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HLA-B27 Frequency in Korean Patients with Ankylosing Spondylitis[1]

Sung Jae Choi and Myoung Hee Park*[2]

Department of Internal Medicine and Department of Clinical Pathology, College of Medicine, Seoul National University, Seoul 110, Korea*

= Abstract = In 90 Korean patients with ankylosing spondylitis (AS), HLA-B27 was examined. HLA-B27 frequency in patients was 83.3 percent, compared to 4.0 percent in healthy Korean controls (345 persons). The positive rate for HLA-B27 was found to be about 21 times higher than that in the control group and the relative risk of HLA-B27 for developing AS was 120, which indicates a strong association of HLA-B27 with AS in Korean population.

Key words: ***Ankylosing spondylitis, HLA-B27***

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic systemic inflammatory disorder of undetermined etiology that primarily affects the axial skeleton; sacroiliac joint involvement is the hallmark of the disease. Another striking feature is the high frequency of occurrence of fibrosis and bony ankylosis, perhaps as a secondary consequence of the primary inflammatory process (Bluestone 1985; Calin 1985; Khan 1984).

The origin of AS is unknown, but recent studies may provide valuable pathogenetic clues. This disease is associated with the histocompatibility antigen B27 (HLA-B27) throughout the world (Bywaters 1980; Schlosstein *et al.* 1973). Thus, approximately 90 percent of Caucasian patients with AS are HLA-B27-positive (Ryder *et al.* 1979). The incidence of HLA-B27 in black Afro-Americans with AS appears to be lower (approximately 50 percent), but it is still higher than the prevalence of the antigen in control groups of 2 to 4 percent (Good *et al.* 1976; Khan *et al.* 1976; Khan *et al.* 1977). The strength of the association is emphasized by Japanese survey in which the normal prevalence of HLA-B27 is less than 1 percent, whereas the antigen is found in about 85 percent of patients with the disease (Sonozaki *et al.* 1975; Tsujimoto 1978).

In Korea, antigen frequency of HLA-B27 in healthy persons is reported as 4.0 percent (Aizawa 1986), but there has been no report in patients with AS. In this paper, we present HLA-B27 frequency in patients with AS in Korea.

MATERIALS AND METHODS

Materials

During the period from January 1981 to June 1987, 100 patients visiting the department of Internal Medicine, Seoul National University Hospital were found fulfilling the New York criteria for definite AS (Table 1). All patients were Korean. Blood samples were obtained from 90 patients with AS.

Methods

Detection of HLA-B27 on lymphocytes by micro-lymphocytotoxicity test (Histognost^{R}-B_{27}: Behring institute) according to Terasaki (1976) was done.

RESULTS

Male to female ratio of patients with AS was about 7.3:1. The peak age at the time of diagnosis was between 16 and 40 years (85%; Table 1.).

Of the 90 case of AS, 75 (83.3%) were HLA-B27 positive, whereas only 14 persons of the 345 (4.0%) were positive in the healthy Korean controls (Table 2). The fact that the positive rate for HLA-B27 was about 21 times higher than that in

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[2] Author for correspondence.

Table 1. Age and sex distribution in 100 patients with ankylosing spondylitis, at the time of diagnosis

Age (Years)	Male	Female	Total	(%)
16 - 20	17	3	20	(20.0)
21 - 30	35	3	38	(38.0)
31 - 40	23	4	27	(27.0)
41 - 50	9	0	9	(9.0)
51 - 60	3	0	3	(3.0)
61 -	1	2	3	(3.0)
Total	88(88.0%)	12(12.0%)	100	(100.0%)

Table 2. HLA-B27 frequency in Korean patients with ankylosing spondylitis(AS) and in controls

	Patients with AS		Controls*	p-value[2)]
	Male	Female		
Number	88	12	345	
HLA-B27(+)	67	8	14	
HLA-B27(−)	11	4	331	
ND[1)]	10	0		
HLA-B27 frequency	75/90(83.3%)		14/345(4.0%)	$p < 0.01$

1) ND: HLA-B27 test not done
2) Statistical significance was tested between patients with AS and controls by proportion Z-test.
*Aizawa M, 1986.

the control group indicates a strong association of HLA-B27 with AS. The relative risk of HLA-B27 for developing AS in Korean population is 126.

