amyloid deposits in the grafts became evident histologically in five patients with AL amyloid at 5, 11, 12, 28, and 30 months after transplantation, and in one patient with familial amyloid at 60 months. Echocardiography showed no evidence of left ventricular systolic impairment at the time of recurrence. Seven patients died, at 3, 11, 26, 32, 49, 85, and 116 months after transplantation; four of these deaths were related to amyloidosis. Actuarial survival at one and two years was 60% and at five years, 30%.

Conclusions—Heart transplantation for amyloid heart disease remains controversial because of the scarcity of hearts for transplantation, the systemic nature of amyloidosis, and the potential for amyloid deposition in the graft. Postoperative mortality was high (20%), reflecting extracardiac amyloid. Heart transplantation for end stage cardiac amyloidosis is feasible but, without treatment of the underlying process, it is a palliative procedure.

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Keywords: heart transplantation; amyloid heart disease; heart failure

Amyloidosis is the generic term for a group of disorders caused by the extracellular deposition of protein in a characteristic abnormal fibrillar form. The amyloidosis syndromes may be hereditary or acquired and are heterogeneous with respect to their pathogenesis and clinical features. In AL amyloid (primary systemic amyloidosis), the amyloid fibrils are derived from monoclonal immunoglobulin light chains and most cases are associated with subtle plasma cell dyscrasias. Some patients can benefit from chemotherapy directed towards the underlying monoclonal gammopathy, but the median period required for a clinical response to this treatment is about one year. Patients who present with severe cardiac involvement do not usually survive beyond six months and are unlikely to benefit from such treatment alone. Hereditary systemic amyloidosis is associated with mutations in the genes coding for several different plasma proteins, most commonly transthyretin (TTR). TTR related disease usually presents as the syndrome of familial amyloid polyneuropathy. Genetic variants of apolipoprotein A1 (apoA1), lysozyme, and fibrinogen are associated with amyloidosis that is often clinically indistinguishable from the AL type but which carries very different implications for treatment.

Despite the extremely poor prognosis of cardiac amyloidosis, few heart transplants have been performed for this indication. This is because of concerns about amyloid deposits in other organ systems, the poor prognosis of associated conditions such as myeloma, and the possibility of amyloid deposition in the donor heart.

We report our experience of heart transplantation in 10 patients with amyloid heart disease. Six of these patients underwent preoperative I labelled serum amyloid P component (SAP) scintigraphy to visualise amyloid deposits in visceral organs. Four underwent additional therapeutic measures in the hope of improving their long term outcome.

Methods

SUBJECTS

We reviewed the clinical records of 10 patients who underwent heart transplantation for amyloid heart disease in the 13 year period 1984 to 1997, together with the histology of endomyocardial biopsies, surgical specimens, and necropsy material.

DIAGNOSIS AND EVALUATION OF AMYLOIDOSIS

The diagnosis was confirmed histologically before transplantation. The fibril type was identified by immunohistochemical analysis supported by the demonstration of a clonal plasma cell dyscrasia, or mutations in the genes for TTR and apoA1 as appropriate. Six patients had undergone I-SAP component scintigraphy.

PRETRANSPLANT CLINICAL EVALUATION

Assessment included electrocardiographic and echocardiographic studies, right and left sided
Table 1  Patient demographics, amyloid type, organ involvement on SAP scan, severity of heart failure, and organs transplanted

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)/sex</th>
<th>Amyloid type</th>
<th>Organs involved on preoperative SAP scan</th>
<th>Preoperative heart failure class (NYHA I–IV)</th>
<th>Organs transplanted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>59 M</td>
<td>AL</td>
<td>Heart, kidney, spleen</td>
<td>IV</td>
<td>Heart</td>
</tr>
<tr>
<td>2</td>
<td>46 M</td>
<td>AL</td>
<td>Heart, spleen</td>
<td>IV + IABP</td>
<td>Heart</td>
</tr>
<tr>
<td>3</td>
<td>59 M</td>
<td>AL</td>
<td>–</td>
<td>IV</td>
<td>Heart</td>
</tr>
<tr>
<td>4</td>
<td>50 F</td>
<td>AL</td>
<td>–</td>
<td>IV + IABP</td>
<td>Heart</td>
</tr>
<tr>
<td>5</td>
<td>61 M</td>
<td>AL</td>
<td>Heart</td>
<td>IV</td>
<td>Heart</td>
</tr>
<tr>
<td>6</td>
<td>56 M</td>
<td>AL</td>
<td>Heart, liver, kidney, spleen</td>
<td>III</td>
<td>Heart and liver</td>
</tr>
<tr>
<td>7</td>
<td>52 M</td>
<td>AL</td>
<td>Heart</td>
<td>IV</td>
<td>Heart</td>
</tr>
<tr>
<td>8</td>
<td>55 F</td>
<td>AL (MM)</td>
<td>Heart, liver, kidney, spleen</td>
<td>III</td>
<td>Heart</td>
</tr>
<tr>
<td>9</td>
<td>62 M</td>
<td>TTR</td>
<td>–</td>
<td>III</td>
<td>Heart and liver</td>
</tr>
<tr>
<td>10</td>
<td>35 F</td>
<td>ApoA1</td>
<td>Heart, liver, kidney, spleen</td>
<td>IV</td>
<td>Heart and kidney</td>
</tr>
</tbody>
</table>

