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Should the Ruptured Renal Allograft Be Removed?

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• During a 16-month period when 93 renal transplants were performed, eight kidney graft ruptures were detected within 18 days of transplantation, without evidence of venous obstruction. Six grafts were removed at the time of an exploratory operation for rupture and only one showed signs of probable irreversible rejection when examined by microscopy. Two graft ruptures were repaired and one of these grafts has had good long-term function 22 months later. These observations suggest that if bleeding at the site of graft rupture can be securely controlled and if the conditions of the patient and of the graft are favorable except for the rupture, it may be possible to save more than one of eight grafts.

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During a 16-month period (January 1976 to April 1977) when 93 renal transplants were performed at the University of Colorado Medical Center, Denver, and the Denver Veterans Administration Hospital, there were nine acute graft ruptures (9.6%). One of these ruptures was caused by renal vein thrombosis that was not discovered until after the graft was removed on the seventh day after transplantation. In the other eight cases, there was evidence of varying degrees of rejection when examined by microscopy. These eight cases were analyzed with respect to the question of whether the acutely ruptured graft should be removed or whether it should be left in the patient if bleeding can be controlled at the time of exploratory operation.

MATERIALS AND METHODS

All eight cases of graft rupture associated with rejection occurred in recipients of kidneys from cadavers. The patients' ages were 17 to 58 years. In five cases, the ruptured graft was the first transplant; in one case, it was the second; in two cases, the graft was the fourth transplant. None of the 25 patients who received grafts from relatives during this period of time are known to have had a graft rupture, although this could have happened in occult form.

The number of mismatched human leukocyte antigens were three in seven cases and two in the eighth case. None of the eight patients had had detectable levels of preformed antibodies against a panel of lymphocyte donors before transplantation.

Preservation times were six to 25 hours. Renal preservation by pulsatile perfusion with cryoprecipitated plasma was performed in four cases and by cold storage after perfusion with Collins' solution using an intracellular electrolyte solution without the addition of procaine hydrochloride in the other four cases.

The techniques of transplantation into the iliac fossa that were used have been previously described,[1] except for those used in one patient in whom the graft was placed in the right upper quadrant with anastomoses to aorta and portal vein. Graft capsulotomy was not performed at the time of transplantation.

All patients received azathioprine and prednisone for immunosuppression, as previously described.[2] All of the five recipients of primary transplants received antilymphocyte globulin/antithymocyte globulin for periods of up to four weeks postoperatively; none of the patients who underwent retransplantation received this agent.

Five of these eight grafts made more than 50 mL/hr of urine after transplantation, before reexploratory surgery was performed for rupture; the other three grafts (cases 5, 6, and 7, Table) produced little or no urine between the times of transplantation and of rupture. During the six to 12 hours prior to exploratory operation for rupture, the renal function was poor in all cases except case 4. Four patients were dialyzed before exploratory operation was performed. The diagnosis of ruptured allograft was strongly suspected in all cases because of the explosive onset of pain, tenderness, and swelling. All patients were taken to the operating room as quickly as possible.

The ruptures occurred one to 18 days after transplantation; in seven cases, it was within seven days after transplantation. In three cases, the ruptures were along the convex border of the kidney; in the other five cases, the sites of rupture varied.

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Clinical Courses of Eight Patients With Ruptured Renal Allografts

Case	Transplant No.	Operation	Course	Outcome
1	1	Graft nephrectomy	Retransplant	Functioning retransplant
2	1	Graft nephrectomy	Dialysis	Awaiting retransplant
3	4	Graft nephrectomy	Dialysis	Awaiting retransplant
4	1	Rupture repaired	Urinary leak	Functioning transplant
5	4	Rupture repaired	Wound infection	Graft nephrectomy; death
6	1	Graft nephrectomy	Retransplant	Functioning retransplant
7	1	Graft nephrectomy	Retransplant	Sepsis; death
8	2	Graft nephrectomy	Dialysis	Awaiting retransplant

RESULTS

Clinical

In six of the eight cases, the transplanted kidneys were removed at the time of reexploratory surgery for graft rupture; in two cases (4 and 5), the ruptures were repaired with electrocautery and interrupted sutures (Table). One of the six patients whose graft was removed had a kidney retransplanted seven days later and died ten weeks after retransplantation because of sepsis (case 7); the other five patients have survived and two of the five have had successful retransplantations.

One of the two repairs of rupture was complicated by urinary leakage caused by distal ureteral necrosis, and ureteroureterostomy was necessary; this graft has had normal function 1¾ years after transplantation (case 4). In this case, the graft rupture was on the posterior surface of the kidney; at the time of the exploratory operation, there did not seem to be enough pressure in the renal pelvis to ascribe the graft rupture to hydronephrosis associated with distal ureteral necrosis. The other graft that was repaired functioned for approximately six months, but required large amounts of prednisone for recurrent rejections; a persistent wound infection necessitated prolonged hospitalization (case 5). This graft was removed six months after transplantation and the patient was returned to dialysis; he died 12 months after transplantation because of uncertain causes, but he had previously expressed suicidal thoughts and his death was probably a veiled suicide.

