The Effect of Blanks and Antigen Sharing in the HLA System on the Paternity Index

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INTRODUCTION

The HLA system is the single most polymorphic, well defined, genetic system in use today as a component of the testing profile in cases of disputed parentage. Over 40,000 phenotypes can be detected utilizing HLA-A and HLA-B locus markers. In spite of this, antigen sharing between the alleged father (AF) and mother (M) is relatively common. Missing antigens, blanks, are also commonly observed, especially in blacks, but also in whites as well. This study was undertaken to determine the effect of HLA-A and/or B antigen sharing between the AF and M, and blanks at these loci, on the HLA Paternity Index (PI) in white non-exclusion cases where the AF was assumed to be the true father.

METHODS

All paternity cases involving 1 child in whites processed from Aug 1981 to Apr 1989 were reviewed independently by the authors. The case material was limited to non-exclusion trios in which the Combined PI (CPI), using an average of 10 genetic systems, exceeded 18. Therefore, it was assumed that the study cases involved true fathers since the minimum probability of paternity was 98% using 0.7 as a realistic prior probability (based upon the observed exclusion rate of 30% from experience in casework over this time). The combined power of exclusion of this test panel was 99% or higher. Each case was classified into a subgroup according to HLA-A and/or B antigen sharing between the AF and M. In addition, the cases were also classified independently into subgroups based upon the presence or absence of HLA-A and/or B blanks in each of the three parties of the case. Frequency distributions of the HLA PI values were constructed for the entire study group (n = 516) and for the various subgroups of the study. Comparisons between the groups were made using the Mann-Whitney U Test for significance.

RESULTS

There were 537 non-exclusion cases in the total study material resulting in a median HLA PI of 25. 21 cases had a CPI below 19. These cases were excluded from the study group which consisted of the remaining 516 cases with CPI values all exceeding 18 (true father cases). The median HLA PI value of this group and the subgroups are displayed in Tables 1 and 2.

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Table 1. HLA A,B antigen sharing between white true fathers and mothers in paternity cases

Antigens Shared	No	%	Median HLA PI	p
None	219	42	31	
One A	148	29	28	ns
One B	67	13	24	ns
One A & B	64	12	15	0.003
Other Combinations	18	4	12	0.002
Total Cases	516	100	26	

Table 2. HLA blanks at the A & B loci in 516 white true father paternity cases

	Blanks Present			No Blanks		
A locus blanks	n	%	Median HLA PI	n	Median HLA PI	p
Alleged father	89	17	22	427	27	ns
Mother	88	17	31	428	26	ns
Child	84	16	19	432	28	0.006
B locus blanks						
Alleged father	62	12	40	454	25	0.060
Mother	57	11	29	459	26	ns
Child	50	10	20	466	27	ns
A or B locus blanks in AF,M,C	265	51	28	251	25	ns

DISCUSSION

Intuitively, one would expect the HLA PI values to be reduced whenever there is antigen sharing between the AF and M since there would be less diversity and therefore less discrete information available. The data in this study support this expectation. However, the differences in the distributions of the HLA PI values in the study groups are not marked unless the AF and M share two or more HLA antigens (Table 1). The most

commonly shared HLA A and B antigens between the AF and M are the most common antigens at these loci. Sharing of a single such antigen resulted in only a slight decrease in the HLA PI. However, if the AF and M share 1 A and 1 B, or other combinations of two or more antigens, then the HLA PI was significantly decreased. Analysis of the 1 A and 1 B AF/M antigen sharing group (n = 64) reveals that the low HLA PI values are usually associated with 1 of 3 types of situations: 1) the child has a blank and the AF and M share the one antigen detected at that locus, 2) M and C are HLA identical, or 3) the AF's "other" haplotype (unshared with mother) is common and is the obligatory haplotype.

The HLA PI is also reduced when the child has either an A locus or B locus blank. Analysis of the antigens detected at the locus with a blank reveals, as expected, that they are usually the more common antigens. Therefore, the child is usually homozygous for a relatively common antigen. The Y value in the denominator of the PI is increased relative to cases in which the paternal antigen is less frequent. This results in a lower quotient - the PI value. However, when the AF has a B locus blank, the HLA PI value tends to increase due to his apparent homozygosity for the B locus antigen. The resulting X value of the numerator is increased relative to the Y value. The Y value of the B locus genes tends to be low due to the B locus gene frequencies. Common A locus antigens tend to have higher frequencies. Therefore, an A locus blank in the AF does not have a strong influence on the PI.

SUMMARY

HLA antigen sharing between a true father and mother can result in a significant reduction of the HLA PI if the father and mother share more than one HLA antigen. HLA blanks in the child, and a B locus blank in the AF, can also produce a significant change in the HLA PI when compared to cases with no blanks. These variances can be attributed to the gene frequencies of the HLA system. Relatively low HLA PI values result when the AF and C share a common antigen but they may also be caused by other factors.

CONCLUSIONS

In non-exclusion cases where the AF is the true father:

Low HLA PI values may be associated with:

1) Sharing of relatively common obligatory antigens between AF and C.
2) Sharing of two or more antigens between the AF and M.
3) A or B locus blanks in the child.

High HLA PI values may be associated with:

1) Sharing of a relatively rare obligatory antigen between AF and C
2) B locus blank in the AF
3) No antigen sharing between the AF and M