AL, light chain amyloidosis; ApoA1, apoprotein A1 mutation; F, female; IABP, intra-aortic balloon pump; M, male; MM, multiple myeloma; SAP, serum amyloid P component scintigraphy; TTR, transthyretin variant; –, not performed.

Cause of death and distribution of amyloid was ascertained by review of histological material from necropsy. If a necropsy examination was not done the cause of death was ascertained from the death certificate or from the patient’s general practitioner.

STATISTICAL METHODS
Survival data were summarised using Kaplan–Meier survival curves. Data are reported as mean (SD) and range.

Results
DEMOGRAPHIC DATA
Between 1984 and 1997, 10 patients with end stage amyloid heart disease underwent transplantation, representing 0.83% of the 1204 patients treated at our centre during this period. Demographic data are summarised in table 1. There were seven men and three women, mean (SD) age 54 (8) years, range 35–62 years; nine were white and one black.

Eight had AL amyloidosis, one in association with previously treated myeloma. The other two patients had familial amyloidosis associated respectively with variant transthyretin Tyr77 and apolipoprotein A1 Arg60. Biopsy confirmation of amyloidosis was obtained from heart (8), kidney (4), and nerve (1). Before transplantation, three patients were in NYHA functional class III and seven were in class IV. Two of the patients with class IV heart failure required intra-aortic balloon pump and inotropic haemodynamic support. Eight of the 10 patients survived the postoperative period for a mean of 50 (40) months (range 3–116 months).

BASELINE CLINICAL FEATURES BEFORE TRANSPLANTATION
Clinical and biochemical evidence of organ dysfunction was present in eight of the 10 patients (table 2). Important renal dysfunction, identified by proteinuria (> 0.5 g proteinuria/24 hours) or a urinary creatinine clearance reduced to < 50 ml/min was present in four and six patients, respectively. In the six patients who had SAP scans before transplantation, extracardiac amyloid was identified in the spleen in four cases, in the kidneys in four cases (two with renal dysfunction), and in the liver in three cases (fig 1). Atrioventricular block requiring permanent pacing was present in three of the 10 patients, and the mean limb lead voltage in the remaining seven was uniformly low (table 2). Mean arterial pressures were low, with high right atrial and pulmonary wedge pressures reflecting the restrictive physiology (table 3).

Table 2  Clinical features of organ function at pretransplant assessment

<table>
<thead>
<tr>
<th>Organ</th>
<th>Variable</th>
<th>Mean (SD); range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Mean left ventricular wall thickness* (cm)</td>
<td>1.8 (0.3); 1.3–2.4</td>
</tr>
<tr>
<td></td>
<td>Mean limb lead ECG voltage (mV)</td>
<td>0.32 (0.03); 0.28–0.35</td>
</tr>
<tr>
<td>Liver</td>
<td>Bilirubin (µmol/l)</td>
<td>22 (9); 13–40</td>
</tr>
<tr>
<td></td>
<td>Alkaline phosphatase (IU/l)</td>
<td>169 (86); 65–328</td>
</tr>
<tr>
<td></td>
<td>Aspartate transaminase (IU/l)</td>
<td>51 (60); 19–209</td>
</tr>
<tr>
<td>Kidney</td>
<td>Serum creatinine (µmol/l)</td>
<td>150 (112); 84–460</td>
</tr>
<tr>
<td></td>
<td>Blood urea (µmol/l)</td>
<td>11 (7); 6–30</td>
</tr>
<tr>
<td></td>
<td>Creatinine clearance (ml/min)</td>
<td>51 (27); 13–86</td>
</tr>
<tr>
<td></td>
<td>Proteinuria (g/24 h)</td>
<td>1.13 (2.27); 0.7–7.43</td>
</tr>
<tr>
<td>Diuretic treatment</td>
<td>Frusenide daily dose (mg)</td>
<td>156 (136); 40–500</td>
</tr>
</tbody>
</table>

*Mean left ventricular wall thickness for each patient was derived from the sum of interventricular septal thickness plus left ventricular posterior wall thickness divided by 2.

