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ORIGINAL ARTICLE

Clinical outcome of cadaveric renal allografts contaminated before transplantation

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Summary

This analysis was performed to define the incidence of pretransplant microbial contamination of donor kidneys, and to assess the resultant morbidity including infections requiring therapy, and graft loss. Case records of all 638 renal allograft recipients patients transplanted in our centre during the period June 1990 to October 2000 were studied. All the recipients were given a single dose of intravenous antibiotics at the time of induction of anaesthesia. A total of 775 microbiology reports on perfusion fluid, kidney swabs and ureteric tissue were retrieved. Fifty-eight of 638 (9.1%) patients were transplanted with a graft that showed preoperative contamination. 18 of these 58 patients (31%) subsequently required antibiotic treatment. Thirty of 32 patients who received kidney contaminated with skin flora had a benign course (i.e. no unexplained, no positive blood cultures or graft infection). By contrast, seven of nine recipients with grafts whose perfusion fluid yielded lactose fermenting coliforms (LFCs) required antibiotics and three of nine of them suffered graft loss as a result. Two of these patients had bacteraemia caused by LFC, and one died. Three of five patients with positive cultures due to yeast required treatment with antifungals. None of the four patients who had graft contaminated by *Staphylococcus aureus* became infected. One-year 49/58 (85%) of these patients survived with functioning graft. Overall 1-year patient survival was 53/55 (92%). These data suggest that contamination of renal allografts by LFCs or yeasts need to be treated preemptively before the onset of clinical manifestations. By contrast, contamination with skin contaminants does not pose a risk to the graft.

Introduction

Contamination of allografts [1] is an important preventable cause of post-transplantation infective complications which may happen either during explantation or packing. The potential consequences in these immunosuppressed range from wound infection to graft-threatening and even life-threatening complications such as septicaemia, pyelonephritis and primary nonfunction [1–6]. There is a great deal of variation with regard to the approach towards pretransplantation microbial contamination. On the basis of review of literature, it is unclear whether to follow the policy of prophylactic antibiotics or opt for preemptive antibiotics. Small number and lack of long-term follow-up is a major limitation of published series of contamination of renal allografts. In our unit we follow the policy of single dose of prophylactic antibiotics and opt for therapy if there is a clinical indication. This analysis was carried out to define the frequency of pretransplant microbial contamination, its likelihood of developing into infection requiring therapy and the eventual outcome.

Patients and Methods

Case records of 638 renal allograft recipients patients transplanted at our centre in between 1990 and 2000 were

analysed retrospectively. A total of 775 microbiology reports of perfusion fluid, kidney swabs and ureteric tissue were retrieved for each recipient from computerized data base, case files and data base in microbiology department.

Our policy has been to provide single dose intravenous antibiotics prophylaxis (mostly Co-amoxyclav) at the time of induction of anaesthesia. Cyclosporine monotherapy was the primary mode of immunosuppression with intention to treat. Oral prednisolone, azathioprine (mycophenolate mefotil since 1996) are added later for recurrent/severe rejection. Conversion from cyclosporine to tacrolimus-based immunosuppression was carried out for cyclosporine failure or toxicity. Acute rejection episodes were treated with methyl prednisolone (0.5–1 g, intravenously, for 3 days). None of the recipients who received a contaminated graft had required anti-Thymocyte Globulin (Merieux) which is used in this unit, though infrequently, for the treatment of steroid-resistant rejection.

Swabs from perfusion fluid for culture and sensitivity were sent as a routine at the time of 'bench' dissection of the renal graft before transplantation. Postoperative cultures were taken from wound discharge, drain fluid, blood, urethral catheter and midstream urine. Appropriate antibiotics were commenced according to the microbiological sensitivity of the organism isolated from perfusion fluid, only if there was a clinical indication for treatment, such as unexplained fever or leucocytosis or graft dysfunction associated with polymorphonuclear infiltrates on histopathology. The patients were classed as having a benign course if they had the following features: (i) absence of bacteraemia, (ii) lack of graft dysfunction or pyelonephritis, (iii) positive culture, other than blood culture, from one source at one time only, and (iv) positive urinary or wound cultures without fever. An infection was classed as related to perfusion fluid contamination if the microbial agent isolated within 2 weeks following transplantation has been same as in the perfusion fluid. Data of only those patients who had 1 year follow-up was included.

