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Effect of CMV Serology on Outcome After Clinical Intestinal Transplantation

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OVER the last 5 years, intestinal transplantation has become a feasible therapeutic option for patients with irreversible intestinal failure.[1] Cytomegalovirus (CMV) infection was shown to be the most frequent viral infection in the intestinal transplant recipients and to be related to high mortality and morbidity.[2,3] In this study, we analyzed the effect of CMV serology of donors and recipients on the outcome of patient and graft survival after intestinal transplantation.

MATERIALS AND METHODS

From May 1990 to September 1995, 76 intestinal transplantations were performed in 72 patients (25 isolated intestine [I], 35 intestinal and liver [I/L], and 12 multivisceral [MV]) at our center. There were 31 adults and 41 children, with ages ranging from 6 months to 58 years. Postoperative immunosuppression was with tacrolimus (FK 506), steroids, and in selected cases azathioprine (AZA). Donor and recipient procedures are described elsewhere.[4] Tissue sampling for CMV was performed when it was clinically indicated. Invasive CMV disease was diagnosed by histopathologic findings and/or by isolation of the virus from tissue specimens. Tissue invasion was determined by detection of typical CMV inclusion bodies along with predominant neutrophilic infiltration and/or unequivocal immunoperoxidase staining of the virus. Isolation of the virus was confirmed by either the shell vial technique or by standard culture.

Fifty-three of 72 recipients received ganciclovir prophylaxis (5 mg/kg twice a day for 2 to 3 weeks in children, and for 3 weeks to 3 months in adults) followed by acyclovir for several months. CMV disease was treated either by ganciclovir (5 mg/kg twice a day), foscarnet (60 mg/kg three times a day), CMV immunoglobulin (100 mg/kg every 2 weeks), or a combination of these agents. The effect of donor and recipient CMV serology on patient and graft survival was studied. Chi-square, Kaplan-Meier, and log rank tests were used for statistical analysis. Statistical significance was achieved if the P value was less than 0.05.

RESULTS

Twenty-four (33%) of 72 recipients developed CMV disease after transplantation during a 1-month to 5-year follow-up period. In these 24 patients, CMV disease occurred a total of 52 times; 14 patients developed only one episode and 10 patients developed two to eight episodes of CMV disease. The type of CMV diseases seen were graft enteritis (n = 43), native gastroduodenitis (n = 3), hepatitis (n = 2), pneumonia (n = 3), and retinitis (n = 1). Table 1 shows the frequency of CMV disease and 4 year patient and graft actuarial survival rates, differentiated by the CMV serology of the donor and recipient. Comparing survival based on donor CMV serology showed that patients who received CMV-seropositive intestinal grafts had significantly worse patient and graft survival than patients who received CMV-seronegative grafts ($P = 0.02$). However, recipients' CMV serology did not affect outcome. The four year actuarial patient and graft survival rates of the CMV seronegative recipients were 51 and 41%. The actuarial patient and graft survival of the CMV seropositive recipients were 33% and 29%.

DISCUSSION

CMV disease occurs more frequently after intestinal transplantation than other types of whole organ transplantation. The increased incidence of CMV disease in intestinal transplantation may be related to higher levels of immunosuppression needed to prevent rejection.[2] This study shows

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Table 1.

CMV Serology					Four Year Survival	
Donor	Recipient	n	Median Follow-up	Incidence of CMV Disease	Patient	Graft
Negative	Negative	28	32 mo	0	62%	53%
Negative	Positive	16	34 mo	56%	43%	37%
Positive	Negative	19	19 mo	58%	32%	20%
Positive	Positive	9	17 mo	44%	16%*	15%
Negative		44	32 mo	20%	57%	49%
Positive		28	19 mo	54%	27%**	17%**

*$P < .05$ vs donor negative, recipient negative.
**$P < .05$ versus donor negative.

that patients who receive CMV-positive grafts had significantly higher morbidity and mortality than the patients who received CMV-negative grafts. Although CMV disease was not necessarily a direct cause of the graft failure or patient death, CMV infection itself or management of CMV infection possibly induced subsequent rejection and rejection-related morbidity and mortality.[5] To avoid CMV related mortality, CMV-seropositive grafts should not be used for intestinal transplantation unless the candidate are in dire need of life-saving organ (liver) transplantation.

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