Retroperitoneal fibrosis in four cats following renal transplantation

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- Fibrosis within the retroperitoneal space is an uncommon complication following renal transplantation in cats.
- Possible causes of retroperitoneal fibrosis in renal transplant recipients may include operative trauma, infection, deposition of foreign material in the operative field, urinary leakage, or hemorrhage during the transplant procedure.
- Recurrence of azotemia within the first few months after surgery, in conjunction with specific ultrasonographic findings, may be supportive of a diagnosis of retroperitoneal fibrosis.
- Surgery appears to be the treatment of choice to relieve the urinary obstruction and restore normal renal function.

A 9-year-old male castrated domestic shorthair cat (cat 1) was referred to the University of Pennsylvania Veterinary Medical Teaching Hospital for renal transplantation. Six weeks previously, the referring veterinarian determined that the cat had renal insufficiency. Prior treatment included SC administration of fluids (100 mL of lactated Ringer's solution) every other day, erythropoietin[a] (unknown dosage) twice weekly, and potassium supplementation. Prior to transplantation, abnormalities detected on biochemical analysis included high BUN concentrations (105 mg/dL; reference range, 15 to 29 mg/dL), and high serum concentrations of creatinine (6.8 mg/dL; reference range, 0.5 to 2 mg/dL), phosphorus (14.9 mg/dL; reference range, 2.5 to 6.0 mg/dL), and globulin (5.6 g/dL; reference range, 2.6 to 5.1 g/dL). The serum albumin concentration was in the low end of the reference range (2.8 g/dL; reference range, 2.7 to 3.9 g/dL). A CBC determination revealed a low hematocrit (25%) and a mild leukocytosis (19,800 WBC/μL; reference range, 5.5 to 19,500 WBC/μL). Abnormalities detected on urinalysis included a urine specific gravity of 1.010 and a pH of 6.

Renal transplantation was performed 1 week following admission to the veterinary teaching hospital. Cyclosporine[b] (2 mg/kg [0.9 mg/lb], PO, q 12 h) was administered beginning 48 hours prior to surgery. Prednisone (0.5 mg/kg [0.23 mg/lb], PO, q 12 h) treatment was started the morning of surgery. During the first 24 hours after surgery, the cat received hydralazine hydrochloride[c] (2.5 mg, SC) on 2 occasions to control 2 episodes of hypertension. One day after surgery, abnormalities detected on biochemical analysis included high BUN (33 mg/dL) and serum creatinine (3.2 mg/dL) concentrations, and a low serum albumin concentration (2.1 mg/dL). A biopsy specimen of the native kidney had been obtained at the time of transplantation; histologic evaluation revealed moderate chronic interstitial nephritis with extensive interstitial fibrosis. The cat was discharged 1 week following surgery with a gastrostomy tube. Because the cat was immunosuppressed, amoxicillin-clavulanic acid[d] (13.75 mg/kg [6.25 mg/lb], PO, q 12 h) was administered for 2 weeks following surgery until the gastrostomy tube was removed.

A biochemical analysis was performed 2 weeks following surgery and revealed a high BUN concentration (36 mg/dL). Serum concentrations of creatinine (2.0 mg/dL), phosphorus (6.5 mg/dL), albumin (2.5 g/dL), and globulin (6.0 g/dL) were within or near reference range values. A CBC determination revealed persistence of the anemia (hematocrit, 22%) and, despite antimicrobial treatment, a mild leukocytosis (21,400 WBC/μL). A urinalysis revealed a urine specific gravity of 1.026.