†Five patients had proteinuria of more than 0.5 g/24 h, and three had no detectable proteinuria.

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163 (60) minutes. The cause of donor death was intracerebral haemorrhage in seven cases; suicide, postoperative cardiorespiratory arrest, and road traffic accident head injury accounted for the remaining three donor deaths. Before organ retrieval, nine of 10 donors were on inotropic support.

TREATMENTS FOLLOWING TRANSPLANTATION

Antithymocyte antibody preparations (RATG or HATG) were used as part of the induction therapy in all seven patients with AL amyloid surviving beyond day 1 postoperatively. One patient also received OKT3. Maintenance immunosuppressive treatment in the eight surviving patients consisted of prednisolone and cyclosporin. In one patient, cyclosporin was subsequently changed to tacrolimus for refractory acute rejection. Azathioprine was used initially in all eight patients but was replaced by cyclophosphamide in three because of liver dysfunction. Chemotherapy for the underlying plasma cell dyscrasia in AL amyloidosis was given following surgery in one patient (case 7) and consisted of eight cycles of epidoxorubicin, carmustine, and cyclophosphamide. 

INCIDENCE OF ACUTE REJECTION

The incidence of acute cellular rejection was similar to that occurring in our transplant population as a whole, at 2.1 (1.5) rejection episodes/patient. All eight surviving patients had at least one episode of rejection requiring pulsed steroid treatment. One patient (case 8) had an episode of severe acute rejection (ISHLT grade 4) complicated by cardiac arrest. This patient required supportive treat-

Table 3 Haemodynamic variables at pretransplant assessment and at most recent assessment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pretransplant*</th>
<th>Post-transplant†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>107 (25); 70–150</td>
<td>125 (36); 70–180</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>70 (13); 70–90</td>
<td>81 (17); 70–100</td>
</tr>
<tr>
<td>Right atrial pressure (mm Hg)</td>
<td>16 (4); 12–17</td>
<td>7 (2); 3–9</td>
</tr>
<tr>
<td>Pulmonary artery pressure (mm Hg)</td>
<td>23 (6); 16–32</td>
<td>29 (8); 12–38</td>
</tr>
<tr>
<td>Pulmonary wedge pressure (mm Hg)</td>
<td>20 (6); 13–28</td>
<td>16 (4); 11–22</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>3.1 (0.4); 2.6–3.9</td>
<td>3.8 (1.2); 2.7–5.8</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>1.8 (0.3); 1.4–2.2</td>
<td>2.2 (0.6); 1.5–3.3</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>48 (17); 20–72</td>
<td>70 (9); 52–78</td>
</tr>
</tbody>
</table>

Values are mean (SD); range.

*Two patients subsequently deteriorated and were sustained haemodynamically using an intra-aortic balloon pump after these data had been acquired.

†Data from four patients were not available following transplantation because death occurred within the first 12 months after surgery and therefore before their first annual assessment. The mean (SD) time interval between transplantation and invasive cardiac measurements in the remaining six patients was 54 (33) months, range 11–96 months.
ment with inotropes as well as treatment with steroids and OKT3.

**AMYLOID DEPOSITION IN THE GRAFT**

In all, 161 biopsies were reviewed. Amyloid was detected in six of the eight patients (75%) who survived the postoperative period (cases 4, 5, 6, 7, 8, and 10). Microscopic deposits were first noted at 5, 11, 12, 28, 30, and 60 months, respectively, following transplantation (table 4). This histological finding preceded any evidence of graft dysfunction, and no patient had heart failure or an echocardiographic abnormality at that stage (table 4). The single patient who remained alive at the time of writing (case 10, 73 months after transplantation) had developed traces of amyloid in her graft at 60 months without any clinical or echocardiographic abnormality.

