Prevention of Sensitization and Hyperacute Rejection in Liver and Heart Xenografts by FK 506 Plus Donor Antigens


We have observed that FK 506 (FK) prevented the induction of hyperacute rejection (HAR) in hamster-to-rat liver (OLTX) and heart (HTX) transplant models and analyzed the mechanisms. $1.5 \times 10^7$ hamster hepatocytes (HC) or a minced heart as source of xenoantigens were given to prospective recipients on day -6, with or without FK (1 mg/kg/d x 6). OLTX and HTX were performed on day 0.

Xenoantigen alone induced HAR that correlated with high titer of complement-dependent cytotoxic antibody (CDC). Additionally, immunosuppression with FK resulted in prevention of HAR and improved survival of OLTX recipients in the first 3 postoperative weeks ($P < .05$), with evidence of reduced antibody in the grafts. Even though FK did not eliminate total IgM amount and natural antibody titers, target-specific IgM, which is responsible for HAR, was reduced in the antigen + FK-treated group as compared with that with antigen alone. Furthermore, the sera from long-term survivors of OLTX did not inhibit CDC activity of sera obtained from animals experiencing HAR. This is contrary to reports by Braun et al. who showed an inhibitory effect of serum from an immunosuppressed patient, postulating a possible role for anti-idiotypic antibodies. This preliminary evidence suggests that the inhibition of xenoantigen-specific IgM production by FK seems to play an important role in the acceptance of xenografts.

REFERENCE


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0041-1345/95/$3.00/+