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THE SELECTION OF DONORS FOR HIGHLY SENSITIZED PATIENTS

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Summary

Two approaches to the selection of donors for highly sensitized patients were compared. One was based on the prediction of acceptable HLA-A and B mismatches from extensive serological screening. The other relied on donor selection by a negative crossmatch test alone. In 14 out of 33 cases studied, the crossmatch negative kidneys carried additional HLA mismatches not predicted by the screening. Our data show that the most efficient way of finding suitable grafts for highly sensitized patients is by direct crossmatching.

Introduction

Highly sensitized patients are at a disadvantage when being considered as recipients for kidneys. In many cases the specificities of the antibody can be determined and as a result HLA mismatched, crossmatch negative donors can be predicted for these recipients [1,2]. In this study we compared the effectiveness of such an approach with a simpler scheme where donors were selected on the basis of a negative crossmatch alone.

Material and methods

Highly sensitized patients were defined as those patients whose peak reactive serum killed over 85 per cent of a panel of 100 HLA individuals. In 139 recipients whose antibody frequencies ranged between 85 per cent and 98 per cent acceptable HLA antigens were determined from the HLA types of the individuals negative in the lymphocytotoxicity test. Independently 33 highly sensitized patients received a transplant on the basis of a negative crossmatch alone, regardless of the degree of HLA matching. The actual HLA-A and B mismatches in these transplants were compared with the predicted acceptable HLA antigens.

TABLE I. Identified and actual HLA-A and B mismatches in highly sensitized patients

Patient number	PRA %	Sex	Number of previous TX	Acceptable mismatches identified HLA-A**	HLA-B**	Additional mismatch in donor HLA-A**	HLA-B**	Total number of A and B mismatch	
70	85	F	2	*3*†,11,9,26,*19*	8 12,*13*,14,15,18,27	–	–	2	1
68	85	M	2	1,2,11,26,*19*	7,8,*13*,18,25,70	–	60	1	2
34	89	F	2	1,10,*11*,28	w6 incl *35*	–	–	1	1
36	89	F	0	3,11,26,28,29	8,13,14,18,35,17	–	–	0	0
50	91	F	0	2,*3*,9,11,19	w6 incl *40*	–	–	1	1
69	96	F	1	3,23	*7*,18,35,44,70	–	60	0	2
24	85	M	0	*2*,*3*,28,19	w6 incl *35*,27,47	–	–	2	1
60	92	M	1	*3*,11,26,*29*,30,31	w6	–	–	2	0
39	85	F	1	1,*3*,9,28,29	8,22,15	31	37	2	1
23	95	F	0	1,11,10,19	7,13,14,39,40	3	15,35	1	2
26	85	M	1	1,3,*11*,10,28,29	8,13,14,*22*	24	–	2	1
14	95	F	0	2,11,*9*,32	45,13,29	–	–	1	0
82	86	F	0	*1*,3,*11*,26	12,15,35,*22*,27,41	–	–	2	1
98	95	M	1	No pattern *	No pattern	3,32	44,62	2	2
31	98	F	1	None	27,56,53	–	8	0	1
115	96	M	1	*1*,3,11,9,26	14,21,35,47	–	37	1	1
47	88	M	1	1,2,9,*10*,11,28	7,22,15,*17*,18,35,37	–	–	1	1
21	94	M	1	3,10,11,*19*	7,40,*41*,14	–	–	1	1
32	96	F	0	3,25	*7*,*18*,47	–	–	0	1
126	85	F	1	11,10,28,*19*	5,7,8,27,*13*,14,15,18	–	–	1	2
122	95	F	0	2,9,11,30	7,15,18,22,41	–	–	0	1
16	95	M	1	1,*2*,11,19	8,18,22,41	–	14	1	1
84	93	F	0	1,10,11,28	5,35,21,22,15,*27*	–	17	0	2
107	97	F	1	9,32 *	27,37	1	8,14	1	2
64	89	F	0	1,11,*28*	7,22,40,5,35,18,15	–	–	1	1
152	99	F	1	2	72	28	–	1	0
85	96	M	1	9,*10*,11,*29*	7,35,21,47	–	–	2	0
141	98	M	0	1,3,29	45,15	11	–	1	0
131	94	F	0	10,*19*	w4 incl *47*	–	–	1	1
62	98	M	2	2,9,11	13	30	18	1	1
109	86	F	1	3,10,11	7,27,5,35,15,17,21	–	–	0	0
72	85	M	3	3,10,28	w6 incl *70*	–	–	0	1
158	100	M	1	None	None	–	–	0	0

PRA=panel reactive alloantibody; *=patient had cytotoxic autoantibody; †=italic specificities are those that were actually mismatched; **=prefix *W* is dropped for graphical simplicity

Results

The identified acceptable HLA-A and B antigens in the 33 transplant recipients are shown in Table I. The number of acceptable antigens varies between one and eight per HLA locus, depending mainly on the reaction frequency of the serum. In 14 patients additional acceptable mismatches which were not identified in the screening were observed in the crossmatch negative donors. The degree of HLA-A and B mismatching is summarized in Table II. Only three patients

TABLE II. Degree of mismatching in 33 highly sensitized patients

Number of HLA-A, B mismatches	Number of patients
0	3
1	7
2	13
3	9
4	1*

* Patient had an autoantibody

received grafts with no mismatches. One of these patients (No. 158) had an antibody with 100 per cent reaction frequency; no acceptable mismatches could be predicted in this case. One patient (No. 98) received a graft with four HLA mismatches. The screening of this patient's serum did not show a consistent pattern of negativity; further investigations revealed that this patient had a cytotoxic autoantibody.

The range of acceptable HLA mismatches did not always include antigens that were in the same serological crossreactive group as the patient's HLA antigens. Scrutiny of the A2/A28 crossreactive group revealed that in only two of the 13 HLA-A28 positive recipients HLA-A2 was an acceptable mismatch. Seven A28 positive recipients were sensitized against HLA-A2. The remaining four patients carried the phenotype HLA-A28, A2.

Discussion

Most highly sensitized patients are reported to have broadly reactive antibodies directed against serologically well-defined public HLA specificities [3]. In these patients it is possible to predict a crossmatch negative, HLA mismatched donor. However, a proportion of highly sensitized patients have non-HLA antibodies, such as auto-antibodies [4] and in these patients the specificities of the acceptable mismatches can not be predicted. Our results show that despite an extensive screening programme, not all acceptable mismatches can be predicted. Furthermore, crossreacting antigens between the donor and recipient are not necessarily acceptable as mismatches. Highly sensitized patients could be denied a crossmatch

negative graft if donors with predicted mismatches alone were considered. We suggest that the most effective donor selection scheme for highly sensitized patients is one based on a negative crossmatch test.

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References

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