HLA Antigens in Filipinos with Ankylosing Spondylitis*

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ABSTRACT

Ankylosing spondylitis has been shown to be highly associated with HLA-B27 in Caucasian patients. This is also present in other ethnic groups. This study was conducted to determine the frequency distribution of HLA antigens in Filipinos and determine the association of ankylosing spondylitis.

Twenty patients satisfying the criteria for ankylosing spondylitis and 192 unrelated controls were HLA-A and B typed. Blood from these subjects were typed using NIH lymphocyte microcyto-toxicity method.

Of the unrelated controls, the frequencies of HLA A9 (w24), B40, A1, B5, Bw22 were increased and B13, B18, Bw35 were decreased. B27 had a frequency of 5.2%. A very significant high frequency of B27 (90%) was found in patients with ankylosing spondylitis with a very high relative risk of 163. A11 had a frequency of 55% with a relative risk of 3.37 which was not significant while B18 had an 18% frequency and a relative risk of 10.5 which was significant.

This study reaffirms the high degree of association of ankylosing spondylitis with HLA B27 and suggests than B18 may be an additional genetic marker for this disease.

INTRODUCTION

Since the report of Amiel in 1967 on Hodgkin's disease and HLA B locus antigen 4c, a large number of diseases have revealed linkage with HLA-A, B, and C antigens.[1] The most striking of these is the strong association between B27 and ankylosing spondylitis (AS). More than 90% of Caucasian patients with AS possess B27 whereas only 5-9% of controls have this specificity. This close association is also present in other ethnic groups. Among some Canadian Indians, 100% of AS patients have B27. The normal frequency of B27 in this ethnic group is extremely high compared with Caucasians.[2] Among American Black patients, there is a significant lower prevalence of B27 compared to Caucasian patients.[3] Among Japanese where B27 is extremely rare, AS also has strong association with B27.[4] Studies in other racial groups indicate a wide variation in the frequency of HLA alleles among different races. Among normal subjects in Southeast Asia, B27 was present among Chinese 7.1%, Malays 10.4% and Filipinos 6.9% (Table 1).[5] B27 is not found among pure Black Africans or in the aboriginals of Central Australia and AS is reported to be rare or non-existent disease in Africa and in Australian natives.[6]

The aim of this work is to determine the frequency distribution of HLA antigens in Filipinos and the association of ankylosing spondylitis with specific antigen(s).

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Table 1. HLA antigens in Chinese, Malay and Filipino Populations[5]

	Chinese n = 238	Malay n = 106	Filipino n = 335
A-Locus			
1	0.000	0.075	0.018
2	0.529	0.340	0.218
3	0.004	0.028	0.024
9	0.273	0.575	0.666
23 (9)	0.000	0.000	0.003
24 (9)	0.231	0.519	0.513
10	0.050	0.151	0.334
25 (10)	0.004	0.000	0.003
26 (10)	0.046	0.066	0.122
11	0.605	0.274	0.325
28	0.004	0.009	0.003
29	0.013	0.000	0.000
W19	0.206	0.274	0.051
B-Locus			
5	0.126	0.170	0.125
7	0.017	0.047	0.081
8	0.004	0.000	0.006
12	0.034	0.132	0.027
13	0.202	0.075	0.057
14	0.000	0.000	0.000
15	0.223	0.145	0.358
17	0.143	0.151	0.087
18	0.017	0.142	0.069
27	0.071	0.104	0.069
37	0.004	0.019	0.000
40	0.412	0.208	0.313
W16	0.109	0.113	0.331
W21	0.000	0.038	0.009
W22	0.122	0.038	0.036
W35	0.046	0.236	0.230
W46 (Sin 2)	0.227	0.019	0.018

MATERIALS AND METHODS

HLA typing for A and B locus antigens were performed using NIH lymphocyte microcyto-toxicity method on 20 patients with AS and 192 unrelated controls.[7] The diagnosis of AS was based on the ARA criteria (New York).[8]

HLA antisera were obtained from Fukuoka Red Cross Blood Center, Sydney Blood Transfusion Service, commercial pharmaceutical companies and 9 Filipino antisera. The following specificities were included: HLA A1, 2, 3, 9(Aw24), 10 (w26), 11, 20/30/31, 33; HLA b5(w51), 7, 8, 12, 13, 15 (w62), 16(w38), 17, 18, w22, w35, 31 and 40. Specificities of the Filipino antisera were A2, Aw24, A2+Bw35, B5, B7 (Bw60), B15(Bw62), B27+B40, Bw35, B15+B17.

