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HL-A 27 in Crohn's disease

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There has been recent interest in the association between human leucocyte antigen-27 and ankylosing spondylitis. Brewerton, Caffrey, Hart, James, Nicholls, and Sturrock (1973) and Schlosstein, Terasaki, Bluestone, and Pearson (1973) demonstrated this antigen in 96% and 87% of ankylosing spondylitics, respectively, as compared with about 5% in normal controls. It is well known that recurrent Reiter's syndrome leads to spinal changes identical to those of ankylosing spondylitis and this prompted Brewerton to screen 33 patients with Reiter's disease of whom 25 were found to have HL-A 27. These results were confirmed (Aho, Ahvonen, Lassus, Sievers, and Tilikainen, 1973; Zachariae, Hjortshøj, and Kissmeyer-Nielsen, 1973).

It is also known that chronic inflammatory bowel disease, such as ulcerative colitis and Crohn's disease, are associated with sacroiliitis and ankylosing spondylitis (Acheson, 1960). Recently, Haslock (1973) investigated a series of patients with known Crohn's disease and their relatives and concluded that the spinal complications of Crohn's disease arise on a coincidental genetic basis, whereas the peripheral arthropathy is a direct complication of the bowel disease. Patients with Crohn's disease and ankylosing spondylitis have been screened for HL-A antigens (Asquith, MacKintosh, Stokes, Holmes, and Cooke, 1974). However, it seemed pertinent to investigate the HL-A profile of patients with Crohn's disease to determine whether those with HL-A 27 are more likely to have rheumatological disease.

Method

All patients with proven Crohn's disease who were attending the Bristol Royal Infirmary or Frenchay Hospital, Bristol, were asked to take part in this investigation. The evidence for the diagnosis of Crohn's disease was reviewed and only those in whom the diagnosis was confirmed by histology were accepted unless there was good radiological and clinical evidence which was agreed by both the gastroenterologist and radiologist concerned. Certain patients were specifically referred for study because they were known to have both Crohn's disease and ankylosing spondylitis. Their results were analysed separately.

A full history was taken from the patient with particular reference to peripheral joint disease and symptoms referrable to the spine and sacroiliac joints. Particular note was made regarding any of the other extra-bowel manifestations of Crohn's disease and a full family history was also obtained. The patients were examined with particular attention being paid to possible axial or peripheral joint disease.

The HL-A profiles of the patients were determined using a standard microcytotoxicity technique (Dick and Crichton, 1972). The sacroiliac joints of the patients were reviewed from the barium meal and barium enema radiographs using the method of Macrae, Haslock, and Wright (1971). When necessary, further *x*-rays of the sacroiliac joints were obtained.

Results

Of the 118 patients in whom the diagnosis of Crohn's disease had been recorded, the diagnosis was confirmed in 74 who agreed to take part in the investigation. The HL-A profiles of these 74 patients did not differ significantly from the panel of controls of the National Tissue Typing Reference Laboratory (Table I). HL-A 13 was found in twice as many of the Crohn's patients as in the control group, but this difference was not statistically significant. Six patients were found to have HL-A 27 and their HL-A profiles are shown in Table II. Three of these six patients with HL-A 27 had Crohn's disease involving the large intestine, whereas only sixteen of the 68 patients without HL-A 27 had large bowel disease.

Of the 74 patients, thirteen said that they had suffered episodes of back pain. However, in none of these was the history typical of ankylosing spondylitis, but rather that of nonspecific back pain. Sacroiliitis or ankylosing spondylitis were not present in any of these thirteen patients. Limb joint symptoms were noted in two patients, one of whom had had an episode of shoulder pain and another of hip pain. There were no radiological changes in either of these two joints, but it is possible that these were episodes of the synovitis of Crohn's disease. HL-A 27 was not present in either of these two patients.

