Improved Survival With Cytomegalovirus Infection After Intestinal Transplantation in Children

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Intestinal transplantation (ITx) is now feasible with actuarial patient and graft survivals at 24 months exceeding 74% and 59%, respectively. The occurrence of opportunistic infections such as cytomegalovirus (CMV), however, has significantly hindered further improvement in long term outcome. In this study, we focus upon our experience with CMV after ITx in children and analyze the influence of CMV infections upon postoperative outcome.

Materials and Methods

Patient Population

Between 1990 to 1995, 41 children received 44 ITx under tacrolimus and steroid immunosuppression. Transplants included: isolated small bowel (SB) (n = 10), liver-SB (L-SB) (n = 27), and multivisceral (MV) (n = 7) allografts. There were 19 males and 22 females with ages ranging between 0.5 to 18 years (mean of 4.2 years). The donor and recipient surgical procedures were as previously described. Indications as well as graft surveillance, immunosuppression, and nutritional management have been reported elsewhere. All but the last seven recipients have been followed for 1 to 5 years.

Incidence and outcome of CMV disease (CMVD) were analyzed for all recipients by donor (D)-recipient (R) serologic status (e.g. D-/R-, D+/R-, D-/R+, D+/R+) using previously established criteria.

Prophylaxis and Treatment

Eight patients received prophylaxis with acyclovir (5 mg/kg) twice a day for 2 to 3 weeks, and 31 patients received intravenous ganciclovir (10 mg/kg) in 2 daily doses for the first 2 weeks after transplantation. Three of these were given concomitant immunosuppression, and nutritional management has been reported elsewhere. All but the last seven recipients have been followed for 1 to 5 years.

Incidence of CMV disease (CMVD) was analyzed for all recipients by donor (D)-recipient (R) serologic status (e.g. D-/R-, D+/R-, D-/R+, D+/R+) using previously established criteria.

Results

Fifteen patients were serologically negative pretransplant for CMV and received organs from CMV negative donors (D-/R-); none of these 15 patients developed CMVD. Twenty-six children were positive for donor or recipient or both CMV serologies and were distributed as follows: D+/R- (n = 8), three patients (37.5%) developed CMVD; D+/R+ (n = 9), three patients developed CMVD (33.3%); D-/R+ (n = 9), four patients developed CMVD (44.4%); D-/R- cases was 60%. The overall graft survival (excluding D-/R-) in CMVD versus no CMVD was 70% and 44%, respectively, and 60% in D-/R- subgroup.

CMVD occurred in three out of five patients without ganciclovir prophylaxis compared to seven out of 21 receiving ganciclovir prophylaxis (P = NS by Fisher Exact Test).

Discussion

We have observed important differences in CMV-associated morbidity and mortality in children as compared to adults undergoing ITx at our center. An equal frequency of disease occurred in our groups D+/R-, D+/R+, and D-/R+ pediatric ITx recipients. Also, CMVD was not associated with significant morbidity or increased mortality. This contrasts with adult ITx recipients where D+/R- experienced severe morbidity and increased mortality from CMVD. There was, however, a trend towards more persis-
tent CMVD involving the allograft of D+/R− children. Though these persistent episodes were not always symptomatic, they took up to 7 months to resolve histologically.

Mortality rates in patients with CMVD were not increased. Deaths in patients with a history of CMVD were associated with rejection or PTLD. Successful clinical management of CMVD was accomplished in the 93% of episodes. Because of the concurrence of CMV and intestinal allograft rejection, immunosuppression was maintained at a therapeutic baseline and reduced only in the face of clinical deterioration. Maintaining this baseline did not appear to exacerbate the CMVD.

In summary, CMV negative donors are preferred for CMV seronegative ITx recipients because CMVD is a major contributing factor in morbidity in these children. The use of CMV negative donors eliminated CMVD in these CMV seronegative patients. However, when CMVD did occur, the use of appropriate antiviral and immunosuppressive management made it possible to minimize its importance. CMV-associated mortality and graft loss did not occur in our patients, regardless of D/R CMV serologic status. Consequently, we recommend the use of CMV positive donors for our candidates with end-stage liver disease who require transplantation urgently and in whom a CMV-negative allograft can not be found.

REFERENCES