with only a marginal fall in paraprotein level. He progressed to ESRF.

After 3 years of the initial diagnosis, the patient underwent autologous PBSC transplantation using intermediate dose melphalan (100 mg/m²). IgG level fell to 300 mg/dl, with serum kappa free light chains of 83.2 mg/l (3.3–19.4). Severe neutropenic sepsis precluded a planned second PBSC transplant. A year later, the patient underwent HLA-identical living donor kidney transplantation. Post-operatively there was delayed graft function. Serum creatinine improved to a baseline of 2 mg/dl.

Twenty-six months post-renal transplant, IgG level was 500 mg/dl, with serum kappa free light chains of 72.3 mg/l. MRI and sestamibi scans showed active disease in the left femur and right iliac crest. Bone marrow biopsy showed 4% plasma cells, although with considerably more noted on CD138 staining. Thalidomide and dexamethasone were commenced, with a plan for a further autologous PBSC transplant with higher dose melphalan. Renal function was stable at 1.7 mg/dl. A kidney biopsy at this stage showed no recurrence of light chain deposition.

Our patient is the first case of LCDD treated with sequential transplantation. Leung et al. [4] described seven patients with the related disorder primary amyloidosis who underwent sequential kidney transplantation and autologous PBSC transplantation. Kidney transplantation was performed first because of the limitations on drug dosing imposed by ESRF. One patient died, but the rest remained well without recurrent amyloidosis (follow-up period 0.7–4.1 years).

Our decision to perform PBSC transplantation first was based on concerns about additive risks of chemotherapy and post-renal transplant immunosuppression. Chemotherapy dose was modified because of renal impairment. There was still significant treatment-related toxicity with incomplete suppression and subsequent progression of the underlying disease, despite no evidence of recurrent light chain deposition in the renal allograft.

Conflict of interest statement. The content presented in this article has not previously been published in whole or in part. There was no conflict of interest for any of the authors of the article. We have had no involvements that might raise the question of bias in the work reported, or in the conclusions, implications or opinions stated.

Advance Access publication 28 November 2006

Human Urotensin II in the plasma of anephric subjects

Sir,

Human urotensin II (UII), perhaps the most potent mammalian vasoconstrictor known, is thought to be produced by the kidneys. The urotensins are a family of vasoactive peptides first isolated from various fish species over 20 years ago. Homologous peptides have been isolated in numerous species including frogs, rodents, pigs, primates and humans. It has been demonstrated in-vitro that human UII is between 8- and 110-fold more potent than endothelin-1 as a vasoconstrictor, and is the most potent mammalian vasoconstrictor known. The precise metabolic pathway(s) of urotensin metabolism is unknown, though high density of UII and its receptor have been demonstrated in mouse and monkey kidneys [1] and human kidneys, [2] and is thus thought to be synthesized, secreted and cleared by the kidneys [3,4,5]. Also, some researchers have reported higher blood values of UII in patients with kidney disease as well as with hypertension. These reports have stimulated interest in a possible aetiological role of UII in kidney disease and hypertension in people with kidney disease; consequently we sought to determine whether plasma concentrations of UII are detectable in subjects with end-stage renal disease (ESRD) on dialysis, and in particular in surgically anephric subjects.

Thirty-one ESRD subjects undergoing routine haemodialysis were enrolled, including two surgically anephric subjects (i.e. both patients had bilateral nephrectomy at least 6 months prior to enrolment). Blood samples were obtained for UII before initiation of a mid-week dialysis session. UII concentrations were measured in unextracted plasma by radioimmunoassay using human UII-specific monoclonal antibody at GlaxoSmithKline laboratories (NA). The mean UII was compared between anephric and non-anephric subjects with a paired Students’ t-test, using JMP IN statistical software version 4 (SAS Institute, Carey, NC, USA).


doi:10.1093/ndt/gfl669

The content presented in this article has not previously been published in whole or in part. There was no conflict of interest for any of the authors of the article. We have had no involvements that might raise the question of bias in the work reported, or in the conclusions, implications or opinions stated.

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Katherine A. Barraclough
Renal Medicine
John P. Dowling
Department of
Anatomical Pathology
Gregory J. Perry
Bone Marrow Transplant Program,
Alfred Hospital,
Melbourne,
Australia
Email: arbieb@hotmail.com

Fig. 1. Pre-transplant kidney biopsy showing moderate widespread deposition of kappa light chains within and surrounding many tubular basement membranes. Immunoperoxidase staining for kappa light chain; original magnification ×400. Bar = 100 μm.
The study was approved the Institutional Review Boards of the University of Pennsylvania and Gambro Healthcare. Written informed consent was obtained from all subjects. Data was stored in a password-protected laptop computer using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

Concentrations of UII were present (and higher) in the two surgically anephric subjects (20,216 and 21,555 pg/ml, mean = 20,886 pg/ml) compared with the other 29 subjects (16,039 ± 769 pg/ml) though these differences were not statistically significant.

