Urinary Tract Infections after Renal Transplantation with Special Respect to Localisation Studies

V PRÁT, V BOHUSLAV, J JIRKA, M HATALA, M LIŠKA, P MÁLEK, K SLÍŽ, V KOČANDRLE
Institute for Clinical and Experimental Medicine, Prague, Czechoslovakia

Summary

Of the 80 allografted subjects 57 (71%) had 124 episodes of urinary tract infection (significant bacteriuria in at least two consecutive cultures). However, renal infection not attributable to other sources (septicaemia, infected perirenal haematoma) or to urinary tract complications (nephrostomy, permanent bladder catheterization) was found in only two of the 46 grafts available for detailed morphological examination. Localisation studies showed most episodes of infection to be confined to the lower urinary tract. Residual bladder urine volume estimations revealed higher values in transplant than in non-transplant subjects.

Introduction

The incidence of urinary tract infection after renal transplantation is relatively high. With few exceptions (Starzl et al, 1970), figures exceeding fifty percent of transplant subjects have been published (Leight, 1969; Bennett et al, 1970; Hamshere et al, 1974). Many contributing factors have been considered (e.g. immunosuppression, bladder surgery and instrumentation), but little attention has been paid to the site of infection and bladder function. This study was undertaken to shed light on this problem.

MATERIAL AND METHODS

Eighty consecutive subjects with renal allografts were studied. Thirty one — all but two living donor kidney recipients — had been bilaterally nephrectomised
prior to or at the time of grafting. The rest — 49 cadaver kidney recipients — had not. Only patients with first grafts followed up for intervals from one week to nearly 10 years were evaluated. In all patients ureteroneocystostomy was performed with catheters left routinely in the ureter for two to four days and in the bladder for three to five days. Four grams of Oxacillin and one gram of streptomycin were administered for 10 days starting on the day of transplantation. As immunosuppression 2–3 mg/kg/day of azathioprine and 2 mg/kg/day of prednisone were given, with the latter gradually reduced to a maintenance dose of 10 to 20 mg/day in six to eight weeks. Acute rejection episodes were usually treated with higher doses of prednisone, occasionally combined with actinomycin and/or local irradiation. In the last two years methylprednisolone given in large intravenous doses was used. All episodes of urinary tract infection associated with positive bacterial cultures were treated early; antibiotics were chosen according to in vitro sensitivity.

Quantitative bacteriuria was followed daily during the first two weeks, twice a week during the subsequent two weeks, once a week during the second month and once every five to eight weeks thereafter. Whenever a culture was positive the bacteriology was repeated. A diagnosis of infection was considered to be established if significant bacteriuria was present in at least two consecutive investigations.

The presence of renal infection was assessed by the histology of autologous kidneys and grafts available either after transplant nephrectomy or necropsy. Altogether 40 autologous kidneys and 54 renal allografts were examined.

The localisation tests used were the bladder washout technique of Fairley et al (1967), 'kidney washout' with an evaluation of the bacterial excretion rate during furosemide-induced diuresis (Prút et al, 1975) and evidence of antibody-coated bacteria in the urinary sediment as described by Thomas et al (1974).

At least two of these tests were performed in each patient. Altogether 31 tests were performed in 14 subjects with active infection.

Urinary bladder function was estimated indirectly by measuring residual bladder volume using $^{131}$I hippuran as described by Shand et al (1968) and modified by Sifjà et al (1976). Such measurements were undertaken in 14 transplant subjects and in 14 non-transplant patients with recurrent urinary tract infection.

RESULTS

Fifty-seven of the 80 transplant patients had 124 episodes of infection involving the urinary tract, i.e. 71 per cent of the patients studied. Bacteriuria alone accounted for 74 and bacteriuria with leucocyturia for 50 episodes; clinical symptoms were seldom present.

Renal infection occurred rarely. Histology of 40 autologous kidneys revealed no active infection, but confirmed its presence in 10 of 54 renal grafts (Table I).
However, in five of the latter the primary source of infection was elsewhere than in the kidney. Two patients had a nephrostomy and one a permanent bladder catheterisation (10 weeks). Thus of 46 grafts in patients with no other infections or urological complications only two were infected, i.e. 4.3 per cent.

### TABLE I  Histological Studies

<table>
<thead>
<tr>
<th></th>
<th>infected</th>
<th>0</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>autologous kidneys</td>
<td>40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>renal allografts</td>
<td>54</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**graft infection**
- metastatic haematogenous nephritis $^1$ 4
- abscess $^2$ 1
- pseudomembranous pyelitis 1
- suppurative pyelonephritis $^3$ 2
- acute pyelonephritis $^4$ 1
- chronic pyelonephritis $^4$ 1

1 septicaemia from other sources
2 infected perirenal haematoma
3 indwelling catheter in one
4 nephrostomy

Table II shows the results of correlation studies with several factors that may be involved in the aetiology of urinary tract infections. It was found that the shorter the period of time after transplantation and the higher the rate of rejection crises, the higher was the rate of episodes of urinary infection due to Gram-positive and mixed infections. On the other hand, infection episodes were not more frequent in subjects with vesico-ureteric reflux, post-transplant oliguria, during acute rejection and in non-nephrectomised patients.