**COURSE OF EXTRACARDIAC AMYLOID**

Extracardiac amyloid deposits were monitored by serial SAP scintigraphy in four patients. There was progression of amyloid deposition in one patient, no change in two, and regression in the remaining case. This last case (case 7, fig 1) was a patient with AL amyloidosis whose monoclonal gammapathy remitted following the chemotherapy he received after transplantation, and whose 10 year survival has been reported elsewhere.17 Although the underlying myeloma in patient case 8 was in complete remission at the time of surgery, she subsequently developed clinically significant progressive systemic amyloidosis within 60 months of her operation.

**TABLE 4  Incidence of biopsy recurrence in the transplanted heart, and time after transplantation**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)/ sex</th>
<th>Amyloid recurrence</th>
<th>Time post-transplant (months)</th>
<th>Survival post-transplant (months)</th>
<th>Survival post-recurrence (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>59, M</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>46, M</td>
<td>–</td>
<td>–</td>
<td>3.0</td>
<td>2.0</td>
</tr>
<tr>
<td>3</td>
<td>59, M</td>
<td>–</td>
<td>5.0</td>
<td>11.4</td>
<td>6.4</td>
</tr>
<tr>
<td>4</td>
<td>50, F</td>
<td>+</td>
<td>11.5</td>
<td>26.2</td>
<td>14.7</td>
</tr>
<tr>
<td>5</td>
<td>61, M</td>
<td>+</td>
<td>29.5</td>
<td>85.4</td>
<td>55.9</td>
</tr>
<tr>
<td>6</td>
<td>56, M</td>
<td>+</td>
<td>28.0</td>
<td>116.3</td>
<td>88.3</td>
</tr>
<tr>
<td>7</td>
<td>52, M</td>
<td>+</td>
<td>10.5</td>
<td>49.2</td>
<td>38.5</td>
</tr>
<tr>
<td>8</td>
<td>55, F</td>
<td>+</td>
<td>31.7</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>9</td>
<td>62, M</td>
<td>–</td>
<td>60.0 (alive)</td>
<td>67.5 (alive)</td>
<td>7.5</td>
</tr>
<tr>
<td>10</td>
<td>35, F</td>
<td>+ (alive)</td>
<td>6.00 (alive)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

F, female; M, male; + recurrence of amyloid on biopsy histology.

**CAUSE OF DEATH AND NECROPSY DETAILS**

Nine patients, including all of those with AL amyloidosis, have now died. The causes of death are shown in table 5. Both patients who died in the immediate perioperative period (cases 1 and 2) had AL amyloidosis. In case 1, death was caused by acute graft failure and renal failure associated with renal amyloid. In case 2, death resulted from acute right ventricular failure which was associated with severe amyloid deposits in the lung vessels. In the remaining six AL patients, amyloid was directly implicated in their deaths in two instances (cardiac amyloid in case 6, cardiac and renal amyloid in case 8) and may have contributed to death in two further cases, both of whom had ischaemic colitis and associated mesenteric vascular amyloid (cases 3 and 7). In the two remaining patients, the causes of death were herpes encephalomyelitis and pneumonia (case 4) and metastatic adenocarcinoma of the colon (case 5). Of the two patients with familial amyloidosis, one (case 9)—with TTR Tyr77—died of renal failure from obstructive uropathy related to prostatic carcinoma at 32 months, while the other patient (case 10)—with apoA1 Arg60—was alive and clinically well at the time of writing. Two of the 10 patients developed cancer after transplantation; although an increased incidence of cancer is recognised in the post-transplant population, with the small numbers involved in our series this could have been a chance finding.

Necropsy examinations were performed in six of the nine patients who died (cases 1, 2, 6, 7, 8, and 9). We had access to the necropsy reports in all, to histological material in cases 1, 2, 6, 7, 9, and 9, and to the explanted heart and limited pathological material in case 8. In cases 1, 2, 7, 8, and 9 there was extensive amyloid deposition in vessels in organs other than the transplanted heart (table 5). In case 6, there was diffuse interstitial amyloid deposition in the myocardium together with extensive renal amyloid, with smaller amounts of amyloid in other organs. In cases 7 and 8 there was diffuse