Examination of the patients showed that three had limitation of movement in the lumbar spine; however,

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Table I *HL-A antigens of patients with Crohn's disease and HL-A antigens of control population*

HL-A	*No. of patients with each antigen*	*Per cent. of patients with each antigen*	*Per cent. of controls with each antigen*
1	22	29·7	33·6
2	38	51·4	51·7
3	19	25·7	25·6
9	14	18·9	18·3
10	6	8·1	8·4
11	12	16·2	10·2
28	2	2·7	3·7
W 29	6	8·1	6·5
W 32	2	2·7	2·9
YM	6	8·1	7·5
5	8	10·8	8·4
7	17	23·0	25·6
8	18	24·3	25·1
12	26	35·1	23·7
13	8	9·5	4·34
W 5	11	14·86	11·0
W 10	9	12·16	11·2
17	5	6·8	7·6
W 18	5	6·8	3·4
W 21	3	4·1	1·7
W 22	2	2·7	5·3
27	6	8·1	7·4
W 15	6	8·1	4·8
W 6	5	6·8	
W 14	2	2·7	7·0
W 16	1	1·4	

W indicates that the antigen has been given a workshop number. This then becomes an HL-A number when the antigen has been established as a pure antigen.

Table II *Full HL-A profile of six patients with HL-A 27*

Case no.	*HL-A profile*
1	2. 3. 10. 27
2	2. 9. 7. 27
3	2. 5. 27
4	10. 27
5	1. 3. 8. 27
6	1. 11. 27

the restriction was in flexion rather than in the other planes, and radiographs showed degenerative changes in the spine only with no evidence of sacroiliitis.

Three patients showed evidence of sacroiliitis. In one the joints had completely fused and the other two showed typical erosive changes. However, there was no evidence of ligamentous calcification or limitation of spinal movement typical of ankylosing spondylitis. None of these three patients had HL-A 27 and the HL-A profiles of these three are shown in Table III.

Three patients were specifically referred because of known Crohn's disease and typical ankylosing spondylitis. Their HL-A profiles are shown in Table IV. HL-A 27 was only present in one of these patients.

Table III *Full HL-A profile of three patients with sacroiliitis*

Case no.	*HL-A profile*
7	1. 2. 5. 17
8	1. 2. 8. 13
9	2. 10. 12. 14

Table IV *HL-A profile of three patients with ankylosing spondylitis and Crohn's disease*

Case no.	*HL-A profile*
10	2. 32. 14. 27
11	2. 32. 12. 14
12	2. 9. 8. 13

Discussion

Sacroiliitis is a frequent complication of Crohn's disease (Haslock, 1973). However, sacroiliitis does not necessarily lead on to ankylosing spondylitis and indeed, ankylosing spondylitis is a comparatively uncommon complication of Crohn's disease. Haslock found that of 116 patients with Crohn's disease, nineteen had sacroiliitis and of these only eight had ankylosing spondylitis. In the present series of 74 patients with Crohn's disease, sacroiliitis was found in three but none had ankylosing spondylitis. It may be that the presence of the HL-A antigen is necessary for sacroiliitis to progress to typical ankylosing spondylitis, but it was found in only one of the three patients with ankylosing spondylitis. This antigen could act as a genetic marker indicating those who are susceptible to the progression of sacroiliitis to spinal involvement, and its absence might account for the protection of the spines in those patients with benign sacroiliac involvement. There appears to be no specific association between HL-A 27 and Crohn's disease itself or Crohn's disease with sacroiliac involvement alone, but we can speculate that if they should occur together, then it is likely that the more severe spinal disease will develop. If this were the case, then the detection of HL-A 27 could be of some prognostic value in Crohn's disease associated with sacroiliitis.

The frequency of HL-A 9 was found to be the same in patients with Crohn's disease as the control population. This is at variance with the findings of Asquith and others (1974), who found that in 56 patients with Crohn's disease HL-A 9 was significantly reduced.

Summary

74 patients with proven Crohn's disease were screened for human leucocyte antigen 27 (HL-A 27). Six were found to have this antigen which was similar to the

incidence of that of the control panel of the National Tissue Typing Laboratory. None of the six patients with HL-A 27 showed evidence of sacroiliitis and spondylitis. Three patients were found to have sacroiliitis, but HL-A 27 was not found in any of them. Of three further patients with Crohn's disease complicated by typical ankylosing spondylitis, HL-A 27 was only present in one.

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