Distribution of HLA-B27 in patients with juvenile rheumatoid arthritis

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SUMMARY HLA antigens were examined in 27 patients with juvenile rheumatoid arthritis. HLA-B27 was found in none. The result was different from most other previously reported studies. The most likely explanation for this difference is the possibility that some patients with juvenile ankylosing spondylitis may have been included among the patients in the other studies.

Recently there has been an extensive search for an association between histocompatibility antigens (HLA) and specific diseases (Schlosstein *et al.*, 1973). Rachelefsky *et al.* (1974) showed that HLA-B27 was found in 42% of all juvenile rheumatoid arthritis (JRA) patients examined. This report prompted us to investigate whether a similar relationship existed in Japanese patients.

Materials and methods

27 patients (7 males, 20 females) with JRA admitted to Tokyo University Hospital were studied. All were Japanese, and in all onset of the disease occurred before the age of 16 years. Diagnosis was based on the criteria (Brewer *et al.*, 1973) for classification of JRA adopted by the American Rheumatism Association (Table 1).

Each patient was carefully observed and underwent a complete examination. Radiological examination was performed on affected joints and on the sacroiliac joints. Duration of follow-up ranged from 1 to 20 years, with 50% studied for more than 10 years.

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HLA typing was performed by the microdroplet lymphocyte cytotoxicity test. 22 HLA antigens were examined in 181 normal Japanese controls and in 27 patients with JRA. 41 patients with ankylosing spondylitis were also examined as a control group. The same antisera was used in typing both patients and controls.

Results

The incidence of the first and second sublocus of antigens in our patients was compared to those in the controls (Table 2). Although HLA-B27 was found in 74% of ankylosing spondylitis patients, none of the JRA patients or normal controls showed this phenotype.

Discussion

According to the reports by Rachelefsky *et al.* (1974), Carpenter *et al.* (1973), Buc *et al.* (1974), and Sturrock *et al.* (1974), HLA-B27 was found more frequently in patients with JRA than in the normal population. However, Gibson *et al.* (1975) recently reported on the association between HLA antigens and the disease; none was found, but HLA-B7 was found more frequently in patients with JRA demonstrating tenosynovitis than in the population with

Table 1 Clinical characteristics of patients with JRA

	No. of patients	Males	Females	Mean age at onset (yr)	Positive rheumatoid factor (no. of patients)	Uveitis
Acute type (Still's disease)	6	2	4	4.2	0	1
Polyarticular (adult type)	16	3	13	7.8	4	2
Monarticular	5	2	3	7.0	1	3
Total no. of patients	27	7	20		5	6

Table 2 HLA antigen incidence in controls and patients with JRA and ankylosing spondylitis

HLA	Healthy population (%) (n=181)	Patients with JRA (%) (n=27)	Patients with ankylosing spondylitis % (n=41)
HLA-A locus			
A1	1.66	3.7	2.86
A2	33.70	37.04	37.14
A3	1.10	0	2.86
A9	42.54	70.37	54.29
A10	16.89	33.33	17.14
A11	12.15	25.93	25.71
A28	0	0	5.71
Aw33	14.81	9.09	2.86
HLA-B locus			
B5	30.39	25.93	42.86
B7	11.05	14.81	14.29
B8	1.10	0	0
B12	19.89	18.52	2.86
B13	1.10	3.70	2.86
B14	1.66	0	0
Bw17	0	0	0
B27	0	0	74.0
Bw35	6.08	7.41	0
Bw40	18.78	55.56	14.29
Bw15	8.84	18.52	11.43
Bw16	2.21	0	0
Bw21	0.55	0	0
Bw22	18.78	22.22	14.29

JRA with no tenosynovitis, but there was no association with HLA-B27, a finding attributed by the authors to the exclusion of cases of ankylosing spondylitis from their study.

The discrepancy between the findings of most of the above-mentioned authors and our own may be explained by some racial differences between Japanese and Caucasians; however, it is more likely that some patients with juvenile ankylosing spondylitis may have been included among the Caucasian groups. The incidence of HLA-B27 in normal Japanese controls and in 27 patients with JRA was 0%, while it was 74% in Japanese patients with ankylosing spondylitis. These results suggest that the second explanation is the more likely one. We have seen some cases of juvenile ankylosing spondylitis where the early clinical features were almost indistinguishable from those of JRA, but after long-term follow-up these patients showed definite clinical features of ankylosing spondylitis. In fact, diagnosis of ankylosing spondylitis or Reiter's syndrome eliminated those patients from our study. 2 patients with juvenile ankylosing spondylitis were so eliminated after long-term follow-up. The increased frequency of HLA-B27 reported in other studies could indicate that patients with juvenile ankylosing spondylitis were not excluded from the group of JRA patients.

HLA-B27 was never found in our 181 normal controls. We have typed HLA antigens in over 3000

normal persons or patients with disorders other than rheumatic diseases. However, HLA-B27 has been found in only 6 of these (0.2%). Saito *et al.* (1975) reported that the incidence of HLA-B27 was 1.5% in 200 normal Japanese and Tsuji and Fukunishi (1973) found 0% in 248. These reports show that the incidence of HLA-B27 in the Japanese population is much lower than in Caucasians. This may be one of the reasons why in ankylosing spondylitis, also, the incidence of HLA-B27 is lower in Japanese patients. The low incidence of ankylosing spondylitis in Japan may be due to the low incidence of HLA-B27 in the Japanese population. However, Amor *et al.* (1974) and Dick *et al.* (1975) reported recently that the incidence of HLA-B27 in Caucasian patients with ankylosing spondylitis was 81% and 82.4%, respectively. These figures are closer to ours.

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