One month following transplantation, moderate azotemia persisted with a BUN concentration of 77 mg/dL, a creatinine concentration of 2.2 mg/dL, and a phosphorus concentration of 8.2 mg/dL. Other abnormalities detected included mild hypoalbuminemia (2.6 g/dL), hyperglobulinemia (6.3 g/dL), anemia (hematocrit, 23%), and a leukocytosis (20,700 WBC/μL). Abdominal ultrasonography of the allograft revealed that the graft had become larger with a decrease in blood flow. On abdominal palpation, the kidney felt firm and large. An aspirate of the allograft was performed, and histologic evaluation revealed numerous lymphocytes. The findings were consistent with allograft rejection, and the cat was treated with cyclosporine (6.6 mg/kg [3 mg/lb], IV, q 24 h) and corticosteroids (prednisolone sodium succinate; 10 mg/kg [4.5 mg/lb], IV, q 24 h). Despite treatment for allograft rejection, the cat remained mildly azotemic. Because the cat appeared healthy to the owners, they declined further diagnostics at this time. Three months following surgery, the cat started to decompensate, and the owners agreed to further evaluation. Biochemical analysis and CBC determination revealed worsening azotemia with a BUN concentration of 60 mg/dL, a serum creatinine concentration of 4.4 mg/dL, a serum phosphorus concentration of 5.2 mg/dL, hematocrit of 19%, and a leukocytosis (25,600 WBC/μL). Urinalysis revealed a urine specific gravity of 1.014 with a pH of 5.5. Evaluation by use of abdominal ultrasonography and intravenous urography revealed hydronephrosis and proximal hydroureter of the allograft. Contrast material could not be seen entering the bladder; however, because of the close proximity of the allograft to the bladder, an exact site of obstruction could not be determined. During an exploratory laparotomy, fibrous

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tissue with a dense gray-white appearance surrounding the allograft kidney and ureter was identified. The fibrous tissue caused mechanical obstruction of the ureter (**Fig 1**). A cystotomy was performed to evaluate the ureteroneocystostomy site for any abnormalities and for the presence of urine flow. The fibrous tissue surrounding the allograft ureter was slowly peeled off of the allograft kidney and ureter (**Fig 2**) until the ureter was freed of any constriction and urine was flowing normally through the ureteroneocystostomy site. Histologic evaluation of the fibrous tissue revealed that it consisted of smooth muscle and fibrous connective tissue proliferation with few lymphocytes and macrophages (**Fig 3**). Most of the tissue was not inflammatory. Bacterial culture results of the tissue were negative. An abdominal ultrasound of the allograft, performed following exploratory laparotomy, revealed the presence of a capsule surrounding some of the allograft and resolution of the hydronephrosis and hydroureter (**Fig 4**). The cat recovered without complication and was discharged. Ten days after surgery, CBC determination and biochemical analysis revealed a BUN concentration of 38 mg/dL, a serum creatinine concentration of 2.0 mg/dL, a serum phosphorus concentration of 6.7 mg/dL, hematocrit of 19%, and a leukocytosis (22,500 WBC/μL). Thirty-six months following the second surgery, CBC determination and biochemical analysis results were within reference range, except for a mild leukocytosis (23,800 WBC/μL). Urinalysis revealed a urine specific gravity of 1.030.

A 6-year-old male castrated domestic shorthair cat (cat 2) was referred to the veterinary teaching hospital for renal transplantation because of a 3-month history of progressive azotemia, weight loss, anorexia, and vomiting. Bacterial culture of fluid obtained by cystocentesis during the initial screening for transplantation revealed large gram-positive and gram-negative rod bacteria (*Klebsiella pneumoniae*), which were thought to be a contaminant. The cat received a course of antibmicrobials (amoxicillin-clavulanic acid[d]; 13.75 mg/kg [6.25 mg/lb], PO, q 12 h) for 4 weeks. Following discontinuation of antimicrobial treatment, a

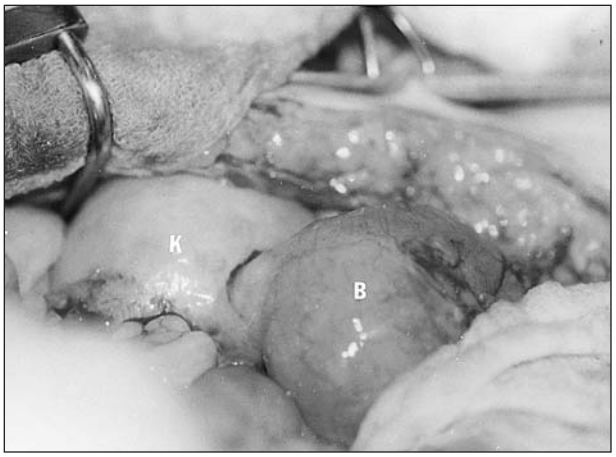

Figure 1—Photograph of exploratory laparotomy in a cat that developed retroperitoneal fibrosis following renal transplantation. Notice the gray-white fibrous tissue surrounding the allograft (K). The allograft is adhered to the bladder (B) by fibrous tissue.

