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HL-A27 AND W10 IN REITER'S SYNDROME AND NON-SPECIFIC URETHRITIS

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Abstract. By means of a standard lymphocyte microcytoxic technique, the tissue types were fully determined in 41 patients with non-gonococcal urethritis and 25 patients with Reiter's syndrome. The antigen HL-A27 was identified in 14 of the patients with Reiter's syndrome and occurred in 3 of the patients with non-gonococcal urethritis. An excess of the genotype HL-A27/W10 was found in patients with Reiter's syndrome. There was no correlation between the duration or the severity of the clinical manifestations of the syndrome and the presence of the antigens. The possibility that the syndrome might result from various pathogenic mechanisms is discussed.

Key words: Reiter's syndrome; Non-specific urethrilis; HL-A27; Sacroiliitis; Uveitis

By the late 'sixties, a considerable body of knowledge had been accumulated on the aetiology of Reiter's syndrome. The disease appeared to have a sexually transmitted origin in certain countries (14) and also to occur in both isolated cases and "epidemic" outbreaks in other geographical locations (10). There had been reports of Reiter's syndrome occurring in the same family (7, 13) and there was an awareness of the close clinical association between ankylosing spondylitis and Reiter's syndrome. The close genetic relationship between ankylosing spondylitis, psoriasis, and Reiter's syndrome had been established by Lawrence (11). While there is little doubt that both the dysenteric and sexually transmitted types of the Syndrome can co-exist in the same community (8), it would be the opinion of the majority of workers that the Syndrome in the United Kingdom follows sexual intercourse (21).

In view of the recent reports relating the presence of HL-A13 and W17 antigen to the occurrence of psoriasis (17) and HL-A27 with ankylosing spondylitis (4, 18) and reactive arthritis (1), an attempt has been made to correlate clinical findings in Reiter's syndrome with the associated HL-A phenotypes. Recently, Woodrow (22) reported that 65%, i.e. 13 of 20 patients with Reiter's syndrome, were HL-A27 positive and Zachariae et al. (23) referred to a series where 11 of 17 patients with Reiter's syndrome had HL-A27. Although the impression has been created (22) that the association of certain antigens with psoriasis and ankylosing spondylitis were major contributions to our understanding of their pathogenesis and genetics, it is important to consider at the outset the actual addition to our knowledge which these observations have made.

Our work was intended to establish whether their results were reproducible in our population, to correlate the clinical manifestations of the syndrome with the presence of other antigen types, and to study the tissue types among patients with uncomplicated non-gonococcal urethritis. The latter group are important since only 0.8% (6) of patients with non-gonococcal urethritis will develop the complete syndrome.

MATERIALS AND METHODS

All 25 patients with Reiter's syndrome had been referred to venereology clinics and with a few exceptions had been under observation for some years. All manifested the triad of polyarthropathy, non-gonococcal urethritis and ocular involvement whilst under our care. Forty-one patients with uncomplicated non-gonococcal urethritis were also studied. Non-caucasians were excluded in order that a homogeneous population could be examined. No females were included since the establishment of a diagnosis of non-gonococcal urethritis in the female presents certain difficulties. Tissue typing was carried out in ignorance of the clinical data. The ages of the patients with Reiter's syndrome ranged from 15 to 57 with an average of 34 years. In addition to the triad of symptoms, 7 had uveitis, 5 had sacroiliitis, 4 had keratoderma blennorrhagica and none had aortitis. The ages of the patients with uncomplicated non-gonococcal urethritis ranged from 16 to 52 with an average of 28 years.

Table I. *HL-A types in Reiter's disease and non-specific urethritis*

HL-A Antigen ($n=27$)	Reiter Obs ($n=25$)	Reiter Exp[a]	NSU Obs ($n=41$)	NSU Exp
1st Segregant Series (LA)				
HL-A1	3	8.5	9	13.9
HL-A2	18	12.0	23	19.7
HL-A3	4	6.7	13	11.1
HL-A9	4	4.5	8	7.5
HL-A10	4	2.2	2	3.6
HL-A11	2	2.7	7	4.5
HL-A28	2	1.0	5	2.1
W29	2	1.7	2	2.9
W30/31	0	2.3	1	3.7
W32	3	0.5	3	0.8
Blank	8	7.9	9	12.2
2nd Segregant Series (FOUR)				
HL-A5	1	2.5	5	4.1
HL-A7	2	6.5	9	10.6
HL-A8	2	5.7	12	9.4
HL-A12	7	7.7	15	12.7
HL-A13	1	1.0	1	1.6
HL-A14	1	1.5	0	2.5
HL-A17	2	2.2	4	3.7
HL-A27	14	2.2	3	3.7
W5	4	3.2	4	5.3
W10	5	2.5	9	4.1
W15	1	3.5	4	5.7
W18	1	1.5	5	2.5
W21	0	0.2	0	0.4
W22	1	0.5	2	0.8
W16	0	0.3	1	0.6
SL-ET	3	0.2	0	0.6
TY	0	0.9	1	1.5
Blank	5	3.7	7	10.2

[a] Expected values obtained from data on 1 000 normal blood donors.

The lymphocyte microcytotoxic test was performed by the method of Gelsthorpe & Doughty (9). Twenty-seven HL-A antigens (Table I) were identified, with at least 3 antisera per specificity, with the exception of W16 (2 antisera) and TY (1 antiserum).

