



Published in final edited form as:

Transplant Proc. 1992 June ; 24(3): 1249–1250.

Infectious Complications After Human Small Bowel Transplantation

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A Clinical trial of liver and small bowel transplantation was initiated at the University of Pittsburgh in May 1990. A total of nine patients received either a combined small bowel and liver graft (n = 8) or an isolated small bowel graft (n = 1). We describe the infectious complications found in this group of patients together with their clinical correlation and outcome.

MATERIALS AND METHODS

Details of the clinical features in these nine patients have been summarized by Tzakis et al.¹ There were three adults and six children. All patients had short gut syndrome and were maintained preoperatively exclusively by total parenteral nutrition. All patients had infectious complications, predominantly line sepsis, prior to surgery. One patient was found to have a splenic abscess (*Staphylococcus aureus*) at the time of transplant, and another child was diagnosed with *Pneumocystis carinii* pneumonia at 4 days posttransplantation and was believed to have harbored this infection preoperatively. Eight patients had signs of liver dysfunction which ranged from severe cholestatic injury and jaundice to frank cirrhosis with portal hypertension, coagulopathy, and bleeding.

Eight patients had combined en bloc liver and intestinal transplantation and one had intestinal transplantation alone, the technical details of which have been previously reported.^{2,3} Immunosuppression was with FK 506 and low-dose prednisone. Azathioprine was used for maintenance immunosuppression when there was evidence of renal dysfunction.

Intestinal decontamination was performed on both donor and recipients. Amphotericin B, tobramycin, and polymyxin E were given by nasogastric tube after mechanical preparation with Golytely. Recipients were maintained on a four times daily regimen for a period of 4 to 6 weeks, and also when there was an episode of small bowel rejection. Prophylactic systemic antibiotics (ampicillin and claforan) were given in all recipients for 5 days.

RESULTS

Clinical features and organisms found in this patient population are summarized in Table 1.

Three patients developed five episodes of positive blood cultures with isolation of the same pathogenic organism from the stool at a concentration of greater than 10^9 occurring between

7 to 57 days after transplant with persistent positive blood cultures from 3 to 7 days. The organisms isolated were bacterial (five *Enterococcus*, one *S aureus*, and one *Enterobacter cloacae*) and fungal (one episode with *Candida albicans*). Two patients had episodes involving more than one organism. Only one infection occurred together with histologic evidence of severe acute cellular rejection of the intestinal graft at 58 days posttransplant. One patient developed pseudomembranous enterocolitis due to *Clostridium difficile* at 60 days after transplant. Another patient had a wound infection at 1 week secondary to *Enterococcus*. These infections presented usually with fever and leukocytosis. In the patient who had associated rejection of the intestinal allograft there was an abnormal D-xylose absorption study, otherwise, no evidence of graft dysfunction was obvious.

Five viral infections were found in three patients, occurring from 9 to 217 days after surgery. Two patients had CMV infections that were not severe and presented with fever, malaise, and positive buffy coat for CMV. The transplanted intestine was involved in one child. Adenovirus was found in the intestinal graft of one recipient while recovering from a bout of severe rejection for which he had received supplemental steroids and FK 506. *Herpes stomatitis* was found in one patient. One child had severe meningoencephalitis with primary EBV infection, which was documented by serology and spinal tap. The patient presented with fever, headaches, and photophobia which progressed to coma. It was unclear whether this progression was due to the encephalitis or to a subarchnoid hemorrhage from the spinal tap. There was full upper cerebral function recovery. However, the child remains paraplegic.

There were three fungal infections found in two patients presenting from 4 to 57 days posttransplant. *C albicans* was found in the blood and stool of an adult recipient experiencing severe rejection of the transplanted intestine. This organism was also isolated from the lungs of a child with a right lower lobe infiltrate at 7 days, who later, at 17 days, was found to have *Aspergillus fumigatus* isolated from a bronchoalveolar lavage specimen.

All of these infectious episodes were successfully treated with specific antimicrobial agents. Changes in immunosuppressive therapy involved reducing or stopping steroids and maintaining therapeutic blood levels of FK 506.⁴

One patient whose upper intestinal anastomosis dehisced 8 days postoperatively had management deviations from protocol and irregular immunosuppression as a consequence. This child died after 22 days, possibly as a consequence of graft-versus-host disease (GVHD). This important case is reported in detail elsewhere.

CONCLUSION

There was a high incidence of infectious episodes in this patient population, which included bacterial, fungal, and viral organisms. Translocation of bacteria or fungi occurs in the early postoperative course of small bowel transplantation and can be an early indicator of small intestinal graft rejection. Adequate immunosuppression to prevent graft rejection as well as prophylactic use of antimicrobials, both enteral and parenteral, is effective in protecting against episodes of infection as well as treating documented sepsis. All infections resolved with appropriate antibiotic therapy, maintaining therapeutic levels of FK 506 without steroids.

Acknowledgments

Supported by Research Grants from the Veterans Administration and Project Grant No. DK 29961 from the National Institutes of Health, Bethesda, Maryland.

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Table 1

Infections in Clinical Small Intestinal Transplantation

Patient	Sex	Age (y)	Cause of Short Gut Syndrome	Graft	Organisms		
					Bacteria	Fungus	Virus
1	M	31.1	Gun shot injury of SMA	Small bowel	<i>Enterococcus</i>	<i>Candida</i>	
2	F	2.3	Necrotizing enterocolitis	Small bowel-liver	<i>Enterococcus Staphylococcus aureus</i>		CMV
3	F	26.7	SMA thrombosis	Small bowel	<i>Clostridium difficile</i>		
4	M	4.3	Gastroschisis	Small bowel-liver	<i>Enterococcus Enterobacter</i>		EBV
5	M	2.8	Intestinal atresia	Small bowel-liver	<i>Enterococcus</i>		CMV, adenovirus
6	F	0.6	Intestinal atresia	Small bowel-liver	<i>Enterococcus</i>		
7	F	1.1	Volvulus	Small bowel-liver			
8	F	1.7	Volvulus	Small bowel-liver		<i>Aspergillus Candida</i>	Adenovirus
9	M	22.4	Motor vehicle accident—injury of SMA	Small bowel-liver	<i>S aureus</i>		