Renal Transplantation in Cats with Chronic Renal Failure

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ABSTRACT. Renal transplantation was performed on 6 cats with chronic renal failure. Clinical signs and the blood chemistry findings (BUN, Cr, IP) improved one week after renal transplantation. Renal anemia also improved 3–4 weeks after surgery. Two cases had the same complications, hydronephrosis and hydroureret within 1 or 2 weeks of surgery, evidenced by marked elevations of BUN and Cr. Suggesting that ureteral obstruction at the site of ureterocystostomy is the main complication of renal transplantation in cats. As a new resolution for this problem, we transplanted the ureter with the intact ureteral opening of the bladder from the donor in the remaining 4 cats. Ureteral obstruction was not observed in them, thus the procedure was considered to be useful for avoiding this complication. Two cats died of pneumonia and other complications within 3 months. There were no acute rejections or side effects from the immunsuppressants during the observation period in the remaining four cats. — KEY WORDS: feline, renal transplantation.


Despite the increase in the number of clinical cases of small animals with chronic renal failure, the treatments are limited to symptomatic therapy and drug therapy consisting of fluid therapy. More active treatment with various dialysis have been used, however this is only executed for the filtration aspect of the renal function, and it is, therefore, not necessarily the essential treatment for chronic renal failure. Renal transplantation has been enumberated as a radical treatment for chronic renal failure and a high rate of success has been obtained in the treatment of human beings, but transplantation has not been clinically performed on animals except for dogs and cats as reported by Gregory et al. [4–6]. We performed renal transplantation on 6 cats, diagnosed as having chronic renal failure.

MATERIALS AND METHODS

Recipients: Renal transplantation was performed on 4- to 10-year-old cats with chronic renal failure (Table 1). All had been managed medically, primarily with fluid therapy, but without improvement in the clinical signs and blood chemistry findings. When medical therapy was judged to be insufficient to prevent further renal deterioration, the surgical treatment of renal transplantation was employed. None of the cats had any complications associated with heart disease, malignancy, hepatic dysfunction or infection. All the cats were negative for FeLV, FIP and FIV.

Donor: Adult cats were selected as donors from the colony of the First Department of Veterinary Surgery, School of Veterinary Medicine, Azabu University. The cats were clinically healthy, showing normal findings for complete blood cell count (CBC), serum chemical analysis and general urinalysis. They also had erythrocyte type and blood-crossmatch compatibility. All of them were negative for FeLV, FIP and FIV.

Informed consent from owners: At the stage of treating

<table>
<thead>
<tr>
<th>No</th>
<th>Patient</th>
<th>Preoperative BUN/Cr/IP&lt;sup&gt;a&lt;/sup&gt; (mg/dl)</th>
<th>Preoperative PCV (%)</th>
<th>Postoperative BUN/Cr/IP&lt;sup&gt;a&lt;/sup&gt; (mg/dl)</th>
<th>Postoperative ureteral stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Himalayan, male, 4 yr</td>
<td>83.8/5.6/11.8</td>
<td>19.7</td>
<td>21.5/1.6/2.8</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>Japanese cat, male, 7 yr</td>
<td>104.1/8.3/15.5</td>
<td>14.5</td>
<td>46.5/1.1/2.7</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>Japanese cat, male, 10 yr</td>
<td>114.3/4.6/10.9</td>
<td>15.0</td>
<td>50.8/1.0/2.7</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>Japanese cat, female, 5 yr</td>
<td>106.0/4.2/8.2</td>
<td>20.5</td>
<td>14.7/1.2/2.2</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>Japanese cat, female, 5 yr</td>
<td>187.3/13.8/20.3</td>
<td>14.0</td>
<td>36.7/1.4/2.6</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>Japanese cat, female, 8 yr</td>
<td>99.0/11.0/15.0</td>
<td>14.0</td>
<td>19.1/0.8/1.8</td>
<td>–</td>
</tr>
</tbody>
</table>

<sup>a</sup>Creatinine. <sup>b</sup>Serum phosphorus.
including part of the bladder wall in the vicinity of the ureteral opening was totally excised. The excised kidney was perfused with heparinized physiological saline solution cooled to 4°C, and stored in ice water before the transplantation. In the recipient, the external iliac artery and vein were separated and exposed after a median inferior incision was made. After the transplantation bed had been prepared on the iliac fossa, the renal vein was end-to-side anastomosed with the right external iliac vein of the recipient and the renal artery was end-to-end anastomosed with the right external iliac artery of the recipient. The total ischemia time (warm and cold ischemia time) of the donor kidney was kept to 60 min or less. In Cases 1 and 2, a submucosal tunnel of the bladder was prepared for ureterocystostomy and routine ureterocystostomy was performed. In Cases 3–6, total ureteral transplantation was performed; i.e., part of the bladder wall including the intact ureteral opening of the donor was excised and connected with the bladder wall of the recipient by sutures (Fig. 1a,b). The kidney of the recipient was not excised.

