

## Inclusion of Spleen in Pediatric Multivisceral Transplantation

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### ABSTRACT

Inclusion of the donor spleen may be beneficial for small children who receive multivisceral transplantation (MVT) because asplenia is associated with increased risk of bacterial sepsis. Beginning in 2003, the spleen was transplanted together with multivisceral transplantation in 17 children under daclizumab induction (spleen group). The results were compared to 23 children who received multivisceral transplantation without the spleen (control group) with the same immunosuppression regimen. Median age of 17 patients who received a spleen was 0.80 years (range 0.54–1.66). Platelet counts at 30 and 60 days posttransplant were significantly lower in the spleen group (average values: day 30: 399,000 vs 636,000,  $P = .015$ ; day 60: 413,000 vs 622,000,  $P = .0056$ ). WBC counts at 30 and 60 days posttransplant were also decreased in the spleen group but the difference was not statistically significant. Median rejection-free survival was 205 days in the spleen group and 101 days in the control group ( $P = \text{NS}$ ). Median length of hospital stay was 39 days in the spleen group and 61 days in the control group. With a median follow-up of 398 days (spleen group) and 1232 days (control group), 3 of 17 (17%) in the spleen group developed graft versus host disease (GVHD), whereas 1 of 23 (4.5%) in control group did ( $P = \text{NS}$ ). In one patient in each group, GVHD was fatal. No patient developed posttransplant lymphoproliferative disorder (PTLD) in the spleen group, whereas 4 of 23 (17%) in the control group developed PTLN. One-year patient survival was 84% in the spleen group and 86% in the control group. Recipients of the spleen as part of a multivisceral graft had significantly lower platelet counts. Rejection-free survival may be prolonged, but the risk of GVHD may be increased.

MULTIVISCERAL TRANSPLANTATION has been successfully performed in children with intestinal and liver failure.<sup>1</sup> The results of multivisceral transplantation have dramatically improved in recent years.<sup>2</sup> Traditional procedure for the multivisceral transplantation is to transplant the stomach, pancreas, small intestine, and liver en bloc. The spleen of the recipient is removed during this procedure, leaving recipients in an aplenic state after transplantation. Since the asplenic state is associated with increased incidence of sepsis in children, we recently started to include an allograft spleen as part of the multivisceral graft. In animal models, donor splenic transplantation or splenocyte infusion is known to induce tolerance to the donor antigen.<sup>3–5</sup> No literature is available concerning the effect of human splenic allograft for the tolerogenicity in multivisceral transplantation.

### PATIENTS AND METHODS

Beginning in 2003, the spleen was transplanted together with multivisceral transplantation in 17 children under daclizumab

induction therapy (spleen group). The results were compared to 23 children who received multivisceral transplantation without the spleen (control group) with the same immunosuppression regimen.

### RESULTS

Patient demographics are summarized in Table 1. Median age of the 17 patients who received a spleen was 0.80 years (range 0.54–1.66). They included 10 boys and 7 girls. Their causes of intestinal failure were gastroschisis ( $n = 5$ ), necrotizing enterocolitis ( $n = 3$ ), intestinal atresia ( $n = 3$ ), volvulus ( $n = 2$ ), Hirschsprung's disease ( $n = 2$ ), and megacystis microcolon syndrome ( $n = 2$ ).

Platelet counts at 30 and 60 days posttransplant were significantly lower in the spleen group. Average values on

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**Table 1. Baseline Characteristics**

	Spleen Group	Control Group	P
Number of patients	17	23	
Mean age*	0.92	3.13	.03
Mean weight*	7.75	12.97	.04
Pre-Tx total bilirubin*	15.8	16.4	.40
Pre-Tx albumin*	2.9	3.0	.73
Patient from home	10/17 (58%)	12/23 (52%)	.69
Donor age*	0.62	2.40	.04
Donor weight*	7.31	12.83	.08

\*Mean values.

day 30 were 399,000 vs 636,000 ( $P = .015$ ), and on day 60, 413,000 vs 622,000 ( $P = .0056$ ). WBC counts at 30 and 60 days posttransplant were also decreased in the spleen group but was not significantly. Average values on day 30 were 11480 vs 14020 ( $P = .29$ ), and on day 60 they were 10,110 vs 14,620 ( $P = .055$ ).

Median rejection-free survival was 205 days in the spleen group and 101 days in the control group ( $P = NS$ ). Median length of hospital stay was 39 days in the spleen group and 61 days in the control group. With a median follow-up of 398 days (spleen group) and 1232 days (control group), 3 of 17 (17%) in the spleen group developed GVHD, whereas 1 of 22 (4.5%) in the control group did ( $P = NS$ ). In one patient in each group, GVHD was fatal. No patient developed PTLD in the spleen group, whereas 4 of 23 (17%) in the control group did. One-year patient survival was 84% in the spleen group and 86% in the control group.

## DISCUSSION

The spleen is the largest single secondary lymphoid organ and the most important organ of the reticuloendothelial system. The organ plays a role in both adaptive and innate immune responses. Healthy individuals that have undergone posttraumatic splenectomy have long-term impairment of humoral and cellular immunity.<sup>6</sup> These patients are extremely susceptible to encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B. The polysaccharide capsules of these bacteria elicit a T-cell independent immune response that depends on the function of the spleen's marginal B cells.<sup>7</sup> Splenectomized patients have diminished responses to these antigens.<sup>8</sup> In children less than 5 years of age, the risk of overwhelming postsplenectomy sepsis may be increased 60- to 100-fold compared to children who have not had a splenectomy.<sup>9</sup>

The tolerogenic effect of donor spleen has been reported in animal models.<sup>3-5</sup> It is known that in some rodent strain combinations, allogeneic spleen transplantation induces tolerance for other donor-specific organs. In 1980s, the spleen was transplanted in humans as a composite pancreas-spleen transplant.<sup>10-12</sup> This practice has been abandoned due to increased risk of GVHD.

In our study, the recipients of spleen together with multivisceral transplantation showed a relatively uneventful postoperative course. Increased incidence of GVHD was observed; however, two of three patients who developed GVHD responded to the therapy. GVHD was fatal for one patient in both the spleen group and the control group. Rejection-free survival was relatively long in the spleen group. The difference in freedom from rejection was not statistically significant.

In conclusion, recipients of spleen as part of the multivisceral graft showed significantly lower platelet counts. Rejection-free survival seems to be prolonged, but risk of GVHD seems to be increased.

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