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COMPARISON OF THE EFFECT OF HORSE ANTI-DOG LYMPHOCYTE GLOBULIN (HADLG) ON RENAL AND LIVER TRANSPLANTS IN DOGS *

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Effect of Horse Anti-Dog Lymphocyte Globulin (HADIgG) on kidney and liver allotransplant survival in dogs was compared. ALIgG served as a sole immunosuppression. The agent was given i. m. in a daily dose of 15 mg/kg body weight for 15 days (from −2 to +13). Significant prolongation of renal allografts survival was observed (MST of 31±12 days). The same ALIgG preparation administered according to the same protocol to liver transplant recipients failed to modify the course of graft rejection.

Horse anti-dog lymphocyte sera and their globulin fraction (HADLG) prepared against thoracic duct lymphocytes are capable of prolonging canine renal allograft survival (Diethelm et al., 1969; Rowiński et al., 1971; Matsukura et al., 1971). The same agent, however, used as a sole immunoppression in canine liver allograft recipients seen to be less efficient (Moreaux et al. 1972). There is still uncertainty, however, as to the extent to which the differences are dependent on the method of ALG preparation and the immunosuppressive protocol after the transplantation. The present work was undertaken to compare the effect of Horse anti-dog lymphocyte globulin (HALIgG) on kidney and liver allotransplant survival in dogs.

MATERIAL AND METHODS

Immune sera were raised in horses using thoracic duct lymphocytes. Two different batches of ALG were used, one from a horse immunized intravenously over a long period (ALIgG–1) and the other from a horse immunized by the six-pulse procedure (ALIgG–2). Details of the immunization protocols and preparation of IgG fraction of the sera are given elsewhere (Rowiński et al., 1973).

* With technical assistance of W. Słuzewska.

Lymphocytotoxic and lymphoagglutinating titers as well as opsonizing and rosette-inhibiting activity of both ALIgG preparations were examined in vivo in dog liver and/or kidney allograft recipients. Experiments were performed in two groups. In group I 16 bilaterally naphrectomized dogs received kidney allograft. Kidneys were transplanted into the illiac fossa using common technique. Half of the animals were treated with ALIgG–1, remaining dogs with ALIgG–2. In group II, orthotopic liver transplantation was carried out in 14 dogs. Technical aspects of liver transplantation as performed in our laboratory are described elsewhere. As in the group I, half of the animals were given ALIgG–1, others were treated with ALIgG–2.

ALIgG served as a sole immunosuppressive agent. In all animals ALIgG administration was commenced 2 days before transplantation and was continued for 15 days. The agent was given intramuscularly in a daily dose of 15 mg/kg body weight. This dose was temporarily increased up to 25 mg/kg body weight during first three days after transplantation. Thirteen days after the operation ALIgG administration was discontinued and surviving animals were left without any immunosuppression.

In all animals total WBC count, absolute lymphocyte count and platelets count in the peripheral blood were checked every other day. Blood urea and serum creatinine were determined every other day in kidney transplant recipients. Serum aminotransferases and alkaline phosphatase activities as well as serum bilirubin concentration were determined daily in liver transplant recipients.

RESULTS

Results of *in vitro* testing are shown in a Table 1. Both ALIgG preparations shown similar lymphocytotoxic titers and opsonizing activity and differed in rosette-inhibiting activity.

In all animals a marked rise of WBC was observed. Absolute lymphocyte count decreased during ALIgG administration but no profound lymphopenia was observed. No significant alterations in platelets count or hematocrite were noted.

Group I. The mean survival time for kidney allograft recipients treated with ALIgG–1 and ALIgG was 17 ± 10 and 31 ± 12 days respectively (MST of nontreated controls $8{,}8 \pm 2$). Although both ALIgG preparations prolonged the survival time of kidney graft recipients in comparison to untreated controls, better results were obtained with ALIgG–2 — prepared from the serum of a horse with short immunization protocol. Serum creatinine and blood urea were within normal limits as long as ALIgG was administered and started to rise a few days before the graft rejection. All animals died of uremia and on the autopsy kidneys presented typical changes of rejection.

Group II. The results of ALIgG treatment in dogs with orthotopic liver tansplantation were much worse. Survival times of the recipient dogs are shown in a Table 2. Serum bilirubin concentration as well as aminotransferases activity were raising up gradually from the second postoperative day. All dogs died of liver insufficiency. At autopsy in all but one dogs typical rejection pattern in the liver were found.

Table 1. Results of *in vitro* testing of ALIgG-1 and ALIgG-2

	ALIgG-1	ALIgG-2
Lymphocytotoxic titer	1:512	1:256
Lymphoagglutinating titer	1:256	1:64
Opsonizing activity	10^{-3}	10^{-3}
Rosette- inhibiting activity	1:16000	1:32000

Table 2. Survival of liver transplant recipients treated with ALIgG-1 and ALIgG-2

	Survival, days	MST *
ALIgG-1 n=7	1, 3, 3, 5, 8, 9, 10	6·33 ±2·80
ALIgG-2 n=7	1, 2, 2, 4, 4, 9, 12	7·25 ± 3·42
Controls n=10	2, 3, 4, 6, 8, 2, 3, 6, 7, 7	5·5 ±1·84

* Animals dying before the third postoperative day were excluded as technical failures.

DISCUSSION

It has resulted from this study that administration of HADLIgG to recipient animals prolonged renal allograft survival. Even less potent ALIgG-1 caused two-fold prolongation of a mean survival time in comparison to untreated controls. These ALIgG preparations however, administered acording to the same protocol to liver transplant recipients failed to modify the course of graft rejection. It may well be that the amount of antigen, as present in much larger liver, then kidney, graft require higher doses of ALG to obtain adequate immunosuppression. Further studies are carried on to find the appropriate immunosuppressive protocol for liver transplantation in dogs.

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