Postoperative management: After renal transplantation, cyclosporin (7.5 mg/kg/12 hr; intravenous instillation; 1–100 dilution), prednisolone (0.25 mg/kg/12 hr; S.C.) and an antibiotic were administered. After internal medication became possible, the administration was changed to oral antibiotics, cyclosporin (7.5 mg/kg/12 hr) and prednisolone (0.25 mg/kg/12 hr). The administration of the antibiotics was stopped when the leukocyte count became stable. Depending on the cats’ conditions, diuretics, fluid therapy, or blood transfusion were performed. During hospitalization, serum chemical analysis, general urinalysis, intravenous pyelography (IVP), and ultrasonography of the transplanted kidney and the ureter were performed. After discharge from the hospital, the cats underwent blood and serum chemical analysis at one-month intervals. Doses of cyclosporin and prednisolone were altered as warranted by the individual course of each case.

RESULTS

In all cats receiving renal transplantation, the clinical signs improved within one to three days post-operation. Additionally, the serum chemical findings, BUN, Cr and IP recovered to normal levels within one week. Since the packed cell volume (PCV) transiently decreased to about 10%, blood transfusions were necessary in some cases. Resolution of the anemia took 3 to 4 weeks.

Cases 1 and 2 showed BUN>80 mg/dL, Cr>4 mg/dL at 10 to 16 days after transplantation. IVP and ultrasonography revealed enlargement of the renal pelvis and the ureter. Postrenal renal failure due to ureteral stenosis was suspected, and reoperation was performed. In Case 1, the clinical signs and renal function were favorably maintained after the reoperation. In Case 2, however, the clinical signs and serum chemical findings worsened after the reoperation, therefore, ureterocystostomy was performed. To prevent restenosis, a catheter was retained in the anastomosed ureter.

The recipient cats by medicine, the risks of surgery and anesthesia for renal transplantation, complications such as postoperative infection and rejection, and the significance of immunosuppressive therapy were explained to all of the owners. With regard to the donor cats, consent for renal transplantation was obtained after confirmation that the recipient’s owner would be willing to maintain the donor cat as an adopted pet.

Preoperative management for recipient: Recipients were maintained on fluid therapy (70–100 mL/kg/day), and on selective blood transfusion therapy prior to surgery. Cyclosporin (intravenous instillation; 1:100 dilution; 7.5 mg/kg/12 hr) and prednisolone (0.25 mg/kg/12 hr; S.C.) were administered, starting 24 hr prior to surgery.

Surgical procedure for renal transplantation: After a median incision had been made on the donor, the peripheral tissue of the left kidney was separated, followed by excision of the free renal artery, vein and ureter. Then, the ureter was ligated and transected at the site where the ureter enters the bladder in Cases 1 and 2, but in Cases 3–6, the ureter is
for 5 days. Subsequently, the clinical signs and renal function were favorably maintained. In contrast, Cases 3 to 6, which were treated using the new method, showed no ureteral stenosis. The vesical wall was re-sutured in Case 3, because leakage from the sutured site of the bladder had occurred as a result of vesical suture failure.

There were no deaths within 2 weeks of transplantation. All six cats were ultimately discharged from the hospital. Cases 1 to 3 were hospitalized for approximately one month because reoperations were necessary, however, Cases 4 to 6 were discharged from the hospital about two weeks after transplantation.

With regard to doses of immunosuppressive drugs after discharge, cyclosporin and prednisolone were maintained at dosages ranging from 7.5 to 10 mg/kg/24 hr and from 0.25 to 0.5 mg/kg/24 hr, respectively.

After discharge, Case 1 had an infection (feline viral rhinotraceitis), and the renal function deteriorated transiently. Subsequently, this cat was treated with fluid therapy, administration of feline interferon (Intercat™, TORAY Co., Ltd., Japan: 10 MU/kg/day) and antibiotics, and the renal function improved, however, the cat died from pneumonia on day 92 after renal transplantation. Case 3 died suddenly for unknown reasons on day 90 after renal transplantation. Postoperative courses have been uneventful, without rejection or infectious complications, for 2 to 5 months, to date, in the remaining cats. Case 2 has been alive for approximately one year, to date, since transplantation.