Statistical analysis utilized the X^2 test with Yates correction.[9] Relative risk (RR) values were computed according to Woolf.[10]

RESULTS

Control Filipino Population

Increased antigen frequency was observed for HLA-A9 (Aw24) occurring in 68.7% and HLA B40 noted in 45.8% (Table 2). Antigen A11, B15, and Bw16 reported to be occurring in high frequency in previous studies[5,11,12] had a lower frequency in this study (Tables 3 and 4). Other antigens found to have increased frequency compared to previous reports are A1, B5, and Bw22. Antigens noted to

Table 2. HLA Antigens and Gene Frequencies in the Filipino Population (n = 192)

Antigen	No. Positive	Antigen Frequency (Pf)	Gene Frequency (Gf)
A–Locus			
1	11	0.057	0.029
2	42	0.218	0.116
3	6	0.031	0.016
9 (w24)	132	0.687	0.440
10 (w26)	33	0.171	0.089
11	51	0.265	0.143
29/30/31	3	0.0015	0.007
33	7	0.036	0.018
B–Locus			
5 (w51)	39	0.203	0.107
7	18	0.093	0.048
8	1	0.005	0.002
12	9	0.046	0.023
13	3	0.015	0.007
15	39	0.203	0.107
W16 (w38)	41	0.213	0.113
17	20	0.104	0.053
18	2	0.010	0.005
W22	13	0.067	0.034
27	10	0.052	0.026
W35	22	0.114	0.059
37	2	0.010	0.005
40	88	0.458	0.264

Table 3. HLA Antigen Frequencies in Filipinos

Antigen	Present Study (Manila)	Chan et al. 1979 (Manila)	Smith et al. 1975 (Cebu)	Payne et al. 1972 (San Francisco)
A–Locus				
1	0.057	0.015	0.000	0.007
2	0.218	0.218	0.160	0.215
3	0.031	0.024	0.020	0.021
9	0.687	0.666	0.620	0.694
10	0.171	0.334	0.160	0.097
11	0.265	0.325	0.300	0.382
W19	-	0.0036	0.060	0.101
28	-	0.003	0.0.20	0.014
B–Locus				
5	0.203	0.125	0.040	1.0104
7	0.093	0.081	0.020	0.069
8	0.005	0.006	0.000	0.007
12	0.046	0.027	0.020	0.049
13	0.015	0.057	0.040	0.056
15	0.203	0.358	0.260	0.347
W16	0.213	0.331	0.320	0.319
17	0.104	0.087	0.080	0.069
18	0.010	0.069	0.020	0.069
21	-	0.009	0.020	0.007
22	0.067	0.036	0.020	0.035
27	0.052	0.069	0.080	0.049
W36	0.114	0.230	0.000	0.215
40	0.458	0.313	0.389	0.200

Table 4. HLA Antigens Occurring in High Frequency Among Filipinos

Antigen	Present Study	Chan et al.	Smint et al.	Payne et al.
A–Locus				
9	0.687	0.666	0.620	0.694
11	0.265	0.325	0.300	0.382
B–Locus				
15	0.203	0.358	0.260	0.347
W16	0.213	0.331	0.320	0.319
40	0.458	0.313	0.200	0.389

Table 5. HLA Antigen in Ankylosing Spondylitis (n=20)

Antigen	Pf	Gf	X^2	RR
A–Locus				
1	0.000	0.000	0.000	0.000
2	0.200	0.106	0.037	0.892
3	0.100	0.052	2.357	3.444
9/w24	0.600	0.368	0.636	0.681
10/26	0.100	0.052	0.678	0.535
11	0.550	0.330	7.078	3.379
B–Locus				
5	0.150	0.079	0.321	0.692
7	0.500	0.026	0.424	0.508
12	0.100	0.052	1.039	2.259
15	0.050	0.026	2.774	0.206
18	0.100	0.052	7.852	10.555
27	0.900	0.684	113.605	163.800
40	0.250	0.134	3.192	0.393

have decreased frequency are B13, B18, and Bw35. B27 has frequency of 5.2%.

Ankylosing Spondylitis

Table 5 shows the frequency and relative risks of HLA A and B antigens in ankylosing spondylitis. A very significant high frequency of B27 is present in this condition with a very high relative risk of 163. There is a high frequency of A9/w24 but it is less than the control. An increased frequency is observed with A11 (55%) with a relative risk of 3.37. B18 has a frequency of 10% and a relative risk of 10.55.

DISCUSSION

The HLA A and B system of the Filipino population is characterized by increased frequencies of A9/w24, A11, B15, Bw16 and B40 compared to other Southeast Asian ethnic groups such as the Chinese and Malays.[5] Compared to previous studies, the present study showed higher frequency of A1, B5, Bw22 and decreased frequency of B13, B8 and Bw35. Differences in antisera used and the fact that the Filipino race is not a pure race can account for these differences. B27 occurs in 5.2% of the control population.

This study reaffirms the high degree of association of ankylosing spondylitis with HLA B27 as it is present in 90% of patients and has a relative risk of 163. The high frequency of A11 (55%) and relative risk of 3.37 is not significant as it is found as the 2nd or 3rd highest antigen frequency in the Filipino population even in other studies.[5,11,12] HLA B18 is significant as its $x^2 = 7.852$ with $p < 0.005 > 0.010$ and a high relative risk of 10.55. This suggests that B18 may be an additional genetic marker for ankylosing spondylitis.

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