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Fourteen-year experience of human leucocyte antigen typing in cases of disputed parentage in Hong Kong

BR Hawkins

Seventy-seven cases of disputed parentage were studied using the human leucocyte antigen system over a 14-year period in Hong Kong. Of these, 30 (39.0%) related to the amendment or verification of birth registration details, 20 (26.0%) were for divorce or affiliation proceedings, and 19 (24.7%) were related to overseas resident visa applications. An exclusion of parentage of at least one of the alleged parents was shown in 23 (29.9%) cases; none of the cases related to overseas resident visa applications showed an exclusion. The study illustrates that human leucocyte antigen testing is a very powerful tool in the elucidation of disputed parentage in Hong Kong.

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Key words: HLA Antigens; Paternity; Sensitivity and specificity

Introduction

Typing for human leucocyte antigens (HLA) is a well-established method for the elucidation of disputed or unclear parentage.[1-3] The technique is used extensively in some societies, but considerably less so in others. The types of cases in which the technique is used inevitably differ from one culture to another, and will reflect the prevailing social need for the test. Only 77 cases of disputed parentage have been tested using HLA typing over a 14-year period in Hong Kong. This paper reviews those cases.

Subjects and methods

Study population

Between 7 December 1982 and 31 December 1996, 77 cases of disputed parentage involving 226 subjects were tested at the Tissue Typing Laboratory of the Department of Pathology at The University of Hong Kong. The majority of the subjects tested were ethnic Chinese, but also included were five Filipinos, one Indian, one Thai, one Nepalese, and three Caucasians.

Human leucocyte antigen typing

Human leucocyte antigen typing was performed by serological techniques using antisera that were standardised for use in a Chinese population. Most antisera were obtained from sources in Hong Kong and were supplemented where necessary by antisera and typing trays which were purchased from commercial suppliers. The panel of antisera covered a minimum of 17 specificities for HLA-A, 34 for HLA-B, and 16 for HLA-DR. Tissue typing that was performed prior to 1984 was restricted to testing for HLA-A and HLA-B specificities only. Tissue typing that was performed subsequently included testing for HLA-DR specificities, except in cases in which a clearly defined exclusion of parentage was shown by HLA-A and HLA-B typing alone.

Results

The reasons for performing HLA typing in the 77 cases are shown in Table 1. The greatest proportion of referrals (39.0%) related to the amendment or verification of birth certificate details and were performed at the request of the Hong Kong Immigration Department. Twelve of 30 (40.0%) of these cases showed the exclusion of at least one of the alleged parents. Of the 20 cases studied for divorce or affiliation proceedings, five (25.0%) showed the exclusion of at least one putative father. None of the 19 applications for resident visas showed an exclusion of the claimed relationship. Eight others were tested for various reasons, including adoption or medical reasons. The number of parties tested in any particular case ranged from two to five. The configurations of the 77 cases and the outcome of the tests are shown in Table 2.

Discussion

The use of inherited markers for the elucidation of dis-

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Table 1. Reasons for performing human leucocyte antigen typing

Reason	Exclusion	Non-exclusion	Total No. (%)
Amendment of birth certificate details	12	15	27 (35.1)
Verification of birth certificate details	0	3	3 (3.9)
Late registration of birth	0	1	1 (1.3)
Adoption	5	0	5 (6.5)
Divorce or affiliation proceedings	5	15	20 (26.0)
Application for US resident visa	0	18	18 (23.4)
Application for Canadian resident visa	0	1	1 (1.3)
Medical reasons	0	1	1 (1.3)
Not specified	1	0	1 (1.3)
Total	**23**	**54**	**77**

Table 2. Number of subjects tested per case type and outcome of investigation

Subjects tested					Outcome		Total
PF1*	PF2†	M‡	C1§	C2‖	Exclusion¶	Non-exclusion	
+		+	+		6	30	36
+		+	+	+	0	4	4
+			+		3	11	14
+	+	+	+		11	0	11
+	+	+	+	+	1	0	1
+	+		+		2	0	2
+	+				0	1	1
		+	+		0	7	7
		+	+	+	0	1	1
				Total	**23**	**54**	**77**

*PF1 one putative father
†PF2 second putative father
‡M alleged mother
§C1 one alleged offspring
‖C2 second alleged offspring
¶One or more alleged parents excluded from parentage
+HLA test performed for this individual

puted or unclear parentage relies on two fundamental principles: a genetic marker cannot appear in a child unless it is present in one or both of the child's biological parents; and, if an individual is homozygous for a genetic marker, that marker must appear in any child of whom that individual is a biological parent. As a corollary to the first of these principles, an additional rule may be established that if an individual is heterozygous for a genetic marker, one of those markers must appear in any child of whom the individual is a biological parent.