Our findings of measurable (and perhaps elevated) concentrations of UII in anephric subjects are inconsistent with the conclusion that the kidneys are the primary source for production of UII. The high density of UII and its receptor in renal tissues suggest that UII is metabolically active in the kidney even though it is produced in sites outside of the kidneys.

Conflict of interest statement. The authors report the following financial conflicts of interests: R.R.T. is a speaker for BMS, Merck and Pfizer and has grant support from Novartis, Sankyo and DMV—international. TD and NA are employees and stockholders of GlaxoSmithKline.

1Department of Medicine, Renal Electrolyte and Hypertension Division University of Pennsylvania School of Medicine Philadelphia 2GlaxoSmithKline King of Prussia, PA

Email: townsend@mail.med.upenn.edu

5Matsushita M, Shichiri M, Fukai N et al. Urotensin II is an autocrine/paracrine growth factor for the porcine renal epithelial cell line, LLCPK1. Endocrinology 2003; 144: 1825–1831

doi:10.1093/ndt/gfl697

Advance Access publication 23 November 2006

Plasma exchange in the treatment of acute renal failure of myeloma

Sir,
The article by Haubitz and Peest, ‘Myeloma—new approaches to combined nephrological–haematological management’ [1] addresses a very important issue in clinical practice. However, very little is said on the management of myeloma patients presenting with acute renal failure (ARF), particularly on the role of plasma exchange (PE) in this setting. PE has been used to reduce plasma concentrations of light chains in patients with renal insufficiency [2], and it has been recommended in the management of ARF in myeloma patients [3]. However, findings from a recent large, prospective, randomized trial of PE in the treatment of ARF in patients with newly diagnosed myeloma, failed to show any benefit [4]. We reviewed our single-centre experience over a 10-year period (January 1995–December 2005) on the effect of PE in 55 myeloma patients (31 men, 24 women; mean age 71 ±11 years) presenting with ARF or either survival and rate of recovery of renal function. ARF was defined as a doubling of serum creatinine with respect to the basal level, over a 48 h period, and/or reduction of urine output <500 ml/24 h in spite of correction of hypovolaemia, hypercalcaemia and metabolic acidosis. Twenty-seven patients received 5–8 (median 6) PE treatments (3 on consecutive days and the others on alternate days) with 50 ml/kg body weight of 5% human albumin and saline as replacement fluid. Twenty-eight patients did not receive PE treatment and were considered as control group. VAD or dexamethasone were administered to all patients according to haematologist’s prescription. Table 1 shows the baseline clinical and laboratory characteristics of the patients. No significant differences were observed between groups. Figure 1 shows Kaplan–Meier analysis for all-cause mortality (left panel), and renal death (need for dialysis) (right panel) in the two groups of patients. No significant effect of PE on either patients or renal survival was observed at 36 months. Twenty-three patients (42%) died. Causes of death were: sepsis 11%, pulmonary infection 34%, cachexia 22%, other causes 33%. Our data agree with those of Clark and Colleagues [4]. We acknowledge that our observations are neither prospective nor randomized, however, they are representative of a large and widespread clinical approach to this problem worldwide. Extension of follow-up to a 36-month period did not show any significant benefit of PE, not only on

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control group patients (28 patients)</th>
<th>Plasma exchange group (27 patients)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)a</td>
<td>69 ± 10</td>
<td>67 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)a</td>
<td>7.4 ± 4.1</td>
<td>9.3 ± 4.5</td>
<td>NS</td>
</tr>
<tr>
<td>Serum calcium (mg/dl)a</td>
<td>9.1 ± 1.2</td>
<td>9.0 ± 1.5</td>
<td>NS</td>
</tr>
<tr>
<td>Diuresis (ml/day)b</td>
<td>1048 ± 759</td>
<td>1006 ± 784</td>
<td>NS</td>
</tr>
<tr>
<td>Oliguria (&lt;500 ml/24 h; n; %)b</td>
<td>6/28 (21)</td>
<td>5/27 (18)</td>
<td>NS</td>
</tr>
<tr>
<td>Osteolytic lesion (n; %)b</td>
<td>16/28 (57)</td>
<td>12/27 (44)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercalcaemia (n; %)b</td>
<td>3/28 (11)</td>
<td>5/27 (18)</td>
<td>NS</td>
</tr>
<tr>
<td>Monoc. BJ proteinuria (n; %)b</td>
<td>23/28 (82)</td>
<td>20/27 (74)</td>
<td>NS</td>
</tr>
<tr>
<td>K (mmol/l; %)b</td>
<td>10/28 (35)</td>
<td>10/27 (37)</td>
<td>NS</td>
</tr>
<tr>
<td>λ type (n; %)b</td>
<td>16/28 (57)</td>
<td>13/27 (48)</td>
<td>NS</td>
</tr>
<tr>
<td>Dialytic treatment (n; %)b</td>
<td>16/28 (57)</td>
<td>18/27 (66)</td>
<td>NS</td>
</tr>
</tbody>
</table>

aPlus-minus values are mean ± SD; comparison between mean: unpaired Student’s t-test.
bComparison between categorical data: χ2 test.