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# Successful Sequential Liver-Kidney Transplantation in a Patient With Preformed Lymphocytotoxic Antibodies

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**S**ENSITIZATION of potential transplant recipients by formation of lymphocytotoxic antibodies can be a result of prior blood transfusions, pregnancy, or failed allograft transplantation. While the presence of preformed anti-HLA-A and -B lymphocytotoxic antibodies does not appear to influence the survival of liver allografts,<sup>1</sup> this has been a contraindication in renal transplantation because of the high incidence of hyperacute rejection.<sup>2</sup>

We report a case of successful transplantation of a renal allograft, in the face of a positive warm T cell crossmatch sequentially following a prior hepatic allograft transplantation from the same donor.

## MATERIALS AND METHODS

### Patient

A G<sub>3</sub>P<sub>3</sub>A<sub>0</sub>, 43-year-old white female, with the diagnosis of primary biliary cirrhosis and renal failure due to interstitial nephritis, presented for combined liver-kidney transplantation. Preoperatively, serum BUN was 42 mg/dL, serum creatinine (Cr) of 3.6 mg/dL, with a Cr clearance of 22 cc/min. Liver and renal allografts were harvested from a single donor and transplanted in a standard manner<sup>3,4</sup> with baseline cyclosporine and steroids, placing the liver and then the kidney allografts. Allograft function was monitored by biochemical and radiologic studies.

### Histocompatibility Studies

These studies consisted of determination of the percent panel reactive antibodies (PRA), and donor lymphocytotoxic crossmatches using serum samples obtained as follows: (1) pretransplant (PRE-OT/KT), (2) postliver, prekidney transplant (POST-OT/PRE-KT), and (3) posttransplantation (POST-OT/KT). Donor lymphocytotoxic crossmatches (DLC) were done using a standard modified Amos Technique.

### Immunoabsorptions

Immunoabsorptions of test samples were done on pooled human platelets at a 1:1 dilution for 60 minutes x 2, while absorptions of mouse antibodies were done on solid phase antimouse antibody beads at a 2:1 dilution.

## RESULTS

### Posttransplant Course

Following completion of both the liver and kidney transplant, immediate function of both grafts was noted. Posttransplant evaluations of renal function by both renal ultrasound and radionuclide flow scans indicated normal function, and that the allograft was largely responsible for urinary excretory function.

Posttransplant liver function tests demonstrated a similar fall in both total bilirubin (TBIL) and transaminase levels. However, nine days following transplantation, elevation of TBIL and biopsy-proven rejection occurred in the hepatic allograft, with normal kidney function. An 11-day course of OKT3<sup>5</sup> was used to reverse the hepatic rejection. Follow-up of 15 months revealed normal renal and hepatic function without further episodes of rejection.

### HLA Evaluation

PRE-OT/KT sample was strongly positive (1:64 dilution) in DLC assays. Eight hours following completion of the liver transplant, the POST-OT/PRE-KT sample was negative by standard crossmatch techniques.

POST-OT/KT samples were analyzed for reappearance of DLC. All samples remained negative for DLC until day 9 posttransplant, when OKT3 was started. This monoclonal murine antibody has been shown to bind complement. As shown in Fig 1, PRA in nonabsorbed POST-OT/KT, also increased

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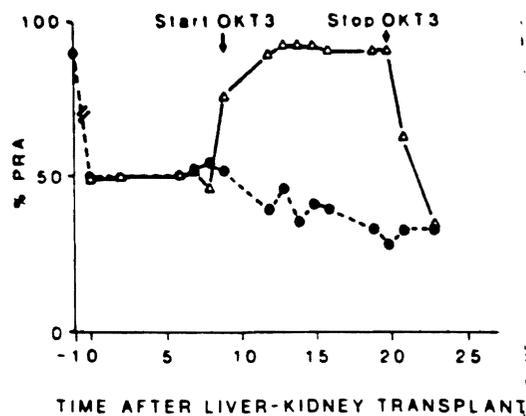


Fig 1. Percent panel reactive antibody (%PRA) is expressed as a function of time following sequential liver-kidney transplantation. OKT3, given (intravenously) IV, was started on day 9, and finished on day 20. Open triangular points reflect %PRA prior to absorption on a solid phase antimouse IgG immunoabsorbent. Closed circles are the corresponding %PRA values following immunoabsorption.

during the period of OKT3 therapy. This artifactual rise in DLC and PRA during the period of OKT3 therapy was shown by absorption of POST-OT/KT samples on antimouse antibody solid phase beads. Following absorptions, a fall in the % PRA to near levels found prior to and following OKT3 therapy was noted (Fig 1). Similarly this absorption removed DLC in the same period.

Immunogenetic analysis of the antibody population present in PRE-OT/KT and absent in POST-OT/KT samples revealed a HLA-B-35-associated specificity. This was

confirmed by elimination of DLC and PRA in PRE-OT/KT samples.

#### DISCUSSION

The mechanism by which the liver is protected from preformed antibody states in transplantation is not known.<sup>1</sup> It has not been clarified whether this reflects the unique architecture of the liver, the distribution of HLA antigens within the liver, or the possibility that the liver is able to "neutralize" specific antibodies by release of soluble HLA antigens. Starzl and coworkers first demonstrated that sequential liver-kidney transplants in presensitized dogs could protect the renal limb from acute rejection.<sup>6</sup> This has been subsequently confirmed in the murine model.<sup>7</sup>

The current study demonstrates the ability of sequential liver-kidney transplantation in the prevention of hyperacute renal rejection in a patient with demonstrated preformed anti-HLA lymphocytotoxic antibodies. The dramatic and sustained fall of DLC was temporally related to placement of the liver allograft. This was most likely due to absorption or neutralization of antibodies by the donor liver, and not by dilutional effects.

The applicability of the concept of multiorgan transplantation in transplanting potential presensitized renal transplant candidates is, of course, limited, but the mechanisms of protection using this model, if defined, may provide clues for less drastic therapeutic approaches.

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