Histocompatibility antigens in psoriatic arthritis

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Lambert, J. R., Wright, V., Rajah, S. M., and Moll, J. M. H. (1976). *Annals of the Rheumatic Diseases*, 35, 526-530. **Histocompatibility antigens in psoriatic arthritis.** Histocompatibility (HL-A) antigen typing was performed on 82 patients with psoriatic arthritis. The prevalence of HLA-B27 was increased (28%) compared with that in a control group (7.5%), and this was most marked in those with spinal changes. The prevalence in patients with sacroiliitis and syndesmophytes was 75%, with sacroiliitis alone 78%, but with syndesmophytes and normal sacroiliac joints only 36%. The overall prevalence in psoriatic spondylitis was 60%, with a prevalence of 71% in those fulfilling the New York criteria for ankylosing spondylitis. The prevalence was not increased in those with only peripheral arthritis (11%).

The prevalence of HLA-B13 was decreased in those with psoriatic spondylitis, though this was not statistically significant. The overall prevalence of HLA-BW17 was increased, this being particularly so in those with syndesmophytes, but values were not significant.

The association of the histocompatibility antigen (HL-A) B27 and ankylosing spondylitis is now firmly established (Table I). A high prevalence has been shown in probands and relatives (Brewerton and others, 1973a; Schlosstein and others, 1973). It is also generally accepted that a high prevalence of HLA-B27 is found in various other seronegative inflammatory arthritides with spinal involvement. These include Reiter's disease (Brewerton and others, 1973b; McClusky, Lordon, and Arnett, 1974; Morris and others, 1974), the arthritis of inflammatory bowel disease (Brewerton and others, 1974a; Bluestone and others, 1975) and Still's disease (Edmonds and others, 1974; Hall and others, 1975).

While a raised prevalence of HLA-B27 has also been found in patients with psoriatic arthritis, especially in those with spinal involvement, the level of this increase is disputed (Table II). Brewerton and others (1974b) found a prevalence of 64% in those with spinal involvement, and Karvonen and others (1974) obtained similar figures. However, Metzger and others (1975) found a prevalence of only half this value. In contrast, McClusky and others (1974) and Medsger and others (1974) found

Table I HLA-B27 in ankylosing spondylitis and related conditions

	No. in group	% with HLA-B27	Reference
Controls		7-10	
Ankylosing spondylitis	75	96	Brewerton and others (1973a)
	40	83	Schlosstein and others (1973)
Reiter's disease			
Peripheral	23	65	Brewerton and others (1973b)
Spinal	10	100	
Peripheral	19	95	Morris and others (1974)
Spinal	6	100	
Peripheral	19	53	McClusky and others (1974)
Spinal	11	82	
Inflammatory bowel disease			
Peripheral	8	12.5	Brewerton and others (1974a)
Spinal	20	65	
Peripheral	14	0	Bluestone and others (1974)
Spinal	12	67	
Still's disease			
Peripheral	22	14	Edmonds and others (1974)
Spinal	8	100	
Peripheral	63	25	Hall and others (1975)
Spinal	3	100	

Table II Prevalence of HLA-B27 in psoriatic arthritis related to spinal involvement

	No. in group	% positive for HLA-B27	Reference
Peripheral	47	23	Brewerton and others (1974)
Spinal	22	64	
Peripheral	17	24	Karvonen and others (1974)
Spinal	19	58	
Peripheral	8	0	McClusky and others (1974)
Spinal	6	100	
Spinal	8	87.5	Medsger and others (1974)
Peripheral	17	18	Metzger and others (1975)
Spinal	23	35	

values of 100% and 87.5%, respectively. Hence, in the study of Metzger and others (1975) more patients with spinal involvement were negative for HLA-B27 than were carriers. In those patients with only peripheral arthritis all studies show a prevalence similar to that in control populations, with the exception of McClusky and others (1974) who found no carriers in this group. In several of these studies, however, small numbers of subjects and different definitions of spinal involvement were used.

The reported prevalence of HLA-B13 and BW17 and more recently BW16, in uncomplicated psoriasis has varied (Russell, Schultes, and Kuban, 1972; White and others, 1972; Krulig and others, 1975). However, Karvonen and others (1974) noted that the frequency of HLA-BW17 was decreased in psoriatic arthritis, with or without spinal involvement, perhaps indicating a different pathogenesis for the psoriatic symptoms, while the prevalence of HLA-B13 was increased in patients with spinal involvement, but not in those with only peripheral arthritis or with uncomplicated psoriasis. They felt that this antigen was not associated with inherited psoriasis but with severe arthritic involvement.

We have studied the HL-A grouping of patients with psoriatic arthritis to determine the prevalence of this association and have also related this to its radiological characteristics, particularly of the spine. The patients formed part of a group observed over many years in a prospective study of the natural history of the condition. The clinical characteristics were known in detail. The findings in patients with psoriasis and other coincidental arthritic complaints are reported.

