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Infectious Complications After Small Bowel Transplantation in Adults: an Update

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WE have reported our experience with the first 21 adult patients after small bowel transplantation (Tx) on tacrolimus immunosuppression regimen in the Paris meeting.[1] The present report represents an update of the infectious complications that occurred in this patient population.

METHODS

Patient Population

Between May 1990 and February 1995, 29 adult patients underwent small bowel Tx in the Transplantation Institute, University of Pittsburgh. Fifteen patients underwent small bowel transplant (SBTx), 8 had small bowel together with liver transplant (SBTx/L), and 6 patients underwent multi-visceral Tx (MV), which included SBTx/L together with other organs. In 11 patients (8 SBTx, 3 MV) Tx of the bowel included also colonic segment. Patients were prospectively followed for infectious complications using previous definitions of infection.[2]

Immunosuppression

Tacrolimus was given intravenously at 0.1 mg/kg/day and later orally at 0.15 mg/kg every 12 hours. Steroid induction was given with 1 gm methylprednisolone and steroid maintenance with 20 mg prednisone. Acute rejection was treated with a "bolus" or "recycle" of methylprednisolone. Steroid resistant rejection was treated with OKT3 monoclonal antibody.

Prophylaxis

Antimicrobial prophylaxis included intravenous cefotaxime and ampicillin 4 g/d for 3 days, oral nystatin 2 million units a day, intravenous ganciclovir 10/mg/kg/d, oral trimethoprim/sulfamethoxazole 80 mg/400 mg a day, and selective bowel decontamination with colistin, gentamicin, and nystatin.

RESULTS

Twenty-nine adult patients underwent small bowel Tx and were prospectively followed for infectious complications. The median follow up was 643 days (Range 21 days to 4.7 years). The mean age was 33 years (Range 19 to 58 years), and the Female/Male ratio was 1.2/1.0. The Kaplan-Meier 1-year patient survival was 68% ± 9%, and overall mortality was 55% (16/29). Twenty-eight of 29 (97%) patients had at least one infectious episode, and the median number of infectious episodes was 5 per infected patient (Range 1 to 11). The percentage of patients with bacterial infection was 93%, viral infection 69%, and fungal infection 59%. The median number of episodes per infected patient in the three transplant types, SBTx, SBTx/L, MV, was 3.5, 5.0, and 6.5, respectively (P = .056, Kruskal-Wallis Test). The percentage of SBTx patients with bacterial infection at the first 3 months after Tx with and without colonic segments was 87% (7/8), and 43% (3/7), respectively (P = .20, Fisher Exact Test).

There were total of 140 episodes of infection and their occurrence at 1 to 3 months, 4 to 6 months, and later than 6 months following Tx was 40%, 16%, and 44%, respectively. These included: bacterial (90): line infection (25), peritonitis (12), abdominal abscess (11), primary bacteremia (11), pneumonia (8), wound infection (8), Clostridium difficile colitis (6), others (9); viral (26): CMV (19), EBV (3), HSV (1), hepatitis C (3); fungal (20): candidiasis (16), aspergillosis (1), coccidioidomycosis (1), others (2); bacterial/fungal (4). Twenty-one of 29 (72%) patients had at least one episode of bacteremia or fungemia, and the median number of episodes was 2.0 (Range 1.0 to 7.0). The source of infection for these episodes of positive blood culture was: intravascular line (43%), abdomen (19%), others (11%), and unknown source (28%). There were total of 54 positive blood cultures which included: aerobic gram positive organisms in 62%, aerobic gram negative organisms in 28%, anaerobic organisms in 2%, and candida species in 9%. Sixteen of 29 (55%) patients developed symptomatic CMV infection. Of these, 10 patients had primary infection, and 6 patients had reactivation. These infections included: gastroenteritis (90%), hepatitis (5%), and retinitis (5%).

DISCUSSION

We reported in the past our experience with the first 21 patients who underwent small bowel Tx at the University of Pittsburgh.[1] In this report we were able to summarize our experience in a larger group of patients with a longer follow-up.

The rate of infectious complication after small bowel Tx is very high, and the risk of infection is still relatively high more than 6 months after Tx. There was a trend for a higher rate of infection in patients who underwent MV compared to patients who underwent SBTx or SBTx/L. There was also a trend of higher rate of early bacterial infections in patients

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with SBTx with a colonic segment. Symptomatic CMV infection and bacteremia/fungemia were the most frequent infections. We have identified the vulnerability of the transplant gut to CMV, and its association with higher amounts of tacrolimus and steroids.[3,4] The high rate of bacteremia/fungemia is mostly due to infection of central lines and abdomen. Bacterial translocation from the gut may explain in part those episodes of bacteremia with "unknown" source, and early bacterial infections in SBTx with colonic segment.

Reduced infectious complications after small bowel transplantation is a very important goal. Possible strategies for the future are: preemptive therapy and limitation of transplant of CMV seronegative recipients with seropositive organs, limitation of colonic segment transplant, paying special attention to management and maintenance of central lines, and innovative strategies in immunosuppression therapy.

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