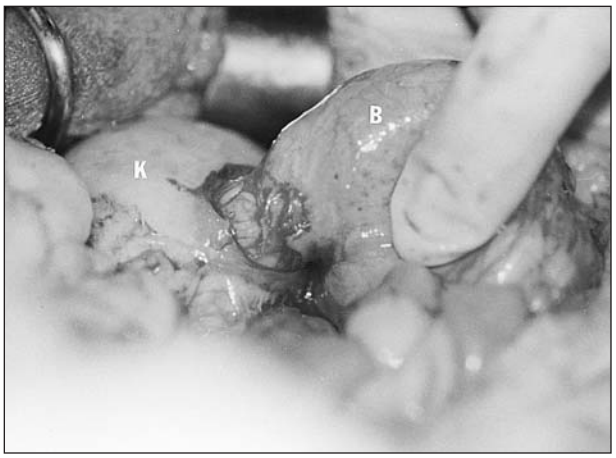

Figure 2—Photograph obtained during exploratory laparotomy in the cat in Figure 1. The fibrous tissue surrounding the allograft was slowly peeled off the ureter until the ureter was freed from constriction. Notice the ureter and periureteral fat that can be seen between the allograft (K) and the bladder (B). Only enough of the fibrous tissue was removed to relieve the urinary obstruction.

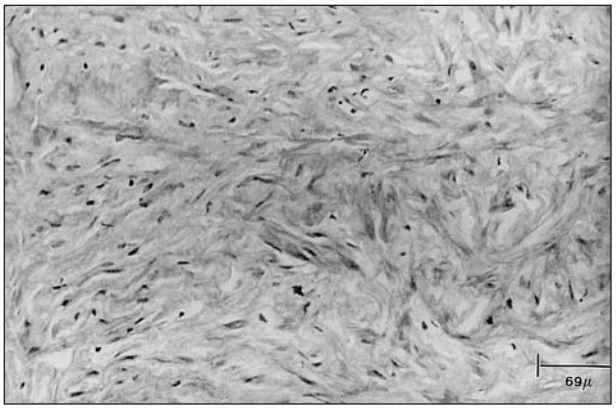

Figure 3—Photomicrograph of a section of a biopsy specimen from a fibrous plaque in the retroperitoneum that encased the ureter of the same cat as in Figure 1. Notice the presence of smooth muscle cells in addition to the fibrotic tissue. H&E stain; bar = 69 μm.

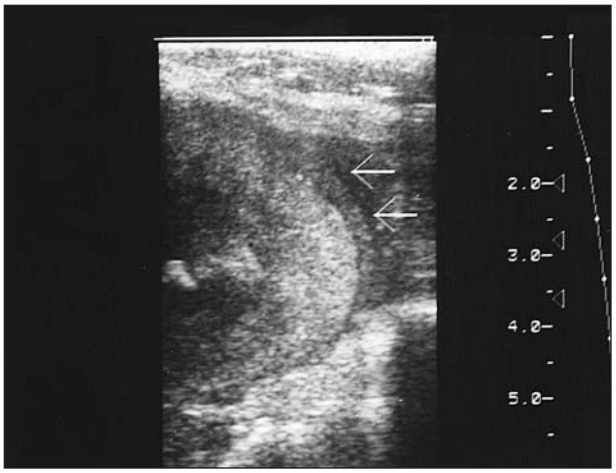

Figure 4—Abdominal ultrasonographic image of the same cat as in Figure 1. The capsule surrounding the allograft was identified (arrows). Abdominal ultrasonography was performed following exploratory laparotomy that was done to relieve the obstruction of the allograft ureter. Hydronephrosis is no longer observable.

cyclosporine[b] challenge was performed to determine whether the cat would redevelop an infection while on immunosuppressive therapy. Results of repeated bacterial cultures of urine samples were negative. The cat was therefore considered a transplant candidate. Prior to transplantation, abnormalities on biochemical analysis included high BUN (63 mg/dL) and serum creatinine (3.6 mg/dL) concentrations. A CBC determination revealed a low hematocrit (19%). Urine specific gravity was 1.011. Renal transplantation was performed without complication. Cyclosporine[b] (2 mg/kg [0.9 mg/lb], PO, q 12 h) was administered beginning 48 hours prior to surgery, and prednisone (0.5 mg/kg [0.23 mg/lb], PO, q 12 h) treatment was started the morning of surgery. The cat was discharged 1 week following surgery.