**Table 5  Duration of survival, cause of death, and pathological features of note**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)/ sex</th>
<th>Survival (months)</th>
<th>Mode of death</th>
<th>Procedure</th>
<th>Amyloid distribution at necropsy/in operation specimen</th>
<th>Other pathological findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>59, M</td>
<td>0</td>
<td>Kidney and heart failure</td>
<td>Necropsy</td>
<td>Kidneys, vessels in liver, spleen, lymph nodes, pancreas,</td>
<td>Subendocardial infarction;</td>
</tr>
<tr>
<td>2</td>
<td>46, M</td>
<td>0</td>
<td>Right heart failure secondary to pulmonary hypertension</td>
<td>Necropsy</td>
<td>Lung, (perivascular ++), vessels in tongue, liver,</td>
<td>Contraction band necrosis</td>
</tr>
<tr>
<td>3</td>
<td>59, M</td>
<td>3.0</td>
<td>Multorgan failure: membranous colitis (operated)</td>
<td>Colectomy</td>
<td>Vascular and interstitial amyloid in submucosa and muscle</td>
<td>Pulmonary infarct</td>
</tr>
<tr>
<td>4</td>
<td>50, F</td>
<td>11.4</td>
<td>Herpes pneumonia and encephalomyelitis</td>
<td>–</td>
<td>Vessels and menentary of colon</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>61, M</td>
<td>26.2</td>
<td>Metastatic colonic adenocarcinoma</td>
<td>Colectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>56, M</td>
<td>85.4</td>
<td>Sudden death</td>
<td>Necropsy</td>
<td>Vascular and interstitial in heart; vessels in kidney</td>
<td>Mild acute rejection (ISHLT grade 1A)</td>
</tr>
<tr>
<td>7</td>
<td>52, M</td>
<td>116.3</td>
<td>Septicaemia; ischaemic colitis</td>
<td>Necropsy</td>
<td>Vessels in colon, stomach, lung, adrenals, liver, spleen, skin, testes, bladder, ureter, pancreas, bone marrow, aorta, splanchnic</td>
<td>Cardiac toxoplasmosis, graft vascular disease</td>
</tr>
<tr>
<td>8</td>
<td>55, F</td>
<td>49.0</td>
<td>Heart and kidney failure</td>
<td>Necropsy</td>
<td>Myocardial vessels in heart; vessels in lung, liver, spleen, wall of colon, myometrium, thyroid, adrenals, peripheral</td>
<td>Graft vascular disease</td>
</tr>
<tr>
<td>9</td>
<td>62, M</td>
<td>31.7</td>
<td>Kidney failure related to prostatic carcinoma</td>
<td>Necropsy</td>
<td>Vessels of lung, spleen, wall of bowel, prostate, adrenals</td>
<td>Oxalate nephropathy; no cardiac amyloid (only one block examined)</td>
</tr>
<tr>
<td>10</td>
<td>35, F</td>
<td>67.5</td>
<td>Not applicable (alive)</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

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cardiac amyloid deposition in intramyocardial arteries and arterioles, and focal deposition in endocardium and interstitium. In cases 7 and 8 there was also diffuse transplant associated graft vascular disease. In case 9 only one block of the transplanted heart was available for examination and was normal.

Two patients, neither of whom had a necropsy examination, underwent colonic resection, one (case 3) for ischaemic colitis and one (case 5) for adenocarcinoma (Dukes stage C). In both, there was extensive intramural and mesenteric vascular deposition of amyloid. The remaining patient (case 4) did not have a necropsy examination.

Discussion

This study shows that heart transplantation in systemic amyloidosis must be regarded as a palliative procedure unless additional therapeutic measures can be implemented to prevent subsequent amyloid deposition in the graft or progression of systemic disease. We have also demonstrated the feasibility of post-transplantation chemotherapy in AL amyloidosis, and of simultaneous liver transplantation in hereditary TTR amyloidosis or kidney transplantation in apoA1 amyloidosis.

Early Mortality

There were two perioperative deaths and a total of four deaths within the first year. These all occurred in patients with AL amyloidosis. It should be noted, however, that four of the 10 patients transplanted were critically ill at the time of surgery. Two of these four were in a recognised high risk category, being in intensive care and dependent on an intra-aortic balloon pump for haemodynamic support before their surgery, while the remaining two patients both had severe renal dysfunction. One patient (case 1) with nephrotic range proteinuria had extensive amyloid infiltration of renal parenchyma at biopsy. The second patient (case 2) had become oliguric immediately before surgery and at necropsy was found to have extensive vascular and interstitial deposition of amyloid in the lung which had not been detected on the preoperative SAP scan.