Materials and methods

Eighty-two patients with psoriatic arthritis diagnosed on the criteria of Moll and Wright (1973) were studied. A full history and examination were carried out with special reference to the spine. Neck movement was assessed

subjectively in three planes, and chest expansion and mobility of the lumbar spine by the criteria of Moll and Wright (1971, 1972). Anteroposterior x-rays of the sacroiliac joints were available in 73 patients; oblique views were taken in doubtful cases. Complete sets of spinal x-rays were available in 29 of these patients. X-rays of the cervical spine were available in a further 17, of the dorsal spine in 4, and of the lumbar spine in 15. 19 patients who had had x-rays of the sacroiliac joints had no spinal x-rays. X-rays of the hands and feet were available in 44 patients, of the hands only in 6, and of the feet alone in one patient.

Ankylosing spondylitis was diagnosed and graded by the New York criteria (Bennett and Wood, 1968) except that estimation of joint space was not included in the assessment of sacroiliitis (Macrae, Haslock, and Wright, 1971). Syndesmophytes are generally accepted as a manifestation of spondylitis (Collins, 1949; Séze, Lacapère, and Amoudruz, 1952) and their presence was noted. It is sometimes difficult to distinguish early cases from osteophytes and later examples from senile ankylosing hyperostosis. We followed the recommendations of Riley, Ansell, and Bywaters (1971), who reviewed the situation fully. X-rays were read without reference to the HL-A status. HL-A typing was performed for 21 antigens by the National Institutes of Health, lymphocyte microcytotoxicity technique (1972). The results obtained in over 1100 normal Caucasian blood donors, laboratory staff, and family members of patients awaiting renal transplant were used as controls. Significance values of differences in prevalence were determined by multiplying the P value, obtained by a χ^2 test, by 21 the number of variables (antigens) tested. This has been shown to give a more accurate estimate of significance where attributes are linked (Croxtton, 1959). In χ^2 tables with small numbers of results, Yates's correction was used.

Results

Table III gives the prevalence of HLA-B27 in all patients with psoriatic arthritis, and relates this to spinal involvement. There is a statistically significant

Table III Prevalence of HLA-B27 in psoriatic arthritis (PsA) related to spinal involvement

	No.	% positive for HLA-B27
PsA total	82	28*
PsA with syndesmophytes and sacroiliitis	8	75*
PsA with sacroiliitis and no syndesmophytes	9	78*
PsA with syndesmophytes and normal sacroiliac joints	11	36*
Ps spondylitis	28	60*
Ps + ankylosing spondylitis	7	71*
PsA — peripheral only (complete spinal x-rays)	9	11
PsA — peripheral only (no clinical and/or radiological evidence of spondylitis)	54	9
Controls	1000	7.5

* $P < 0.01$ when multiplied by 21.

increase of HLA-B27 in the total group, even more marked in those with spinal changes. Sacroiliitis and syndesmophytes both show a significantly raised prevalence of HLA-B27, particularly so for patients with sacroiliitis with or without syndesmophytes. Of the 9 patients who had complete spinal x-rays with no abnormality, only one was positive for HLA-B27—the same prevalence as in controls. A similar prevalence was found in those patients without clinical and/or radiological evidence of spinal involvement. Psoriatic spondylitis was diagnosed when either sacroiliitis or syndesmophytes were observed and the prevalence of HLA-B27 was raised in these 28 patients. A high prevalence was noted in the 7 patients who fulfilled the criteria for ankylosing spondylitis.

Syndesmophytes were often situated either anteriorly in the midcervical region or laterally at the thoracolumbar junction. Table IV gives the prevalence of HLA-B27 to syndesmophytes in these different sites. The difference in prevalence between those patients with only cervical or only thoracolumbar syndesmophytes is significant. In Table V the clinical characteristics of those with the HLA-B27 antigen are contrasted with those without. There was a significantly higher male preponderance among those with HLA-B27, and also a significantly higher prevalence of iritis, syndesmophytes, and fulfilment of the criteria for ankylosing spondylitis, but these differences were not statistically significant. There was no difference in the age of onset or duration of joint, skin, or nail disease. Those without HLA-B27 were more likely to have had severe arthritis and less likely to have had severe skin changes. There was no statistical difference between the prevalence of erosive changes and distal interphalangeal joint involvement between those with and those without HLA-B27.

The prevalence of HLA-B13 and BW17 (Table VI), showed no significant differences. No patients with spondylitis had HLA-B13. The prevalence of HLA-BW17 was raised especially in those with syndesmophytes, but this increase was not significant.

HL-A typing was also done in a small number of patients with psoriasis and other rheumatic

Table IV *Prevalence of HLA-B27 related to location of syndesmophytes*

<i>Location of syndesmophytes</i>	<i>No.</i>	<i>% positive for HLA-B27</i>
Cervical region only	4	75*
Thoracolumbar junction only	6	33½*
Both sites	8	62.5

* Difference between cervical and thoracolumbar, $P < 0.02$.