DISCUSSION

The investigation of the tissue types of patients with Reiter's syndrome has revealed an excess of patients with HL-A27. The figure of 14 out of 25 is very much in keeping with the results of similar series reported by Zachariae et al. (23) and Woodrow (22). An attempt to relate the individual components of the syndrome with the tissue type has not indicated marked differences between patients with and without HL-A27. No correlation was found between the severity of the illness and the presence of HL-A27, as judged by frequency of attacks or the duration of the illness (Fig. 1). However, while the numbers are small, it does appear that sacroiliitis and uveitis only occur in those patients with HL-A27. Thus, a knowledge of the tissue type may be of particular value in the anticipation and early recognition of the latter complications.

Although not expressed in Table I, an excess of the type HL-A27/W10 (both antigens of the second sub-locus which segregate independently) was found in patients with Reiter's syndrome. It should be noted that W10 and HL-A27 can be recognised as discrete antigens by the use of specific antisera, even though they are members of a cross-reacting group (12). Five cases of Hl-A27/W10 were observed against an expected 1.4. Since the numbers investigated are not large enough to be significant, we feel this point is worthy of further investigation.

As there is a high male/female ratio in Reiter's syndrome and ankylosing spondylitis (3, 16), the possibility that HL-A27 had a similarly high distribution ratio was excluded. In 1 000 random Caucasian blood donors (Sheffield region), the antigen HL-A27 frequency was 9% in males and 8% in females.

A parallel study of 41 patients with non-gonococcal urethritis showed the incidence of HL-A27 to be the same as for a normal random population (Table I). Therefore the possibility that the presence of the HL-A27 antigen could be effective in selecting for the initial infection of non-gonococcal urethritis is very unlikely.

This would seem to suggest that the HL-A27 antigen can influence the subsequent development of Reiter's syndrome in a patient with non-gonococcal urethritis. Since shigella (15), Mycoplasma (2), *Yersinia entercolitica* (19), and chlamydia (20) have all been related to the occurrence of the syndrome in certain populations, it would be of value to relate the relevant organism to the presence of HL-A27. Alternatively, HL-A27 may be a passive marker for a genetic complex which influences the development of Reiter's syndrome after infection by any arthrogenic agent.

As can be seen from Fig. 1, there was little difference in the mean duration of the illness between those patients who had HL-A27 and those who lacked the antigen. The apparent relationship between the presence of HL-A27, sacrioliitis and uveitis as observed by Brewerton et al. (5) and ourselves,

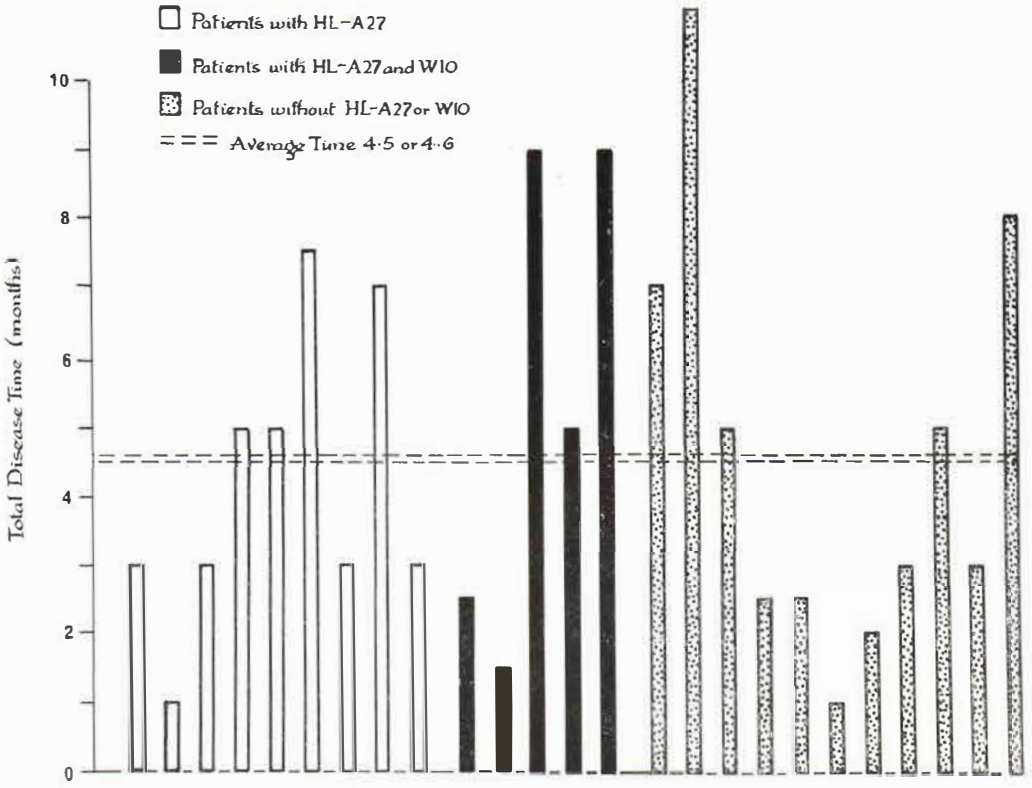

Fig. 1. The duration of the illness in patients with Reiter's syndrome analysed with reference to the presence or absence of HL-A27 and W10.

leads us to postulate that a proportion of those patients who develop the Reiter's syndrome do so by a pathogenic mechanism different from that in the remaining patients who possess HL-A27. If this is the case then Reiter's syndrome is in fact a syndrome complex grouping together at least two distinct conditions which have a markedly similar presentation.

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