The current scarcity of donor organs suitable for heart transplantation has led to a consensus that strict selection criteria should be used. Patients with amyloidosis now should meet the same selection criteria as candidates for transplantation with other causes for heart failure.

Stringent selection of patients with minimal involvement of extracardiac sites, using SAP scanning and histology, might be expected to minimise early mortality. The proportion of patients with cardiac AL amyloidosis and minimal systemic disease at the time of diagnosis is, however, small and in one study such patients accounted for only 4% of all patients presenting to a major amyloid referral centre.

Additional Treatment for AL Amyloidosis

Our experience of progression of systemic amyloidosis in extracardiac sites and in the cardiac allograft is similar to that reported by others. However, systemic amyloidosis should no longer be regarded as an incurable disease. Although there is no treatment which specifically disperses amyloid deposits, prospective quantitative monitoring of amyloid using radiolabelled SAP has shown regression of amyloid deposits within 6–36 months of treatments that reduce the supply of amyloid fibril precursor proteins. Severe cardiac involvement remains a major problem in the treatment of AL amyloidosis. For those who have end stage amyloid heart disease and who are suitable for heart transplantation, a transplant may be life saving in the short term and may provide a window of opportunity for additional therapeutic measures to achieve an effect. Recent studies have suggested that dose intensified chemotherapy with autologous stem cell rescue can produce much higher response rates in AL amyloidosis than low dose regimens.

The use of chemotherapy after transplantation is illustrated anecdotally by one of our patients with AL amyloid (case 7) who lived for over nine years following treatment with a combination myeloma regimen. In that patient, follow up SAP scans at seven years showed that the major visceral amyloid deposits that had been demonstrated shortly after transplantation had regressed to undetectable levels.

Combined Transplantation for Hereditary Amyloidosis

In the case of TTR amyloidosis, liver transplantation effectively eliminates the supply of the genetically variant TTR, as transthyretin is almost exclusively produced by hepatocytes. Associated cardiac amyloidosis can regress in this situation, but the process is very slow and may be dependent on the specific mutation.

No treatment is known to reduce the progression of hereditary apoA1 amyloidosis, and its natural history after heart transplantation is uncertain. However, the absence of progressive disease in our patient after seven years is encouraging and indicates that her amyloid deposition is extremely slow.

Limitations of this Study

The results of our series of patients must be interpreted with caution because of the small numbers involved. Nevertheless, because of the rarity of amyloidosis and the infrequent use of heart transplantation for this condition, the cases reported here form a significant part of the information available on this topic.

SAP scanning has limitations and is poor for imaging the heart itself. While a positive scan can be of use in identifying extracardiac amyloid involvement, a negative SAP scan cannot exclude the presence of amyloid in other organs. This was illustrated by case 2 in whom extensive pulmonary amyloid was not detected.

The “time to recurrence” of amyloid (table 4) reflects the timing of heart biopsies. Routine surveillance biopsies were performed during the first year after transplant but were thereafter determined by clinical indications. In consequence the time of recurrence is approximate.
We have compared survival figures after heart transplantation in general, in the series presented here, and in patients with non-transplanted cardiac amyloid (fig 2). The limitations of this comparison include the small number of patients in our series, the heterogeneity of amyloidosis, and the varying approaches to treatment. Owing to the selection bias of patients with amyloidosis who were transplanted, this graph cannot be interpreted as indicating that transplantation improved survival in our patients.

CONCLUSIONS

The use of heart transplantation for cardiac amyloidosis is palliative, providing only short to medium term benefit because it does not influence the underlying disease process. On the basis of our experience, we feel that heart and liver transplantation is feasible in disease. This approach will, however, need to intensity chemotherapy to treat the underlying proportion of patients with AL amyloidosis transplantation alone cannot be justified, on the basis of our experience, we feel that heart encephale the underlying disease process. On the medium term benefit because it does not influence the underlying disease process. This approach will, however, need to be tested in future studies. We have shown that heart and liver transplantation is feasible in hereditary TTR type amyloidosis and that combined heart and kidney transplantation can produce worthwhile results in the apoA1 type.

We wish to thank the pathologists who contributed surgical and necropsy data to this study. We also thank Debbie Simpson, Brenda Hollingsworth, and Marguerita Lewis for technical help with the biopsy review.


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Long term results of heart transplantation in patients with amyloid heart disease

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