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Renal Transplantation in the Presence of a Positive Cytotoxic Antibody

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With the exception of the B cell autoantibodies,[1] the positive crossmatch is associated with the development of hyperacute rejection, and contraindication to clinical renal transplantation.[2, 6] The mere historical presence of cytotoxic antibodi.es, is not a contraindication, provided the cross match with a current serum (CS) at transplantation is negative.[7, 8] In addition the occurrence of hyperacute rejection in the presence of a negative cytotoxic crossmatch,[5, 9] prompts the ques: tion of the limitations of the technique in the opposite direction. This report refers to our experience with clinical renal transplantation in the presence of a doubtful or weakly positive crossmatch with CS.

MATERIALS AND METHODS

Case Material

A total of 264 cadaveric kidney transplants were performed at our institution between December 1984 and December 1986.

Tissue Matching

Included in this series are 39 patients with a doubtful (37) or weakly (2) positive, cytotoxic crossmatch with CS. Historical crossmatch was negative in three cases, doubtful positive in 24, weakly positive in six, strongly positive in five, and not available in one case.

The presence of preformed, cytotoxic, donor specific, antibodies was measured using conventional crossmatching techniques (Standard Ames Technique). Eighteen of the patients were males and 21 females, ranging in age from 16 to 69 years. There were 20 primary and 19 retransplantations: second graft for 16 patients, third graft for two patients, and fifth graft for one patient.

HLA matching at the HLA A and B loci averaged 1.38 ± 1.19 SD antigens and at the DR locus 0.56 ± 0.60 SD antigens (Table 1).

The patients were observed for a period of 2 to 28 months (average, 11.8 months).

Immunosuppression

Cyclosporine A (CsA) was administered orally at a dosage of 17.5 mg/kg on admission a few hours before transplantation. The treatment was continued postoperatively starting with 17.5 mg/kg/d in two divided doses, then adjusting the CsA dose according to blood radioimmunoassay (RIA) levels of CsA. Intravenous (IV) CsA was administered when

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needed. A five-day tapered course of steroids, beginning with 200 mg and decreasing by 40 mg/d until a maintenance dose of 20 mg/d was achieved, was administered in four divided daily dosages starting on the first postoperative day.

A total of 23 patients were treated with OKT3 (5 mg IV bolus daily). In 17 of these patients, the treatment was started either intraoperatively or on the first postoperative day. The remaining five required OKT3 treatment for rejection episodes at a later time. For five patients, a second course of OKT3 was required for treatment of rejection episodes. In II patients azathioprine (0.5 to 1.5 mg/kg/d) was added for various periods of time.

Rejection episodes were identified by clinical criteria (fever, graft tenderness and swelling, oliguria with rising serum creatinine) and confirmed by scintigraphy and histologic evaluation (Bx), when in doubt. Reversal of rejection was characterized by significant fall in serum creatinine, restoration of urine output and, in select cases, by needle biopsy histology.

RESULTS

Mortality

There were three deaths (7.69%) in this series, all due to respiratory failure. The cause remains unclear in one patient, a second patient died of dissemination of Tuberculosis, which was undetected at transplantation and the third patient died of H. Influenzae pneumonia.

Graft Survival

Twenty eight of 39 patients have life sustaining renal function from their transplanted graft (average serum creatinine 2.72 mg/dL), 2 months to 2 years and 4 months after transplantation (average 11.18 months), for an overall success rate of 71.2%, 80% for primary, and 63% for retransplantation (Table 2).

Rejection

Two patients (5.13%) had hyperacute rejection. In one case it was a primary kidney allograft while in the other it was a secondary kidney transplant. In both cases, the clinical observation was confirmed by histologic evaluation. The panel-reactive antibody (PRA) for the patient receiving the primary transplant was 100% for both historic and current sera, and was 10% for both historic and current sera in the patient receiving the secondary graft. A third patient lost his graft most likely due to arterial thrombosis. Four other patients (10.26%) lost their grafts to rejection at a later date, one occurring in a primary transplant and the remaining three following kidney retransplantation.

Primary Non Function

Four patients in this series had primary nonfunction of the graft, two each in the primary and secondary transplants, respectively.

Acute Tubular Necrosis

Twenty two of these grafts developed acute tubular necrosis (ATN), for an overall rate of 56.41 %: 70% in the primary transplants and 42% in retransplants. A TN lasted for more than a month in six cases. Life sustaining renal function could not be maintained for more than a few months in two of these patients, due to repeated rejection episodes. The remaining four patients recovered and are stable and dialysis free (average serum creatinine 3.2 mg/dL).

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DISCUSSION

The cytotoxic cross match, since its introduction into clinical practice,[6] has defined the permissibility of clinical renal transplantation, with the notable exception of the cases in which positivity is due to autoantibodies.

The feasibility of successful renal transplantation in patients with a historically positive, but currently (at transplantation) negative cross match has been shown by both Cardella et al[1] and Kerman et al.[7] This report refers to a single institutional experience with renal transplantation in the face of current positive crossmatch, at transplantation. The patients in this series belong to a group of patients who have repeatedly demonstrated positive cross match to a succession of donors, and the presence of a doubtful or weakly positive cross match was thought to represent a unique therapeutic window.

The results, although somewhat inferior to our overall results, can still be considered gratifying, in view of the high-risk population involved. The high mortality observed in this series is probably related to the intense immunosuppression that was required. Additionally, in one case, it was due to failure to recognize pulmonary tuberculosis, predating transplantation.

The ATN incidence in this series (56.41%) is higher than the average (30%) at our center; in six cases, it was unusually long and was followed by graft loss due to rejection shortly after recovery in two of these cases. In addition, the number of cases of primary nonfunction was higher than in our general transplant population. It is our belief, that the above discrepancies from our average case load, represent unrecognized immunologic reactions and are variations of the observations made by Iwaki et al[9] on nonfunctioning kidneys in immunized patients.

Based on the data derived from this initial clinical experience, it is apparent that successful renal transplantation can be achieved in the face of doubtful or weakly positive cross-match, with results approaching those of the general population. Because intense immuno-therapy is expected to be needed, careful patient selection is necessary to avoid unnecessary mortality.

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Table 1

Immunopathological Data

		Average Class 1 Match	Average Class 1 Mismatch	Average Class 2 Match	Average Class 2 Mismatch	Average Peak PRA	Average Current PRA
Primary transplants	20	1.45 ± .28	2.25 ± 1.26	0.47 ± 0.60	1.0 ± 0.56	34.05 ± 30.6	16.3 ± 25.4
Retransplants	19	1.32 ± 1.08	2.47 ± 1.09	0.57 ± 0.62	1.0 ± 0.65	64.5 ± 31.9	47.4 ± 31.8
Total	39	1.38 ± 1.19	2.36 ± 1.19	0.5 ± 0.60	1.0 ± 0.6	48.9 ± 34.8	31.5 ± 31.89

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Table 2

Clinical Data

	Hyperacute (Rejection)	Primary Nonfunction	ATN	Graft Loss (Rejection)	Eventual Satisfactory Result
Primary Tx 20	1	2	14	1	16
ReTx 19	1*	2	8	3	12
Total 39	2	4	22	4	28

Abbreviations: Tx, transplantation; ReTx; retransplantation.

*Additional graft was lost to arterial thrombosis (ReTx).

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