The azotemia resolved following surgery and, according to the owner, the cat appeared healthy. Results of biochemical analysis were within reference range for the first 2 months following transplantation; however, the cat continued to be anemic (hematocrit, 22%) and the urine specific gravity was 1.020. Five months following transplantation, mild azotemia developed with a BUN concentration of 73 mg/dL and a creatinine concentration of 2.3 mg/dL. Abdominal ultrasonography revealed hydronephrosis and proximal hydroureter. Results of an intravenous urography revealed a large hydronephrotic kidney, a dilated proximal ureter, and a delayed nephrographic and pyelographic phase. Differentials for this cat were a pyelonephritis and a partial ureteral obstruction. Bacterial culture of an aspirate from the renal pelvis revealed anaerobic bacteria that were small gram-positive rods and gram-positive cocci. Amoxicillin-clavulanic acid[d] (13.75 mg/kg [6.25 mg/lb], PO, q 12 h) and enrofloxacin[e] (5 mg/kg [2.3 mg/lb], PO, q 24 h) were administered for 4 weeks. Following antimicrobial treatment, the azotemia persisted and, because of the degree of hydronephrosis, an exploratory laparotomy was performed. At surgery, a dense white fibrous tissue surrounding the allograft kidney and ureter that caused mechanical obstruction of the ureter was observed. A cystotomy was performed to evaluate the ureteroneocystostomy site for urine flow. The fibrous tissue surrounding the allograft ureter was slowly peeled off of the allograft kidney and ureter until the ureter was freed of any constriction and urine was flowing normally through the ureteroneocystostomy site. A piece of the fibrous tissue was submitted for histologic evaluation and bacterial culture. The tissue consisted of smooth muscle and fibrous connective tissue proliferation with few lymphocytes and macrophages. Most of the tissue was not inflammatory. Twenty-four hours following surgery, abdominal ultrasonography revealed almost complete resolution of the hydronephrosis. The cat recovered without complication and was discharged 3 days following surgery. Fourteen months following the second surgery, findings on CBC determination and biochemical analysis were unremarkable, and the cat was clinically normal.

An 8-year-old male castrated domestic shorthair cat (cat 3) with a 1-year history of renal insufficiency was referred to the veterinary teaching hospital for renal transplantation. Prior treatment included SC administration of fluids (75 mL of lactated Ringer's solution, q 24 h), erythropoietin[a] (unknown dosage), and aluminum hydroxide[f] (4 mL, PO, q 24 h). Abnormalities detected on biochemical analysis prior to transplantation revealed a BUN concentration of 57 mg/dL and a serum creatinine concentration of 5.6 mg/dL. Abnormalities detected on CBC determination included anemia (hematocrit, 23%) and thrombocytosis (1,063,000 platelets/µL). The platelet count was repeated prior to surgery, which revealed a value of 772,000 platelets/µL. Transplantation was performed; however, infarction of the kidney occurred after a clot formed in the renal artery. The cat received heparin treatment, and a second transplantation was performed 2 weeks following the first surgery. Cytologic evaluation of peritoneal fluid collected at the time of the second transplantation revealed a pure transudate with a mild inflammatory component. On bacterial culture of the peritoneal fluid, a gram-positive cocci *Enterococcus* sp and an anaerobic *Clostridium* sp were identified. During the first 24 hours after surgery, the cat received 1 dose of hydralazine[c] (2.5 mg, SC) for an episode of hypertension. The cat received amoxicillin-clavulanic acid[d] (13.75 mg/kg [6.25 mg/lb], PO, q 12 h) for 4 weeks. The cat was discharged 1 week following surgery. Biochemical analysis at the time of discharge revealed a BUN concentration of 46 mg/dL, a serum creatinine concentration of 2.2 mg/dL, and a serum phosphorus concentration of 5.7 mg/dL.