Results

Of 638 patients, 58 received a renal graft with evidence of preoperative contamination in the form of one or more positive culture from the allograft. Eighteen of 58 (31%) patients had received treatment with antibiotics on the basis of clinical indications.

The organism cultured and the subsequent outcome is shown in Table 1. Thirty-four of 58 (58.6%) had contamination with from skin flora, and thirty of 32 (94.1%) had benign course. The most common skin contaminants were coagulase negative staphylococci and these were associated with benign course in 21/22 (95.4%) of patients. Clinical course of grafts with other skin contaminants including *S. aureus* ($n = 4$), α-haemolytic streptococci ($n = 2$) and diptheroids ($n = 1$) were associated with benign course. Only one patient with mixed skin flora ($n = 5$) as skin contaminant needed treatment.

By contrast, seven of nine recipients (of 58) with positive culture of perfusion fluid because of lactose fermenting coliforms (LFCs) required antibiotics and three of them (33%) suffered graft loss. Two of these patients had bacteraemia as a result of LFC, and one of them died.

Table 1. Clinical and microbiological findings on 58 patients within 4 weeks of receipt of contaminated renal allograft.

Bacteria	Benign course	Need for antibiotics	Drain fluid C/S	MSU C/S	Blood C/S	CSU C/S	PN	Cultures positive from >1 sites	Graft loss
Skin contaminants									
Staphylococcus aureus, α-haemolytic streptococci, diptheroids ($n = 7$)	7	0	0	0	0	0	0	–	0
Coagulase negative staphylococci ($n = 22$)	21	1	4	1	0	1	1	1	0
Mixed skin flora ($n = 5$)	4	1	1	0	1	0	0	–	0
Contaminants of bowel origin									
Enterococci ($n = 3$)	0	3	2	1	0	0	0	–	0
Anaerobe ($n = 2$)	0	2	1	1	0	0	0	1	0
Gram negative rods									
LFCs ($n = 9$)	2	7	4	3	2	2	3	3	3
Pseudomonas ($n = 5$)	4	1	0	0	0	1	0	–	0
Fungal									
Yeast ($n = 5$)	2	3	1	1	0	1	0	–	0

LFCs, lactose fermenting coliforms; MSU, Midstream urine; CSU, catheter specimen of urine; PN, pyelonephritis as seen on histopathology of graft; postop., postoperative C/S culture and sensitivity.

Benign course if in the postoperative course: (i) absence of bacteraemia, (ii) lack of graft dysfunction or PN, (iii) positive culture, other than blood culture, from one source at one time only, and (iv) positive urinary or wound cultures without fever.

Five of 58 (8.6%) patients had positive cultures because of yeast. Three of them required antifungal therapy.

Forty-nine of these patients (85%) survived with functioning graft. One-year patient survival was 53/58 (92%). Excluding the patients who had perfusion fluid contamination because of LFCs, the graft survival figure and patient survival at 1 year was 40/45 (88.9%) and 43/45 (95.6%) respectively.

Discussion

In this study, 58/638 (9.1%) renal transplant recipients received contaminated kidney. Previous studies have reported contamination of perfusion fluid to vary from 4.2 to 28% [1–7], refer to Table 2. A number of dissimilarities in methodology, therapeutic approach to the problem of contamination, and timing of treatment make them difficult to interpret in defining a policy (and therefore, for the sake of clarity, the data of only four of these has been included in Table 2). However one feature of the meta-analysis of 1264 renal graft recipients is that skin contaminants (including *S. aureus*) constitute 136/203 (67%) of all contamination of renal grafts and do not pose a significant risk, irrespective of antibiotics policy. Hayry *et al.* [3] suggested that most patients had no clinical sequelae following perfusion fluid contamination and attributed this to the small size of inoculum which was effectively overcome by prophylactic antibiotics. The lack of serious sequelae has also been reported in a study of 114 allografts by Buchholz *et al.* [6]. Higher incidence of positive cultures of perfusion fluid, in this study, is a reflection of a proactive approach in isolating organism which helped isolate many microbes in otherwise lower numbers.