The vast complexity of the HLA system[4] makes it particularly useful for the elucidation of disputed parentage. There are many more alleles than for any other genetic marker system, the inheritance patterns are well established, and the antigens are well expressed on the target cells (lymphocytes) throughout life. The use of DNA-based techniques has recently allowed the detection of an unprecedented array of subcomponents within the established HLA specificities. As a result, HLA typing now provides a level of success that far surpasses the use of multiple combinations of other genetic systems in the resolution of parentage disputes.[5]

To ensure that a minor's rights are adequately protected and to discourage individuals "who just want to be sure," the Tissue Typing Laboratory at The University of Hong Kong restricts HLA typing for parentage elucidation to three categories: when the test has been ordered by a court of law; at the request of a government immigration department, the Social Welfare or Legal Aid Departments of the Hong Kong Government; or at the request of a medical practitioner when there

are justifiable medical grounds. Within the cases included in this survey, the greatest number of referrals were those from the Hong Kong Immigration Department and related to the verification of birth registration details. These cases consisted of two main types: children whose fathers were originally named on the birth certificates as the mother's husband but who were later claimed to be the offspring of a different father; and, children whose biological fathers were not available when the child's birth was registered and for whom another person falsely claimed to be the father. This is of particular relevance in Hong Kong, because the mother is normally listed on the birth registration certificate under her unmarried surname and the father's name has to be specified for the child to be known under the father's surname.

In one such case it was alleged that the paternal grandfather of two children had been falsely named as the father on the registration documents. Since an offspring shares 50% of its genes with its biological father and 25% with its grandfather, there is only a 50% chance that a grandfather falsely accused of being the father can be distinguished from the true father on the basis of a single genetic system such as HLA. In this case the alleged grandfather was excluded from paternity of one child but not the other, whereas the alleged true father could not be excluded from paternity of either child. In at least two cases it was alleged that the father's brother had been falsely named on the registration documents. In one such case the brother named on the registration certificate was excluded from paternity but the father was not. In another case the two brothers in question had identical HLA phenotypes and could not be distinguished. HLA typing of the alleged offspring would not have been informative in this case and was not performed.

Approximately one quarter of the cases studied were at the request of overseas immigration authorities. Typically, these cases involved an alleged parent or offspring from overseas applying to the overseas immigration authority to sponsor the respective alleged offspring or parent for an overseas visa. HLA testing was requested when, for example, birth registration documents had been lost or destroyed, or for other reasons which attracted suspicion from the investigating officers. These cases often involved only one alleged parent and one alleged offspring, and the chances of showing an exclusion were correspondingly reduced. None showed an exclusion of the claimed relationship.

Only one case was studied for medical reasons. This case involved a child diagnosed as having β-thalassaemia major but whose alleged father did not appear to carry the genetic defect present in the child. HLA typing in this case could not exclude the alleged father from paternity of the patient.

Many of the cases were referred to this laboratory when erythrocyte antigen grouping failed to show the alleged exclusion. It is known that the power of erythrocyte antigen grouping to reveal an exclusion of paternity in a Chinese society is relatively low, compared with that in Caucasians.[6] This study highlights the power of the HLA system as a tool for the elucidation of disputed parentage. Of all the cases studied, 29.9% showed an exclusion of at least one of the alleged parents. Of the 15 cases in which two putative fathers were tested, 14 showed an exclusion of at least one of the two men by HLA typing. The one case that did not show an exclusion involved two putative fathers who were brothers who had identical HLA phenotypes. Identical phenotypes would be expected in 25% of cases in which two brothers are named as possible fathers. The testing of such cases for additional genetic marker systems could be beneficial because identity in one genetic system does not imply identity in another system.

Because of the strict criteria imposed on the acceptance of cases, the 77 cases reported in this paper will clearly not include all the cases of disputed paren-tage occurring in Hong Kong during the study period. Of the cases which would meet the acceptance criteria, not all would have been referred for HLA typing. There is no shortage of medical laboratories offering erythrocyte antigen grouping facilities in Hong Kong and it is now relatively easy to obtain DNA testing in overseas laboratories without the need for the subjects to leave Hong Kong. HLA typing still remains an option in many cases, however, and this study underlines the tremendous power of the HLA system to help clarify what, for the parties involved, is often a highly stressful event in their lives. The involvement of DNA-based technology in HLA typing is rapidly expanding and confers additional sensitivity and specificity over serological methods[7]; we expect to see a greater proportion of cases referred for medico-legal purposes in the future.

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