The cat was readmitted to the veterinary teaching hospital 6 weeks following the second surgery with a recurrence of azotemia. Biochemical analysis and CBC determination revealed a BUN concentration of 65 mg/dL, a serum creatinine concentration of 5.0 mg/dL, a serum phosphorus concentration of 8.3 mg/dL, and a hematocrit of 17%. The cat was initially treated for acute allograft rejection with cyclosporine[b] administered at a dosage of 6.6 mg/kg (3 mg/lb), IV, for 6 hours. No response occurred with allograft rejection treatment, and the degree of hydronephrosis worsened with fluid therapy. Exploratory laparotomy revealed a dense white fibrous tissue surrounding the allograft kidney and ureter that caused mechanical obstruction of the ureter. A cystotomy was performed to evaluate the ureteroneocystostomy site for urine flow. The fibrous tissue surrounding the allograft ureter was slowly peeled off of the allograft kidney and ureter until the ureter was freed of any constriction and urine was flowing normally through the ureteroneocystostomy site. Histologic evaluation of the fibrous tissue later revealed a mixture of fibrous connective tissue and smooth muscle. At a single edge of the tissue specimen there was minimal infiltration of neutrophils and lymphocytes. Bacterial culture results of the tissue were negative. The cat recovered uneventfully and was discharged 3 days following surgery. Seven months after surgery, findings on CBC determination and biochemical analysis were unremarkable.

An 8-year-old female spayed domestic shorthair cat (cat 4) was referred to the veterinary teaching hospital for renal transplantation. The cat had not been clinically normal for 2.5 months. Prior treatment

included SC administration of fluids (100 mL of lactated Ringer's solution, q 24 h), potassium supplementation, famotidine[g] (0.5 mg/kg [0.23 mg/lb], PO, q 24 h), aluminum hydroxide[f] (unknown dosage), and a vitamin supplement[e] (unknown dosage). Prior to transplantation, abnormalities detected on biochemical analysis included a high BUN (54 mg/dL) and serum creatinine (3.5 mg/dL) concentrations. The CBC was unremarkable, except for a slightly low hematocrit of 28%. Renal transplantation was performed 1 week following admission. Cyclosporine[b] (2 mg/kg [0.9 mg/lb], PO, q 12 h) was administered beginning 48 hours prior to surgery. Prednisone (0.5 mg/kg [0.23 mg/lb], PO, q 12 h) treatment was started the morning of surgery. A biopsy specimen of 1 of the native kidneys revealed chronic interstitial nephritis with glomerular sclerosis. The cat was discharged 1 week following surgery. Biochemical analysis at the time of discharge revealed a BUN concentration of 35 mg/dL, a serum creatinine concentration of 1.6 mg/dL, and a serum phosphorus concentration of 4.3 mg/dL.

The referring veterinarian examined the cat 6 weeks following surgery because of a recurrence of azotemia (BUN concentration of 65.4 mg/dL and creatinine concentration of 2.5 mg/dL) and persistence of the anemia (23.8%). A urinalysis revealed a specific gravity of 1.013, trace proteinuria, and 3+ leukocytosis (range, 0 to 3+). Bacterial culture results of urine were negative. Over the next week, the azotemia worsened and CBC determination revealed a leukocytosis (22,600 WBC/μL; reference range, 6 to 18,000 WBC/μL) with a mild neutrophilia (89%). Abdominal ultrasonography revealed moderate renal pelvic dilation and a discreet 2-mm-thick pericortical capsule surrounding the allograft. An exploratory laparotomy was performed, and a thick, white fibrous capsule was found surrounding the allograft kidney and ureter. The ureter was freed of constriction, and a piece of the fibrous tissue was submitted for histologic evaluation and bacterial culture. The ureter was inadvertently traumatized during surgery, and as a result, reimplantation of the ureter into the bladder was performed. Histologic evaluation revealed dense fibrosis characterized by embedded, well-differentiated fibrocytes and fibroblasts supported by collagen bundles. Inflammation was present with rare aggregates of mononuclear inflammatory cells and neutrophils associated with small zones of fat necrosis. On histologic evaluation of a complete cross section of the ureter, no evidence of luminal inflammation with extensive fibrosis was observed. No active cellular infiltrate was identified or was associated with the ureter. The cat recovered uneventfully and was discharged 7 days following surgery. Twenty-two months after surgery, findings on CBC determination and biochemical analysis were unremarkable.