**DISCUSSION**

Renal transplantation is an essential surgical treatment for chronic renal failure. If it is successful, the various complications of chronic renal failure, which cannot be rectified by dialysis, can be overcome. As a result of our present renal transplantation, clinical signs such as loss of appetite and listlessness improved 1-2 days after renal transplantation. The serum chemical findings also showed marked decreases in BUN, Cr and IP, which were restored to normal within one week of surgery. Anemia also tended to gradually improve 3-4 weeks after renal transplantation, thus, blood transfusion should be performed for about 2 weeks after transplantation, according to circumstances.

The main surgical complications of renal transplantation are blood flow disorders due to narrowing and thrombus of the transplanted renal artery and vein, stenosis at the site of ureterocystostomy, vesicoureteral reflux (VUR), and suture failure of the ureter and bladder. Stenosis or obstruction of the site of ureterocystostomy is considered the biggest problem for cats[6]. In humans and dogs, the most common surgical procedure of ureterocystostomy is the submucosal tunnel method [3]. Since the feline ureter lumen is \( \leq 1 \) mm, it is probable that the feline ureter will become stenotic even at the site of anastomosis and in the tunnel. Furthermore, in the report of Gregory et al. [6], ureteral stenosis was observed in 4 (5 kidneys) of 23 cases within 2 weeks after transplantation, and they concluded that the ureteral stenosis was attributable to the drop-in technique of ureterocystostomy. The cases in which submucosal tunnels were prepared in an experiment by Kochin et al. [8], showed enlargement of the kidney, renal pelvis and ureter one week after surgery, whereas 8 weeks after the transplantation there were no problems. The technique described in the study was then applied to 15 ill cats receiving renal allografts, and none required surgical correction of ureteral obstruction [8]. In our cases, hydronephrosis and hydrourereter were observed within 1 or 2 weeks and elevations of BUN and Cr were also marked. Despite submucosal tunnels having been prepared, the operation had to be performed again. As a new trial for this problem, we performed transplantation of the ureter including part of the bladder wall of the ureteral opening of the donor in the present experiment. The recipients showed no ureteral stenosis, it is, therefore, considered useful for renal transplantation in cats.

Immunosuppressive therapy is essential for patients with transplantation, but infection may be caused by excessive administration of immunosuppressants. If the dose is too limited, however, acute rejection may also occur. In the present study, no findings likely to be indicative of rejection were observed. Side effects of prednisolone such as hemorrhage from the digestive tract, and side effects of cyclosporin such as nephrotoxicity and hepatotoxicity can be a problem [1, 12], but it is believed that there are almost no side effects of cyclosporin in animals [4-7]. None of our recipient cats showed any side effects during the course of observation, however, since chronic rejection may also occur, regular screening will be necessary.

Case 1 had an infection and died from pneumonia. The cat was contagious with other diseased cats, and the reduced immunological competence, which was attributed to
excessive administration of immunosuppressants, was not considered to be the only factor in this case. The cause of death in Case 3 was unknown, because the owner's consent for autopsy was not obtained.

In selecting donors, consistence of histocompatibility is necessary because erythrocyte membrane surface antigens and the histocompatibility antigen system are present in the endothelium of blood vessel. In human beings, DNA typing and cross-matching of lymphocytes are performed [11, 13, 14, 17]. In cats, however, many aspects of histocompatibility remain to be clarified. We performed blood crossmatching and typing, and no problems have occurred to date.

The purpose of the preoperative blood transfusion was to improve the anemia of the recipient, however, some reports have shown that the effects of selective blood transfusion therapy (donor specific blood transfusion; DST) increase the survival of transplanted kidney [2, 16]. For this reason, we transfused the donor blood in all cases before transplantation.

In selecting recipients, transplantation is recommended to be performed in a transitional period from the compensatory to the non-compensatory stage of chronic renal failure, since the recipients have to tolerate anesthesia and surgical stress, which will be additive. Transplantation should be performed before hematocrit decreases to a severe degree. Informed consent from the owners is deemed to be important for selecting recipients. For this purpose, correct knowledge and recognition of renal transplantation, as follows, should be provided to owners in as much detail as necessary: renal transplantation is one of the therapeutic methods for treating chronic renal failure; its ultimate purpose is to increase the animal's quality of life; the degree of risk from surgery and anesthesis in renal transplantation; complications of renal transplantation, such as postoperative infection, rejection, etc.; the significance of immunosuppressive therapy. When selecting donors from among cats in a university laboratory, recipients' owners should be obliged to keep it as an adopted pet from the viewpoint of prevention of cruelty to animals, and bring it in regularly for postoperative renal function tests.

The proper kidney was not excised in the present experiment. This will provide reserve function if the donor kidney does not function adequately. There is another opinion, however, that the proper kidney should be excised because hypertension may be induced by hyperactivity of renin-angiotensin system if the proper kidney is left in situ for a long duration [9, 10, 15]. This should also be investigated in the future.

REFERENCES