Isotope renography was performed in six patients prior to suspecting graft rupture because of poor graft function; in these six cases, the interval between performance of the isotope renogram and exploratory surgery for rupture was one half to three days. These renograms were interpreted as showing acute tubular necrosis or rejection; no renogram was considered suggestive of graft rupture.

At the time of exploratory surgery for graft rupture, the kidneys were usually pink, with small patchy areas of blue parenchyma in some cases. These grafts did not appear to be totally infarcted and they did not manifest the speckled appearance characteristic of end-stage rejection that has been allowed to develop fully. In some cases, there was active hemorrhage from the site of rupture.

Pathology

All of the eight ruptured grafts were tensely edematous at the time of exploratory surgery for rupture. The amount of hemorrhage associated with the rupture varied from approximately 200 to 1,000 mL.

Light microscopy and immunohistology were performed in all cases. A biopsy of one of the two kidneys not removed at the time of rupture was done at the time of rupture (case 4), and the other kidney was not examined microscopically until it was removed six months after rupture (case 5). The findings of microscopic examination in the eight cases are as follows: interstitial edema, 3 cases; focal mononuclear cell infiltration, 5 cases; slight glomerular hypercellularity, 5 cases; arterial narrowing by intimal thickening, 1 case; infarction/cortical necrosis, 3 cases; immunoglobulin with or without complement (Ig ± C) in capillary walls, 2 cases; Ig ± C in mesangium, 3 cases; Ig ± C in arteriolar walls, 3 cases.

Only one of the eight cases had histologic signs of advanced rejection (case 3); in six other cases, histologic signs were of mild to moderate rejection. The rejection was predominantly cellular in four cases, humoral in two, and mixed in one. The eighth kidney, which was examined six months after repair of the rupture (case 5), showed no evidence of rejection.

COMMENT

The first reported case of graft rupture was after the second cadaveric transplantation performed at the University of Colorado.[1] The patient had fallen out of bed several days earlier and an etiologic role of this minor trauma was suspected. The removed kidney had histopathologic evidence of cellular rejection similar to those of some of the specimens in the present report.

In 1968, Murray et al[3] reported four ruptures in 110 kidney transplants performed between 1962 and 1968; three of the four occurred in grafts from relatives. The incidence of graft rupture has varied from 0.4%[4] to 8.4%[5] in other series, and rupture generally has been found to happen less frequently in grafts from relatives than in grafts from cadavers, as illustrated by our own experience. Graft rupture may in fact be undetected in some patients and the frequency of rupture is probably higher than is generally recognized. One of the ruptures described by Salaman et al[6] was found incidentally at the time the operation was performed because of continuing anuria on the 22nd day after transplantation.

All ruptures in this series occurred within 18 days of transplantation. This has been the experience of several other authors,[4,7-11] although delayed rupture has been documented by Haberal et al,[12] Lord et al,[13] and Homan et al.[14]

The mechanism of graft rupture is not well understood. Although rupture has been associated with renal vein thrombosis,[15] in our eight patients renal vein thrombosis was not observed. The histopathology observed in our eight cases does differ from the findings in the majority of cases whose unruptured kidneys were removed because of rejection, in that the obliterative vascular changes usually found in the unruptured rejected kidneys are present in only one of our eight cases. The pathology found in our eight cases was not importantly different from the findings of Matas et al in five ruptured kidneys.[16] Focal areas of necrosis, which might be expected to predispose a kidney to rupture, were found in only three of our eight cases. Histologic signs of acute tubular necrosis or ischemic cortical damage were not prominent. The reason for the ruptures of some kidneys is not apparent; the only common factor seems to be a swollen graft.

Four patients had undergone hemodialysis after transplantation but before reexploration was performed for graft rupture. In one of these four patients, severe pain at the graft site and hypotension during hemodialysis devel-

oped; in this patient (case 7), the heparin needed for hemodialysis may have contributed to the volume of the hemorrhage associated with the graft rupture and perhaps to the actual rupture itself. Rupture of the nontransplanted kidney has been described as a complication of anticoagulation.[17,18]

The finding of graft ruptures exclusively in grafts from cadavers in our series and predominantly in grafts from cadavers in other series, except the one of Murray et al,[3] suggests that immunological factors are important in the pathogenesis of rupture. However, none of our patients had detectable preformed antibodies against a panel of lymphocyte donors who represented a broad range of histocompatibility antigens, and the results of microscopic pathologic examination did not suggest violent humoral or cellular rejection.

The site of rupture was the convex border of the kidney in three of eight cases in our experience, but in 18 of 19 cases in the report by Lord et al.[4] They offered a mathematical explanation for this site predilection, having to do with the greatest amount of tension being at the site of greatest curvature; however, this explanation does not fit well with the varied sites of rupture observed in our eight cases.

The method of cadaver kidney preservation did not seem to influence rupture, in that half of all the ruptured kidneys had been preserved by pulsatile perfusion with cryoprecipitated plasma and half had been stored in cold intracellular electrolyte solution. However, the fact that all of the ruptures occurred in kidneys that had been preserved (as compared with grafts from relatives, which were transferred directly from the living donor to the recipient) could indicate that cold preservation, with or without perfusion, predisposes to rupture, although this does not seem likely.