The nature of the organism isolated is important as this analysis shows. Indeed the association of LFC in perfusion fluid with the graft loss has been reported from our unit [4]. Gram-negative organisms ($n = 5$) cultured in perfusion fluid have been reported to be associated with death and graft loss (one and two respectively) in an analysis of 81 allografts by McCoy *et al.* [5]. Majeski *et al.* [7] reported contamination rate of 4.2% (29/514), and suggested that prophylactic antibiotics are seldom required. They suggested discarding grafts if there was evidence of *Escherichia coli* or high number of bacteria on Gram staining.

Contamination of kidneys by Gram positive organism is not thought to be a contraindication for transplantation, as supported by our study [3–7]. Bijnen *et al.* [2] observed graft contamination rate of 24% (83/350). Among them two of five patients with graft contamination by *S. aureus* lost graft and therefore suggested pre-

Table 2. Contaminated cadaveric organs contaminated before transplantation: a review of literature.

Reference: contaminated graft/patients studied	Skin contaminants (benign course/ graft loss/ septicaemia)	Yeasts (benign course/graft loss/total)	Pseudomonas (benign course/graft loss/total)	*Escherichia coli* (benign course/ graft loss/total)	Anaerobes (benign course/graft loss/total)	Other bacteria (benign course/graft loss/total)	Suggested antibiotics policy
McCoy *et al.* [5]: 14/81 (17.3%)	10/0/10	2/0/2	1/2/3 one death	0/0/1	–	0/0/1	Prophylactic: ? Preemptive: for Gram negative and enterococci for 3 days. Therapeutic: only if clinically indicated
Anderson *et al.* [8]: 19/83 (23%)	6/0/6	1/0/2	–	3/0/3	3/0/3	5/0/5	Prophylactic antibiotics in 35/83 patients. Discard graft if multiple or heavy contamination.
Hayry *et al.* [3]: 17/91 (19%)	6/0/6	–	2/0/2	3/0/4	2/0/2	4/0/4	Prophylactic: penicillin for 4 days. Preemptive: for all positive cultures
Buchholz *et al.* [6]: 41/145 (28%)	41/0/41	–	1/0/1	3/0/3	–	–	12-h rapid culture of perfusion fluid pretransplantation preemptive for positive cultures

P.S., skin contaminants include were coagulase negative staphylococci, *S. aureus*, α-haemolytic streptococci, mixed skin flora and dipheroids; preemptive, treatment on getting evidence of contamination but before clinical manifestation.
Benign course if in the postoperative course: (i) absence of bacteraemia, (ii) lack of graft dysfunction or PN, (iii) positive culture, other than blood culture, from one source at one time only, and (iv) positive urinary or wound cultures without fever.

emptive antibiotics (commencing a therapy on identification of culture but before the onset of clinical infection) for *S. aureus* [2]. However, we observed that *S. aureus* does not pose additional risk.

As suggested by Anderson *et al.* [8], we too recommend preemptive treatment if candida is detected in perfusion fluid.

The infection related to contaminated graft may not be clinically obvious in early post-transplant period partly because of immunosuppression (which is at its peak in early post-transplant period). Contamination of renal allografts by LFCs or yeast needs prompt, preemptive and aggressive treatment for about 1 week after first negative culture. On the contrary, the contamination by skin contaminants does not pose a risk as prophylactic single dose of antibiotics, a routine policy in our unit, is enough. We do not support discarding of contaminated graft unless the donor has a urinary tract sepsis because of LFCs. Gram staining as suggested by some authors would not be able to characterize Gram negative rods as LFCs, and therefore has its own limitation as formal culture report would not be available before transplantation. We would like to emphasize that the cultures from perfusion fluid are performed routinely and the report is actively chased to help in subsequent management.

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