DISCUSSION

Ankylosing spondylitis (AS) demonstrates the strongest association of any rheumatic disease with any HLA antigen. Over 90 percent of Caucasian patients with AS have HLA-B27, an antigen that occurs in 6-8 percent of whites in the United States and Europe. The relative risk for AS in person possessing this antigen has been estimated as 100-150 (Woodrow 1977; Woodrow 1978; Schlosstein *et al.* 1973). Approximately 20 percent of "apparently healthy" B27-positive blood donors, both males and females, have been found to have clinical and/or radiographic evidence of spondylitis (Calin and Fries 1975; Cohen *et al.* 1976). Previous estimates of the prevalence of AS have thus been projected upward to 1-2 percent of American Whites (Calin and Fries 1975; Masi and Medsger 1979). This figure is comparable to the prevalence of rheumatoid arthritis.

The frequency of HLA-B27 varies widely from one geographic area to another and in different racial and ethnic groups (Table 3,4. Aizawa 1986; Chan *et al.* 1980; Khan 1984). The prevalence of AS roughly parallels the antigen frquency in divergent populations. The data show that despite race-related differences, the significant association between AS and B27 hold true in all racial groups studied thus far (Table 4).

In this study, it is also clear that there is an extremely close correlation between HLA-B27 and AS. This result is similar to other reports (Table 4). Among healthy Korean, the HLA-B27 positive rate (4.0%) is higher than that of Japanese and similar to that of Chinese (Table 3).

Pre-HLA family studies demonstrated that 7.5-20 percent of relatives of AS patients also had sacroiliitis or spondylitis (Hochberg *et al.* 1978). The application of HLA typing to such families, primarily Caucasian, has proved an almost invariable segregation of B27-bearing haplotypes into affected members (Dick *et al.* 1974; Hochberg 1978; Woodrow 1978). Since HLA haplotypes are

Table 3. HLA-B27 frequency in controls of oriental countries (Aizawa M, 1986)

Ethnic groups	Number of control	HLA-B27 antigen frequency (%)
Korean	345	4.025
Japanese	472	0.424
Chinese (north)	430	4.196
Chinese (south)	407	4.187
Chinese (Sichuan)	266	4.331
Taiwanese	85	8.235
Thai chinese	86	5.814
Thai	138	8.696
Uygur	100	1.000
Nepalese	54	0.000
Philippino	76	5.263
Malay	100	12.000

Table 4. HLA-B27 frequency in Caucasoid and non-Caucasoid patients with ankylosing spondylitis (AS) and in controls (Khan MA, 1984)

Populations	No.of studies	Patients with AS		Controls	
		No.of patients	B27 frequency (%)	No.of controls	B27 frequency (%)
Caucasian	29	2,022	79-100	16,162	4-13
Indian and Pakistans	9	130	83-100	456	2-8
Mexicans	2	68	75	305	6
South African Black	3	9	22	798	<1
American Black	5	67	57	1,330	2-4
Haida Indian (north America)	1	17	100	222	50
Chinese* (singapore)	1	29	97	238	7
Japanese	2	72	82	208	<1

* Chan SH, 1980

transmitted as autosomal codominant traits, the inheritance of HLA-B27 and the predisposition to AS is dominant. The disease itself, however, shows incomplete penetrance in that not all B27-positive relatives of a proband with AS will manifest the disease. In fact, only 20-26 percent of B27-positive relatives of AS probands have the disease (Calin *et al.* 1981; Woodrow 1978). There may be greater penetrance of AS in families where the proband is female (Hochberg *et al.* 1978). The determinants of penetrance, whether genetic, enviromental, or both, remain the keys to understanding the pathogenesis of this disease.

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= 국문초록 =

한국인 강직성 척추염 환자에서 HLA-B27 빈도에 관한 연구

서울대학교 의과대학 내과학교실 · 임상병리학교실*

최성재 · 박명희*

강직성 척추염환자 90명에서 HLA-B27 검사를 시행하여 다음과 같은 성적을 얻었다. HLA-B27 빈도는 강직성 척추염 환자에서는 83.3%인 반면 정상대조군에서는 4.0%이었다. 환자군에서 정상대조군에 비해 약 21배의 높은 HLA-B27의 양성율을 보이고 강직성 척추염 발병에 대한 HLA-B27의 상대위험도가 120배로 높은 사실은 한국인에서 HLA-B27과 강직성 척추염 사이에 강한 연관관계가 있음을 의미한다.