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DIALYSIS + TRANSPLANTATION

Kidney/Bone Marrow Transplantation

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Within the past few years, a new conceptual view of transplantation has emerged, based on the observation that renal transplant recipients with extremely long (27 - 29 years) graft survival have all had evidence of donor cells in their peripheral blood, skin, and lymph nodes.¹ They were thus chimeric. This led to the theory that chimerism is necessary for successful long term engraftment.²⁻⁴ It also led to the next logical step of attempting to augment chimerism by transplanting donor bone marrow at the time of organ transplantation. Early reports of combined organ/bone marrow transplantation have suggested that it is safe and is associated with reasonable outcomes.⁵⁻⁸ In this paper, we discuss the outcome in the first 30 patients undergoing combined kidney/bone marrow transplantation.

MATERIALS AND METHODS

Between December 13, 1992 and September 30, 1994, 30 patients underwent combined kidney/bone marrow transplantation. Nineteen patients undergoing kidney transplantation alone (usually a function of lack of availability of donor bone marrow because of the refusal of the donor family to consent to vertebral body recovery) were studied as controls. Six kidney/bone marrow recipients also received pancreatic islets, and four received pancreases. All but one were undergoing their first transplant. Two of the control patients also received pancreases, and all were undergoing their first transplant. One patient in each group was sensitized, with a panel reactive antibody level over 40%. Mean recipient and donor ages, ischemia time, and quality of HLA matches and mismatches are listed in Table 1.

Bone marrow was isolated from donor vertebral bodies and was infused intravenously at a dose of $3-5 \times 10^8$ unmodified cells/kg at the conclusion of the

transplant procedure.

Immunosuppression was with tacrolimus and steroids; pancreas recipients and occasional control patients also received azathioprine. Radiation, cytoreduction, or induction antilymphocyte therapy was not given to any patient.

Blood was drawn pre- and post-transplantation for various chimerism studies including flow cytometry polymerase chain reaction (PCR), and fluorescent insitu hybridization (FISH), for Y-chromosome analysis in female recipients of kidneys from male donors, and for immunologic studies primarily mixed lymphocyte reaction (MLR).

RESULTS (Table 2)

The mean follow-up for the kidney/bone marrow patients is 8.0 ± 6.4 months. 28 (93%) have functioning kidneys, with a mean serum creatinine of 1.8 ± 0.6 mg/dl and a BUN of 30 ± 9 mg/dl.

The mean follow-up for the control patients is 6.9 ± 3.7 months. 18 (95%) are alive, and 17 (89%) have functioning kidneys, with a mean serum creatinine of 2.3 ± 1.3 mg/dl and a BUN of 35 ± 14 mg/dl.

There were no differences between the 2 groups in the incidence of delayed graft function (17% in the kidney/bone marrow group and 16% in the control group), rejection (73% vs. 58%), need for OKT3 or ATG (13% vs. 11%), or CMV (13% vs. 16%). Graft vs. host disease was not seen in any patients. 21% of the kidney bone marrow and 22% of the control patients have been weaned off steroids.

Chimerism was studied in the first 10 kidney/bone marrow and 8 control patients. Of 9 evaluable kidney/bone marrow patients, chimerism was seen in all, by flow cytometry, PCR, and/or FISH. Of 5 evaluable control patients, 3 (60%) had evidence of

chimerism by PCR and/or FISH.

Evidence of decreasing donor specific responsiveness was seen in 2 of 9 (22% kidney/bone marrow and 1 of 6 (17%) control patients. In 2 patients, rejection was associated with an increase in donor specific responsiveness, but this was not always seen.

DISCUSSION

There have been several goals of our ongoing programs of bone marrow augmentation. The first has been to establish the safety of combined kidney (or other solid organ)/bone marrow transplantation, in terms of both short term patient and graft survival and function, and the absence of graft vs. host disease. Thus far, this goal seems to have been accomplished.⁵⁻⁸ The second has been to augment chimerism in the recipient, and, at least in the short term, this also seems to have been achieved. The remaining goals, of improving long term patient and graft survival, assessing the long term durability of chimerism and the development of donor specific hyporesponsiveness, and perhaps even withdrawal of chronic immunosuppression, will require many more years of follow-up. For now, we can say that combined kidney/bone marrow transplantation is straightforward, safe, is associated with reasonable patient and graft survival and augmentation of chimerism, and is associated with no evidence of graft vs. host disease.

TABLE 1**RECIPIENT AND DONOR CHARACTERISTICS**

N	Kidney/Bone Marrow	Control
Mean Recipient Age (Years)	38.7 ± 11.2	47.7 ± 12.0
Mean Donor Age (Years)	29.3 ± 14.8	41.1 ± 18.3
Cold Ischemia Time (Hours)	23.3 ± 9.5	28.1 ± 6.0
HLA Matches	2.4 ± 1.3	2.5 ± 1.3
Mismatches	3.4 ± 1.6	3.4 ± 1.4

TABLE 2**RESULTS**

MEAN FOLLOW-UP - 8.0 ± 6.4 MONTHS

	Kidney/Bone Marrow	Control
Patient Survival	100%	95%
Graft Survival	93%	89%
Serum Creatinine (mg/dl)	1.8 ± 0.6	2.3 ± 1.3
BUN (mg/dl)	30 ± 9	35 ± 14

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