1701

Infectious Complications After Small Bowel Transplantation in Adults

S. Kusne, R. Manez, H. Bonet, K. Abu-Elmagd, H. Furukawa, W. Irish, A. Tzakis, S. Todo, and T.E. Starzl

THE USE of FK 506 as an immunosuppressive agent at our institution allowed us to initiate a small bowel transplantation program. In this report, we describe the infectious complications that were encountered in the first 21 adult patients following small bowel transplantation.

METHODS

Patient Population

Between May 1, 1990 and May 1, 1993, 21 adult patients underwent small bowel transplantation at the University of Pittsburgh. Patients were followed prospectively for infectious complications until October 1, 1993 or until death, or for 1 month after the graft was lost. The median follow-up was 415 days (range 51 to 1156 days). The female:male ratio was 10:11, and the mean age was 34 years (range 21 to 58 years). There were ten patients who underwent small bowel transplantation only (SBTx), six also had liver transplantation (SBTx/L), and five had multivisceral transplantation which included SBTx/L with other organs (MV).

Immunosuppression

The patients were given a continuous intravenous (IV) infusion of FK 506 at 0.15 mg/kg per day and later orally at 0.15 mg/kg every 12 hours. Steroid induction included 1 g of methylprednisolone and steroid taper followed by maintenance of 20 mg prednisone. Treatment of acute rejection included methylprednisolone bolus and/or steroid taper. Steroid-resistant rejection was treated with OKT3 monoclonal antibody.[1]

Prophylaxis and Infection Definitions

We used our previous definitions of infections.[2] Antimicrobial prophylaxis included: cefotaxime 4 g/d IV together with ampicillin 4 g/d IV for 3 days; 2 million U/d oral nystatin; amphotericin B IV 10 to 20 mg/d; ganciclovir IV 10 mg/kg per day; and oral trimethoprim/sulfamethoxazole 80 mg and 400 mg every day. All patients were given oral colistin, gentamicin, and nystatin for selective bowel decontamination.

RESULTS

Twenty-one patients after small bowel transplantation were prospectively followed for infectious complications. Actuarial 1-year patient survival was 84% ± 8.0%. The overall mortality was 33.3% (7 of 21), and six of seven (85.7%) deaths were associated with infection. There was a total of 91 infectious episodes (eps), shown in Table 1. Four episodes were mixed, and were caused by bacteria and yeast together. Most of the infectious episodes occurred more than 3 months after transplantation. The percentage of bacterial, viral, and fungal infections occurring more than 3 months after transplantation were 55.5%, 52.6%, and 85.7%, respectively.

All 21 patients had at least one episode of infection during the study period. When infectious episodes were subdivided in major categories, the following percentage of patients infected were observed: 81% (17 of 21) had bacterial infections; 76.2% (16 of 21) had viral infections; and 61.9% (13 of 21) had fungal infections. Although there was no statistical difference, MV transplantation patients had higher numbers of infectious episodes per patient. The median numbers of infectious episodes per patient were: 3.0, 3.5, and 7.0 in the SBTx, SBTx/L, MV subpopulations, respectively.

There were 32 episodes of bacteremias and candidemias in 14 patients, with a median of 2.0 episodes per patient. The secondary sites of infection were: intravascular lines in 59.4% (19 of 32); abdomen in 12.5% (4 of 32); lung in 6.3% (2 of 32); joint in 3.1% (1 of 32); and in 18.8% (6 of 32) a source was not identified. Overall, there were 41

Table 1. All 91 Infectious Episodes that Occurred in 21 Patients After Small Bowel Transplantation

Type of Infection	Number of Episodes
Bacterial (n = 54)	
Line infection	18
Wound infection	6
Abdominal abscess	5
Peritonitis	6
Clostridium difficile colitis	5
Pneumonia	4
Bacteremia of unknown source	5
Others	5
Viral (n = 19)	
Symptomatic CMV	17
Symptomatic EBV	2
Fungal (n = 14)	
Candida esophagitis	7
Sinusitis	2
Peritonitis	2
Coccidioidomycosis	1
Line infection	2
Bacterial/Fungal (n = 4)	

From the Departments of Surgery, Medicine, and Infectious Disease, University of Pittsburgh, Pittsburgh, Pennsylvania.

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

Address reprint requests to Dr Kusne, University of Pittsburgh, Transplantation Institute, 3601 Fifth Avenue, 5C Falk Clinic, Pittsburgh, PA 15213.

0041-1345/94/$3.00/+0

isolates, of which 63.4% (26 of 41) were gram-positive bacteria, 24.4% (10 of 41) were gram-negative bacteria, 2.4% (1 of 41) were anaerobes, and 9.8% (4 of 41) were *Candida* species.

DISCUSSION

In this report, we describe the infectious complications that occurred in 21 consecutive patients who underwent small bowel transplantation. The rate of infection was very high and involved 100% of the population studied. The high rate of infection was most likely caused by relatively high immunosuppression therapy, which was given to treat frequent rejection episodes.[1] The timing of infectious episodes was different from liver transplantation, where most of infections occur within the first 2 months after transplantation, and where the rate of infectious complications is relatively low 3 months after transplantation.[3] Here instead, most infections occurred more than 3 months after transplantation, suggesting that patients were getting higher amounts of immunosuppression therapy.

The most frequent infections were: bacteremias secondary to infected intravascular lines, *Cytomegalovirus enteritis* involving the transplanted bowel, and *Candida esophagitis*. Recurrent CMV infection of the transplanted bowel is a unique problem to this population and is described separately in this issue.[4] Bacteremia was quite common in these patients and originated mostly from an infected central intravascular line or from the abdomen. Nineteen percent of bacteremias had no identified source, although we suspect most originated from the abdomen. It is possible that some of these bacteremias were related to bacterial translocation from the transplanted bowel, though this was difficult to prove. *Candida esophagitis* was the most frequent fungal infection and occurred relatively late after transplantation and often occurred multiple times. This was usually associated with prolonged courses of antibiotic therapy in patients heavily colonized with yeast.

Decrease in infectious complications is crucial in this population because of the high morbidity and high association with mortality. This could be obtained by improvement of antimicrobial prophylaxis on one side, and avoidance of heavy immunosuppression on the other side, possibly by using new therapeutic modalities to control graft rejection.

REFERENCES

1. Abu-Elmagd K, Todo S, Tzakis A, et al: Transplant Proc (this issue)

2. Kusne S, Dummer JS, Singh N, et al: Medicine 67:132, 1988

3. Alessiani M, Kusne S, Martin M, et al: Transplant Proc 23:1501, 1991

4. Manez R, Kusne S, Abu-Elmagd K, et al: Transplant Proc (this issue)