In humans, **retroperitoneal fibrosis (RF)** has been classified as primary or secondary. In both instances, the fibrotic tissue, which appears as a dense gray-white fibrous plaque, surrounds the aorta and vena cava within the retroperitoneum and can extend laterally encasing the ureters, occasionally extending to the renal pelvis and resulting in partial or complete ureteral obstructions.[1-5] Although the fibrosing process can surround the aorta and vena cava, obstruction of these vessels is not common. Uncommonly, RF can encase organs of the gastrointestinal tract and the bladder.[6]

In primary or idiopathic RF, the fibrosis is most severe in areas of the aorta with atherosclerotic disease. It is thought in these patients that an immune-mediated process may be occurring in response to a component of the atherosclerotic plaque, which can protrude through the aortic wall.[1,7] The aortitis that initially occurs in these patients is thought to precede the fibrosis. Up to 15% of patients with idiopathic RF have fibrosis outside the peritoneum, suggesting that the RF may be part of a systemic fibrosing disease.[4,5]

Secondary RF is associated with a specific cause such as malignancy, drug treatment, or a sclerotic reaction that occurs as a consequence of retroperitoneal inflammation caused by infection, trauma, hemorrhage, multiple abdominal surgeries, urine extravasation, gastrointestinal inflammation, or an abdominal aneurysm.[3-10] In human transplant patients, possible insults during or after renal transplantation that could result in RF include operative trauma, infection, deposition of foreign material in the operative field, urinary extravasation, and perirenal hemorrhage caused by trauma to the allograft.[11,12] In affected humans, 30% develop secondary RF and 70% develop primary or idiopathic RF.[10] A diagnosis in human renal transplant patients is suggested, based on impaired renal function in conjunction with pyelograph studies. Differentials in humans may include a pyelonephritis and severe transplant rejection.

In the 4 cats of this report, cat 1 was initially treated for allograft rejection on the basis of the presence of moderate azotemia, a large allograft on abdominal palpation, and histologic evaluation of an aspirate of the allograft that revealed numerous lymphocytes. This cat did not respond completely to treatment for allograft rejection, suggesting that another cause of the azotemia may exist. Another possibility is that the abdominal inflammation associated with a possible rejection episode in cat 1 may have been associated with RF identified 2 months later. The cause of the persistently high WBC count in this cat, before and after surgery, was never determined. In cat 2, a pyelonephritis in the allograft detected 5 months following transplantation may have been the cause. The degree of hydronephrosis present in this patient, however, may suggest that the outflow obstruction preceded the pyelonephritis. In cat 3, a septic peritoneal effusion detected at the time of the second transplantation may have potentiated the RF. Cat 3 was also initially treated for allograft rejection on the basis of reoccurrence of impaired renal function and findings on ultrasonographic evaluation. In cat 4, a possible cause could not be determined.

Some pharmacologic agents have been associated with the development of RF in humans. Administration of methysergide, hydralazine, aspirin, methyldopa, ergotamine tartrate, oxprenol, atenolol, propranolol, dextroamphetamine, ephedrine, or strychnine has been implicated as a cause of RF in people.[4,7,8,13,14] Two of the 4 cats received hydralazine (2.5 mg, SC) for hypertension after surgery. One cat received 1 dose and the second cat received 2 doses. The mechanism by which these medications cause RF in humans is unclear. Many of these drugs are vasoactive. It has been hypothesized that repeated vasoconstriction and

vasodilation caused by some drugs may result in perivascular edema, transudation of plasma, and the development of a fibroblastic response.[13] An immunologic mechanism has also been postulated for adverse effects associated with methyldopa and hydralazine. One way β adrenergic blockers may produce RF is by decreasing the ratio of adenosine 3:5-cyclic monophosphate to cyclic glucose monophosphate, resulting in an increase in cellular proliferation.[4] In a retrospective study[14] evaluating the management of hypertension after surgery in feline renal transplant patients, 21 cats were treated with hydralazine SC with no reports of RF occurring following treatment. In that report,[15] there is no mention of the presence of concurrent infections or rejection episodes occurring in any of the cats.

Because RF appears to be a rare complication in renal transplant recipients, it is not thought that hydralazine played a role in causing the fibrosis in the 2 treated cats of this report. However, it is possible that induction of RF may require the interaction of several causative agents of which 1 may be hydralazine. Inflammation alone or inflammation associated with infection may interact with hydralazine to trigger RF. With regards to the 2 cats in this report that received hydralazine, in cat 1, abdominal inflammation may have been associated with a possible rejection episode or the presence of a gastrostomy tube, and in cat 3, a septic peritoneal effusion was detected at the time of the second transplantation.