### TABLE II  Correlation of Urinary Tract Infections with other factors

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>CORRELATION WITH URINARY INFECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>time interval since grafting</td>
<td>yes $r = -0.868$ p &lt; 0.001</td>
</tr>
<tr>
<td>number of rejection episodes</td>
<td>yes $r = 0.680$ p &lt; 0.001*</td>
</tr>
<tr>
<td>abnormal cystoradiogram</td>
<td>no $X^2 = 0.867$ N.S.</td>
</tr>
<tr>
<td>acute rejection</td>
<td>no $X^2 = 0.120$ N.S.</td>
</tr>
<tr>
<td>post-transplant oliguria</td>
<td>no $X^2 = 1.048$ N.S.</td>
</tr>
<tr>
<td>presence of autologous kidneys</td>
<td>no $X^2 = 2.994$ 0.05 &lt; p &lt; 0.10</td>
</tr>
</tbody>
</table>

* valid for gram-positive or mixed infections only

The results of localisation studies are represented in Figure 1. It can be seen that in 4/5 of the subjects studied the source of bacteriuria was the lower urinary tract. All three methods gave uniform results in 71, antibody-coated bacteria combined with kidney washout in 100 per cent of cases.
Figure 1. Results of localisation studies in renal transplant patients with Bacteriuria.

The comparison of residual bladder volumes in transplant and non-transplant subjects is shown in Figure 2.

Figure 2. Residual bladder volume

DISCUSSION

In the present series, the incidence of urinary tract infection was nearly identical to that reported in other studies. Prophylactic administration of antibiotics in urinary tract infection appears to be of little value (Hatala et al, 1974). This seems to be true also of renal infection. The incidence of 4.6 per cent in this study is close to the 6.8 per cent reported by Starzl et al (1970) in their 118 patients with ureteroneocystostomy without prophylactic antibiotic therapy. Whether this low figure is due to early antibiotic treatment of all episodes (used in both studies) or to other factors, still remains speculative. Judging by these data, urinary tract infection in transplant patients — unless due to surgical, urological or septicaemic complications — is a relatively benign condition. At
first sight, this observation contradicts the findings of Myerowitz et al (1972) according to which the urinary tract and the graft or its neighbourhood were the source of bacillaemic episodes in most of their transplant patients. Yet it should be noted that over half of these episodes were associated with ureteral obstruction, urinary fistula or infected perirenal haematoma.

Negative correlation between the incidence of episodes of urinary tract infection and the time after transplantation holds for infections in general (Lagrange et al, 1973). Therefore local factors (except for the quantitative aspect), would seem to be of little importance. However, the observation that in most patients residual bladder volumes were increased shows that this need not necessarily be so. If impaired bladder evacuation can persist for several years after transplantation (seven subjects were investigated after more than three years), the more likely is it to have been present shortly after transplantation, when readaptation of the bladder is necessary after months or years of hypofunction, and after surgery.

The positive correlation between episodes of urinary tract infection and the number of rejection crises resembles that observed by Myerowitz et al (1972) and others, with infections in general. The role of Gram-positive infection in this relationship is obscure. But it is worthwhile reconsidering the experimental studies of Rapaport and Chase (1964) showing that transplantation immunity may be enhanced by streptococcal antigens.

A very important observation in this study is the site of urinary tract infection and hence the source of bacteriuria. Given the prevalence of infections confined to the lower urinary tract, the following prognostic and therapeutic conclusions can be drawn: urinary tract infection carries a very good prognosis and its site in the lower urinary tract may explain why renal tissue is seldom involved; methods attacking lower urinary tract infections directly should be sufficient to control them, and high doses of antibiotics may be avoided as undesirable in transplant patients.

References

Lagrange, Ph, Acar, J F, Idatte, J M, Bedrossian, J and Brisset, J M (1973) Pathologie et Biologie, 21, 981
Myerowitz, R L, Medeiros, A A, O'Brien, T F (1972) American Journal of Medicine, 53, 308
Open Discussion

CANTALUPI (Milan) Our experience in 150 patients is very similar to yours. Now, I will ask you, what is your therapeutic attitude towards simple bacteriuria without leucocyturia?

PRAT We treat these patients usually with a single dose therapy. That means that most of these patients are treated by, for instance, a single dose of Furadantin once a day for a long period of time, because it is known that this bacteriuria has a tendency to recur.

CATTELL (London) I think this is a very interesting paper. We have found similar results. One of the important things is that it explodes all the ridiculous concepts that I fear many transplant surgeons have regarding the need for pre-transplant nephrectomy. What I would like to ask is, in the patients you found with upper tract disease, did you have any difficulty in eradicating infection; did you have any problem with relapsing infection or were they relatively easily treated?

PRAT I think our group of patients is too small to evaluate differences between these two types of patients.

AHLMEN (Gothenburg) I have two questions, the first one is: this seems to be a good opportunity to culture anaerobic bacteria from urine. Have you done this? My second question is: have you any figures telling you if these UTIs have any importance in the long run, for example in graft survival? Because from our figures in Gothenburg it seems to be the other way round. Patients when well-treated for recurring UTI seem to have a better graft survival after 3 - 4 years' transplant function than the other patients without UTI. Perhaps that is because of better immunosuppression, but I don’t know.

PRAT We did not evaluate anaerobic infection and the second question — we did not analyse survival rates of the infected and non-infected patients or the treated and non-treated. In fact, we treat all of these patients with urinary infections because in some instances they have troubles with frequency of micturition and so on.