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Kidney Transplantation With Bone Marrow Augmentation: Five-Year Outcomes

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Bone marrow augmentation in renal transplant recipients has been performed in a small number of centers, in an attempt to augment chimerism and/or provide donor-specific immunomodulation.[1–14] In this report, we present our experience with bone marrow augmentation in renal transplantation over the past 7 years.

PATIENT AND METHODS

Between December 14, 1992, and January 1, 2000, 124 kidney/bone marrow transplants were performed. There were 51 (41%) cadaveric kidney, 59 (48%) kidney/pancreas, 8 (6%) kidney/islet, and 6 (5%) living-related kidney recipients. The mean recipient age was 40.4 ± 10.5 years. The dosage of unmodified bone marrow was 3 to 5 × 10^8 cells/kg, given either as a single infusion (n = 86; 69%), or as multiple infusions (n = 38, 31%).[15] The mean donor age was 33.0 ± 15.5 years, and the mean cold ischemia time was 17.8 ± 9.6 hours. The mean number of HLA matches and mismatches was 1.9 ± 1.3 and 3.8 ± 1.3, respectively. Eighty patients who could have undergone kidney/bone marrow transplantation but did not because of lack of bone marrow availability were studied as controls. There were 45 (56%) cadaveric kidney, 32 (40%) kidney/pancreas, 2 (3%) kidney/islet, and 1 (1%) living-related kidney recipients in the control group. This was not a randomized trial; the availability of donor bone marrow was sporadic, and the total case material accounted for only about 10% of the transplants performed during this time period. The mean recipient age was 43.8 ± 10.8 years. The mean donor age was 36.7 ± 17.3 years, and the mean cold ischemia time was 21.9 ± 10.0 hours. The mean number of HLA matches and mismatches was 2.2 ± 1.5 and 3.5 ± 1.6, respectively.

Immunosuppression was with tacrolimus-based immunosuppression, as previously described.[6,16] Antibody induction was not given, nor was radiation or cytoreduction therapy.

The bone marrow and control protocols were submitted to and approved by the Institutional Review Board of the University of Pittsburgh.

RESULTS

The mean follow up was 36.4 ± 23.2 months. In the K/BM group, the 1- and 5-year actuarial patient survival was 98% and 85%, and the 1- and 5-year actuarial graft survival was 97% and 76%. In the control group, the 1- and 5-year actuarial patient survival was 97% and 85%, and the 1- and 5-year actuarial graft survival was 93% arid 71 % (P = NS).

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The mean serum creatinine in the K/BM group was 1.6 ± .6 mg/dL; in the control group, it was 1.6 ± 1.0 mg/dL.

The incidences of rejection and steroid-resistant rejection in the K/BM group were 60% and 6%; in the control group, they were 69% and 10%, respectively. An analysis of the incidence of chronic allograft nephropathy suggested a relative risk of .71 in the K/BM group relative to the control group, with a 95% confidence interval of 0.46 to 1.09. Although this difference did not achieve statistical significance, it appeared to be progressive over time.

The incidence of symptomatic cytomegalovirus was 17% in the K/BM group and 18% in the control group. The incidence of posttransplant lymphoproliferative disorders (PTLD) was 3% in the bone marrow group and 0% in the control group (P = NS). The initial and final incidences of posttransplant diabetes mellitus were 21% and 11% in the bone marrow group, and 22% and 11% in the control group.

Of patients who had kept their renal allografts for 1 year or more, 65% of K/BM patients and 61% of the control patients were withdrawn from steroids.

Chimerism, by PCR, was seen in 92% of the K/BM group and 64% of the control group. The incidence of decreasing donor-specific reactivity was 45% in the K/BM group, and 32% in the control group. Graft-versus-host disease was not seen in any patient.

DISCUSSION

This analysis confirms earlier reports suggesting that bone marrow augmentation in renal transplant recipients is associated with reasonable patient and graft survival,[5,6,7,9,10] and extends these findings, with 5-year actuarial patient and graft survival rates of 85% and 76%, respectively. As in previous analyses, no significant improvement was noted in graft survival, when compared with control patients not receiving bone marrow.[6,7,10] However, there is a suggestion that bone marrow augmentation had some immunomodulatory effect, with a trend toward a progressive decrease in the incidence of chronic allograft nephropathy. This observation has also been made by the Miami group.[8,11–13] Also noted was a slight increase in the incidence of PTLD. Although not statistically significant, this observation is still worrisome and suggests that it may be necessary to maintain bone marrow augmented renal transplant recipients on somewhat lower levels of chronic immunosuppression.

In our report on the effect of bone marrow augmentation in the simultaneous pancreas/kidney patients, there appeared to be a more significant effect of bone marrow on reducing pancreatic graft loss to rejection.[17] Perhaps this is related in some way to the possible additional effect of transplantation of mesenteric and periduodenal lymph nodes and other lymphatic tissues in the pancreas-duodenal transplant.

Important questions that remain include the impact of chimerism itself on patient and graft survival, and the impact of multiple bone marrow infusions compared to a single infusion. These analyses remain ongoing.

In conclusion, bone marrow augmentation appears to be associated with reasonable patient and graft survival, routine augmentation of chimerism, some increase in the percentage of patients with decreasing donor-specific reactivity, and a trend toward less chronic allograft nephropathy.

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