A diagnosis of RF in people is often difficult early in the course of the disease because the symptoms are often nonspecific and do not necessarily relate to the urinary tract until a ureteral obstruction is present. Middle-aged men are most commonly affected with idiopathic RF, and the most common clinical sign in people with RF is a nagging back pain, not necessarily in the renal area, which often radiates.[4,5,7,12,13,16] Other clinical signs in people may include anemia, nausea, fever, weight loss, hypertension, and lower extremity edema.[2,7,14,17] In the current report, 3 of the 4 cats were male. After transplantation, all of the cats had maintained their weight and none of the cats were febrile. The anemia persisted in all 4 cats. It was not until the second surgery was performed to remove the offending fibrotic tissue and relieve the ureteral obstruction that the anemia resolved.

Laboratory findings in humans with RF support the presence of inflammation and renal insufficiency. A high erythrocyte sedimentation rate is a consistently abnormal laboratory finding in people with idiopathic RF, and there is a correlation between the degree of the increase and the activity of the disease process.[11,16,17] Erythrocyte sedimentation rate was not evaluated in the cats of this report. In some human patients, globulin concentrations have also been found to be high. In this report, serum globulin concentrations were high in only 1 cat after surgery (cat 1). All of the cats of this report were readmitted to the veterinary teaching hospital following their renal transplantation because of recurrence of their azotemia 1 to 5 months following transplantation. Occasionally in humans, a leukocytosis is present.[6,7] This was true for cats 1 and 2 of this report. Urinalysis results are often nonremarkable in humans[16]; however, a transient proteinuria or pyuria may be documented, as was true for cat 4.

In humans, abdominal ultrasonography and excretory intravenous urography are extremely helpful in making a diagnosis of RF. The classic triad in human patients with RF includes a delayed excretion of contrast material with unilateral or bilateral hydronephrosis, tapering of the ureter to a narrowed segment, and medial deviation of the ureter.[4,5,7,17] These appearances can be nonspecific, and up to 18% of control subjects can have findings consistent with this triad.[5] It has been postulated that as the inflammatory mass matures and fibroses, contraction occurs, drawing the ureters medially.[10] Abdominal ultrasonography in humans often identifies a smooth retroperitoneal mass enveloping the aorta and vena cava. In the cats of our report, abdominal ultrasonography revealed a 2- to 4-mm-thick capsule surrounding the allograft in cats 1 and 4, a hydronephrosis in all 4 cats, and a hydroureter proximally in cats 1 and 2. Intravenous urography was performed on cats 1 and 2. Because of the close proximity of the allograft to the bladder, the exact location of the ureteral obstruction could not be determined.

Treatment in humans is often a combination of surgical and medical management. Surgery is typically recommended for primary and secondary RF to relieve the urinary obstruction and restore normal renal function. In many instances, particularly those of primary RF, medical management to prevent continued progression of the inflammation is recommended.[5,6] Surgical treatment of choice in people is ureterolysis, a surgical release of the ureter from surrounding scar tissue. The ureter is then wrapped in omentum to prevent reobstruction.[7] In people, the fibrous tissue does not typically invade the ureteral tissue but surrounds and encases the ureter, leaving a defined plane of normal and abnormal tissue. The obstruction may be a mechanical obstruction of the ureter or may be a functional obstruction by interfering with normal ureteral peristalsis.[17] In humans, results of ureteral catheterization and pressure studies reveal inhibition of peristalsis resulting from intrinsic fibrosis.[1] In all 4 cats of this report, an exploratory laparotomy was performed. At surgery, the aorta and vena cava were not visible because of the presence of a gray-white fibrous plaque that extended at least over the ventral surface of these vessels, encasing the allograft kidney and ureter with fibrous attachments to the bladder. This gross appearance is similar to what is seen in humans. A cystotomy was performed first in all 4 cats to evaluate the ureteroneocystostomy site for urine flow. Blunt dissection was then used to carefully peel the constricting fibrous tissue off of the allograft ureter and the medial aspect of the allograft kidney. A defined plane was present between the graft tissue and the abnormal scar tissue. Once the ureter was released from the constricting tissue, urine flow was observed at the ureteroneocystostomy site. The cystotomy was closed. All 4 cats recovered without complication.