Table V *Characteristics of patients with psoriatic arthritis, related to the presence of HLA-B27*

	<i>HLA-B27 positive</i>	<i>HLA-B27 negative</i>
No. of males	16	22
No. of females	7	37
Ratio males: females	2.3:1	0.6:1†
Mean age at review (years)	49.6	47.6
Mean age at onset of arthritis (years)	35.6	36.6
Mean duration of arthritis (years)	14	11
Mean age of onset of psoriasis (years)	31.7	27.7
Mean duration of psoriasis (years)	17.9	19.9
Severity of peripheral arthritis (%)		
Nil	17	5
Mild	39	25
Moderate	22	21
Severe	22	49†
Severity of skin psoriasis (%)		
Mild	75	65
Moderate	10	29*
Severe	15	6
Prevalence of nail changes (%)	56.5	74
Mean age of onset of nail changes (years)	38.1	37.3
Prevalence of iritis (%)	18	5
Prevalence of sacroiliitis (%)	64	6½
Prevalence of ankylosing spondylitis (%)	22	5

* $P < 0.05$; † $P < 0.02$; ‡ $P < 0.01$.

Table VI *Prevalence of HLA-B13 and BW17 in psoriatic arthritis (PsA), related to spinal involvement*

	<i>No.</i>	<i>% with HLA-B13</i>	<i>% with HLA-BW17</i>
Controls		3.6	6
All PsA	82	7.3	19.5
PsA with sacroiliitis	17	0	14
PsA with syndesmophytes	19	0	23.5
PsA peripheral only (complete spinal x-rays)	9	11	11
PsA peripheral only (no clinical and/or radiological spondylitis)	54	11	24

complaints. 3 had coincidental rheumatoid arthritis, and of these one had HLA-B27, 3 HLA-BW17, and none HLA-B13. 9 had coincidental osteoarthritis, of whom none had HLA-B27, 4 had HLA-BW17, and 2 HLA-B13. 3 patients were thought to have psoriatic arthritis without psoriasis (Baker, Golding and, Thompson, 1963; Ross, 1964) and of these one had HLA-B27, all HLA-BW17, and none HLA-B13.

Discussion

It has been shown that there is an increased prevalence of HLA-B27 in psoriatic arthritis, and that its presence is related to spinal involvement. Our values are similar to those of Brewerton and others (1974b), and are higher than those found by Metzger and

others (1975). It is more usual for patients with psoriatic arthritis to be HLA-B27 negative, as this antigen is not found in 75% of these patients. However, values are raised in those patients with spinal changes. 71% of those fulfilling the New York criteria for ankylosing spondylitis were positive, as were 60% of those with sacroiliitis or syndesmophytes. These values are lower than in idiopathic ankylosing spondylitis (Brewerton and others, 1973a; Schlosstein and others, 1973) and Reiter's disease (Brewerton and others, 1973b; McClusky and others, 1974; Morris and others, 1974), and are lower than the values for psoriatic arthritis found by McClusky and others (1974) and Medsger and others (1974). However, there is a striking similarity between the results obtained in these diseases, findings which add further weight to the Leeds concept of 'seronegative spondarthritis' (Moll and others, 1974).

It is difficult to explain the differences between the results of Brewerton and others (1974a), those of our own study, and those of Metzger and others (1975). The latter have found a high frequency of spinal involvement, 58% of 40 patients, compared with Brewerton's 32% of 69 patients, and our 33% of 82 patients. They defined spondylitis by the Rome criteria (Kellgren, 1962) and according to McEwen and others (1971). Perhaps their criteria were less stringent than ours, though we included patients without sacroiliitis if syndesmophytes were present. The duration of psoriasis and of arthritis was slightly longer in this study, though it is unlikely that this accounts for the discrepancy.

The high prevalence of HLA-B27 in patients with syndesmophytes and normal sacroiliac joints is further evidence of the importance of these findings

in the diagnosis of psoriatic spondylitis. The male preponderance in those patients who were HLA-B27 positive is accounted for in part by the weighting by patients with ankylosing spondylitis.

There is a high prevalence of nail changes in patients with psoriatic arthritis, 81% compared with 30% of those with uncomplicated psoriasis (Moll and Wright, 1973), though the prevalence is lower in those patients positive for HLA-B27 and is higher than in uncomplicated psoriasis.

There was no statistically significant alteration in the prevalence of HLA-B13 and BW17, in contrast to uncomplicated psoriasis where both Russell and others (1972) and White and others (1972) found the prevalence of these antigens to be increased. The findings for HLA-BW17 are in keeping with those of Karvonen and others (1974) though his prevalences were slightly lower. We have not found that HLA-B13 is related to psoriatic spondylitis. The report by Krulig and others (1975) that HLA-BW16 was present in 5% of controls and 22% of psoriatic patients is surprising. We have found this antigen in only 2 or 3 out of several hundred control subjects and in none of the small number of patients with psoriatic arthritis in whom we were able to test for it.

It is concluded that HLA-B27 is an indicator of spinal involvement in psoriatic arthritis and this probably represents further evidence of its relationship to the other seronegative spondarthritides.

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