The relatively mild degree of rejection observed at the time of exploratory surgery for rupture, and later through microscopy, suggests that many of these grafts might be capable of functional recovery if not removed at the time of rupture. However, the mild degree of visible rejection may simply reflect a lack of time for the more recognizable hallmarks of severe rejection to develop. The poor chronic performance of ruptured grafts that were not removed in the series of Matas et al[16] and Homan et al[14] suggests that graft rupture does in fact imply an unfavorable prognosis for long-term graft function. The fact that 75% of all the ruptured kidneys in our series were removed reflected, in part at least, a conviction that this was the preferred treatment.

The treatment of the ruptured kidney hinges on whether or not to remove the kidney. Kootstra et al[9] recommended that if renal function has shown signs of improvement prior to rupture, if the appearance of the kidney is otherwise satisfactory, and if hemostasis can be achieved, it may be possible to save the kidney. However, indifferent renal function may ultimately be achieved[14,16] and deaths from continued hemorrhage and infection caused by an attempt to save the kidney have been documented.[4,8,10] Minale et al[10] described six cases that were repaired with recovery of function but in whom there were two subsequent deaths due to hepatic coma and *Pseudomonas* septicemia.

If acute kidney rupture is suspected clinically in the early posttransplantation period, we believe that the graft should be explored as soon as possible for control of hemorrhage. Although there has been long-term graft function in only one of the two patients in our series in whom the graft was left in place after rupture, this 50% graft survival rate is not greatly different from the long-term graft survival rate in transplants from cadavers that have not ruptured. This uncontrolled observation, combined with the finding of rather little evidence of rejection from microscopy in the six grafts removed immediately after rupture, suggests that the ruptured graft should not be removed if bleeding from the site of rupture can be securely controlled, if the gross appearance of the graft is not characteristic of end-stage irreversible rejection, if the patient's general condition warrants continued immunosuppression, and particularly if the graft has made urine until the time of rupture.

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Nonproprietary Name and Trademark of Drug

Azathioprine—*Imuran.*

References

1. Starzl TE: *Experience in Renal Transplantation.* Philadelphia, WB Saunders Co, 1964.
2. Weil R III, Schröter GPJ, West JC, et al: A 14-year experience with kidney transplantation. *World J Surg* 1:145-156, 1977.
3. Murray JE, Wilson RE, Tilney NL, et al: Five years' experience in renal transplantation with immunosuppressive drugs: Survival, function, complications and the role of lymphocyte depletion by thoracic duct fistula. *Ann Surg* 168:416-435, 1968.
4. Lord RSA, Effeney DJ, Hayes JM, et al: Renal allograft rupture: Cause, clinical features and management. *Ann Surg* 177:268-272, 1973.
5. Ghose MK, Kest LM, Cohen SM, et al: Spontaneous rupture of renal allografts. *J Urol* 109:790-794, 1973.
6. Salaman JR, Calne RY, Pena J, et al: Surgical aspects of clinical renal transplantation. *Br J Surg* 56:413-417, 1969.
7. Flanigan WJ, Caldwell FT, Williams GD, et al: Clinical patterns of renal allograft rejection. *Ann Surg* 173:733-747, 1971.
8. Haimov M, Glabman S, Burrows L: Spontaneous rupture of the allografted kidney. *Arch Surg* 103:510-512, 1971.
9. Kootstra G, Meiger S, Elema JD: Spontaneous rupture of homografted kidneys. *Arch Surg* 108:107-112, 1974.
10. Minale C, Linder E, Largiader F: Spontanrupture von Nierentransplantaten. *Dtsch Med Wochenschr* 97:459-461, 1972.
11. Siedeck M: Beobachtungen bei Rejektion von Nierentransplantaten. *Langenbecks Arch Chir* 325:714-719, 1969.
12. Haberal M, Picache RS, Husberg BS, et al: Late spontaneous rupture in a homografted kidney. *Arch Surg* 109:824-826, 1974.
13. Lord RSA, Belzer FO, Kountz SL: Delayed spontaneous rupture of the allografted kidney. *Arch Surg* 100:607-610, 1970.
14. Homan WP, Cheigh JS, Kim SJ, et al: Renal allograft fracture: Clinicopathological study of 21 cases. *Ann Surg* 186:700-703, 1977.
15. Goldman MH, Leapman SB, Handy RD, et al: Renal allograft rupture with ileofemoral thrombophlebitis. *Arch Surg* 113:204, 1978.
16. Matas AJ, Scheinman JI, Pattazzi LC, et al: Immunopathological studies of the ruptured human renal allograft. *Transplantation* 22:420-426, 1976.
17. Hibner RW: Spontaneous rupture of the kidney with massive hemorrhage: A complication of anticoagulation. *Am J Surg* 118:637-640, 1969.
18. Luna I, Leadbetter RL, Gilbert DR: Spontaneous rupture of the kidney: A complication of anticoagulation: Report of two cases. *J Urol* 109:788-789, 1973.

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