In humans, recurrent ureteral obstruction following surgery has been reported in up to 22% of patients treated with surgery alone.[6] To date, no recurrence has been reported in any of the 4 cats. Adjunctive immunosuppressive therapy in humans using corticosteroids, cyclosporine, azathioprine, or cyclophosphamide has been successful in preventing progression in some patients with idiopathic RF, supporting an immunolog-

ic cause of the disease in these patients.[7,18] Another study[7] found no difference in the outcome of patients receiving surgery and corticosteroids, compared with those receiving surgery alone. It appears that medical management may be most affective in the initial phases of idiopathic RF. As the disease progresses, the cellular infiltrate is replaced by fibroblasts and collagen. In the later stages, the tissue may be completely devoid of cells and this stage is difficult to treat medically.[11] Tamoxifen, which may increase the synthesis and secretion of an inhibitory growth factor, has also been used successfully in humans.[6,7]

In humans with idiopathic RF, biopsy specimens taken along the lateral margins of the fibrous tissue have histologic characteristics of immature connective tissue, whereas midline biopsy specimens (surrounding the aorta) appear mature.[19] Laterally, the fibrous tissue contains many lymphocytes, fibroblasts, and occasional macrophages, eosinophils, neutrophils, and mast cells. Medially, the fibrous tissue is composed of dense connective tissue with few fibroblasts and inflammatory cells. These differences may suggest that there is lateral progression of the process from midline structures such as the aorta and vena cava.[5,6,11,19] In some instances, by the time the process causes clinical complications, there may be little evidence of the initial inflammatory reaction.[13] Sections of plaque taken adjacent to the renal pelvis were submitted for histologic evaluation and bacterial culture from all 4 cats of this report. Histologic evaluation of biopsy specimens revealed smooth muscle (3 cats) and fibrous connective tissue. The reason for the presence of the smooth muscle in biopsy specimens from 3 cats is not known. It is possible that myofibroblasts that were present may have differentiated into smooth muscle rather than fibroblasts. Most of the tissue from the 4 cats was noninflammatory. It is not known for any of the cats early on in the progression of RF whether the lesions were inflammatory. Bacterial culture results for biopsy specimens from all 4 cats were negative.

Prognosis in patients with RF depends on the underlying cause. In patients with idiopathic RF without renal compromise and effective surgical treatment, the prognosis is excellent. The RF itself rarely causes substantial morbidity and mortality. Most of the deaths in humans are attributable to complications with atherosclerotic disease. The prognosis is poor in human patients with malignant RF, with a mean survival of 3 to 6 months after the diagnosis has been made.[5] The cause of fibrosis in the 4 cats described in this report is not known. The abdominal inflammation associated with a possible rejection episode in cat 1 may have been associated with RF identified 2 months later. The cause of the persistently high WBC count in this cat, before and after surgery, was never determined. Infection may have played a role in cats 2 and 3. Cat 2 had a positive bacterial culture result for an aspirate from the renal pelvis, which may have been a cause of fibrosis or may have resulted from the fibrosis causing an outflow obstruction. Bacterial culture of peritoneal fluid collected at the time of the second transplantation in cat 3 revealed a gram-positive cocci *Enterococcus* sp and an anaerobe *Clostridium* sp. In cat 4, a possible cause could not be determined. Other possible causes of RF in the cats of this report may include perirenal hemorrhage or urinary extravasation. In renal transplantation, the renal capsule is sutured to the lateral body wall. Hemorrhage from the capsule can collect in the peritoneal cavity. A cystotomy is performed for ureteral implantation. Urine production from the native kidneys and the allograft can occasionally collect in the peritoneal cavity. Although the peritoneal cavity is lavaged well prior to closure, it is possible that residual hemorrhage or urine may have resulted in fibrosis around the allograft. All 4 cats, regardless of the cause, responded well to surgical resection of the scar tissue that was causing a ureteral obstruction. Recurrence of obstruction did not occur in any of the cats following surgery.

[a]Epogen, Amgen Inc, Thousand Oaks, Calif.
[b]Neoral, Novartis Pharmaceuticals Corp, East Hanover, NJ.
[c]Hydralazine, Sidmak Laboratories Inc, East Hanover, NJ.
[d]Clavamox, Smith Kline Beecham, Philadelphia, Pa.
[e]Baytril, Bayer Corp, Shawnee Mission, Kan.
[f]Alu-Cap Antacid, 3M Pharmaceuticals, Northridge, Calif.
[g]Pepcid, Johnson & Johnson, Fort Washington, Pa.
[h]Hi-Vite drops, Advanced Biological Concepts, Oslo, Ill.

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