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HLA antigens in sarcoidosis

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SUMMARY

The HLA antigens were identified in sixty-five patients with sarcoidosis, comprising forty-five with uveitis, twelve with erythema nodosum and eight with arthritis. In the group with arthritis, B8 was present in seven of eight ($P=0{\cdot}0016$) and the haplotype 1,8 in five of eight ($P=0{\cdot}0053$). A1 was present in 44% with uveitis ($P=0{\cdot}04$). There was no other significant disturbance of antigen frequencies in uveitis or in erythema nodosum, but it was noteworthy that B27 was present in only two patients with uveitis.

INTRODUCTION

It is not known why patients with sarcoidosis present with widely different clinical expressions of the same disease. A possible explanation is that these manifestations are genetically determined, so we have studied the distribution of inherited histocompatibility (HLA) antigens in sarcoidosis patients who developed acute anterior uveitis, erythema nodosum or arthritis. In previous studies of sarcoidosis (Kueppers, Brackertz & Mueller-Eckhardt, 1972; Hedfors & Möller, 1973), patients with particular clinical features were not selected and the overall distribution of HLA antigens was normal, except that individuals with B7 were more likely to retain a negative tuberculin response and to become asymptomatic (Persson *et al.*, 1975).

PATIENTS AND METHODS

During the last 27 years, 1000 patients with sarcoidosis have attended the Royal Northern Hospital Sarcoidosis Clinic; from them were selected patients who had had acute anterior uveitis, erythema nodosum or arthritis due to histologically-proven sarcoidosis. In order to assess these features individually, patients with more than one manifestation were excluded. Thus, the relatively common combination of erythema nodosum and arthritis was excluded in this preliminary study. Of 149 patients selected, sixty-five were able to participate, comprising forty-five with acute anterior uveitis, twelve with erythema nodosum and eight with arthritis. The HLA antigens were identified using a modified two-stage lymphocytotoxicity micromethod, testing the lymphocytes of patients for twenty-two different antigens (Terasaki & McClelland, 1964). The significance of the results was calculated from a Z-variate obtained from the normal approximation to the binominal difference between two proportions.

RESULTS

In this series of sixty-five patients, A1 was present in 44% compared with 28% in controls ($P=0{\cdot}011$), and B8 in 45% compared with 27% of 1300 controls ($P=0{\cdot}006$) (Table 1). The haplotype 1,8 was present in 28% compared with 17% of controls ($P=0{\cdot}039$). In the patients with arthritis, B8 was present in seven of eight ($P=0{\cdot}0016$) and the haplotype 1,8 in five of eight ($P=0{\cdot}0053$). The antigen frequencies were not significantly abnormal in the patients with uveitis or erythema nodosum, except that A1 was present in 44% of those with uveitis ($P=0{\cdot}04$). B27 was present in only two patients with

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TABLE 1. HLA antigens in sixty-five sarcoidosis patients with uveitis, erythema nodosum or arthritis and controls

Antigens $n=22$	Uveitis $n=45$ (%)	Erythema nodosum $n=12$ (%)	Arthritis $n=8$ (%)	Controls $n=1300$ (%)
1	20 (44)	4 (33)	5 (62)	28
2	19 (42)	6 (50)	5 (62)	50
3	12 (27)	5 (42)	0 —	27
9	8 (18)	0 —	3 (37)	18
10	5 (11)	0 —	0 —	9
11	8 (18)	0 —	0 —	11
28	0 —	0 —	0 —	0·5
29	1 (2)	2 (17)	1 (12)	10·5
Blanks	17 (38)	7 (58)	2 (25)	41
5	6 (13)	1 (8)	0 —	10
7	16 (36)	5 (42)	2 (25)	28
8	15 (33)	7 (58)	7 (87)	27
12	13 (29)	3 (25)	4 (50)	30
13	2 (4)	0 —	0 —	3
W35	3 (7)	1 (8)	0 —	8
W40	3 (7)	1 (8)	0 —	9
14	4 (9)	0 —	0 —	16
W15	6 (13)	0 —	0 —	13
W17	4 (9)	1 (8)	0 —	9
18	0 —	0 —	0 —	1
W21	0 —	0 —	0 —	1
W22	0 —	0 —	1 (12)	3
27	2 (4)	1 (8)	1 (12)	8
Blanks	16 (36)	4 (33)	1 (12)	41

uveitis and one patient each with erythema nodosum and arthritis. In the series, resolution of the chest radiograph had occurred in thirty-five of fifty-four patients with intrathoracic disease, and notably in sixteen of eighteen with the haplotype 1,8 and seventeen of nineteen with B7. A negative tuberculin test was not more frequent in patients with B7.

DISCUSSION

The apparent relationship between B8 and arthritis associated with sarcoidosis may be important and requires further study. By analogy with other diseases, it is possible to understand how individuals with B8 who have sarcoidosis might be more susceptible to arthritis. It is known that B8 is associated with several autoimmune disorders, and this antigen has been described as a genetic marker of increased immune responsiveness. More striking is the presence of B27 in only 4% of patients with acute anterior uveitis associated with sarcoidosis, which is in sharp contrast to the findings at Westminster Hospital that B27 was present in 43% of patients with acute anterior uveitis who had no evidence of an associated disease and in 86% of patients who had uveitis associated with ankylosing spondylitis, Reiter's disease and other disorders (Brewerton, 1975). Clinically the types of uveitis associated with B27 are similar to the uveitis of sarcoidosis, and it might have been expected that it too would be related to B27. The absence of such an association in sarcoidosis is important, although difficult to interpret because there are several plausible explanations. The uveitis of sarcoidosis might be a distinct entity despite its clinical similarity; the 43% of patients with B27 and uveitis alone might represent a forme fruste of ankylosing spondylitis without rheumatic disease; or there might be genetic factors predisposing to uveitis which are associated with B27 in some circumstances but not in others. Further investigation is required, including family studies.

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