

Lone aortic regurgitation, sacroiliitis, and HLA B27

Case history and frequency of association

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SUMMARY An account of aortic regurgitation complicating ankylosing spondylitis is given. Twenty patients with lone aortic regurgitation and without overt spondylitis were examined clinically and radiologically and tissue typed. No evidence of sacroiliitis could be found in any patient. HLA B27 was absent from this group, and no significant disturbance in antigen frequency was noted.

The allele HLA B27 is strongly associated not only with ankylosing spondylitis but also with its *formes frustes*, acute iritis and sacroiliitis in isolation, and with Reiter's syndrome. Aortic regurgitation has been reported in association with ankylosing spondylitis in 2 per cent of cases and characteristically occurs with peripheral joint involvement. Ankylosing spondylitis can present as an acute polyarthritis and fever, particularly in younger patients when it used to be mistaken for rheumatic fever. In this paper we describe such a case and give the results of a pilot study on a possible association between lone aortic regurgitation, sacroiliitis, and histocompatibility antigens.

Case report

A 46-year-old instrument mechanic, who had a history of repeated episodes of arthritis from the age of 13 with back pain since the age of 19, had a diagnosis of aortic regurgitation confirmed at the age of 21 years, though a murmur had first been noted at the age of 15. He was able to lead an active life until 2 years before admission when he became troubled with dyspnoea.

Physical examination disclosed a thin man with an obvious kyphosis and a rigid back. He was in sinus rhythm, with a collapsing pulse; the blood pressure was 190/80 mmHg. There was a systolic murmur at the aortic area and a long early diastolic murmur at the left sternal edge.

The chest *x*-ray film showed severe cardiac enlargement with a dilated aortic root. The sacroiliac joints were fused and the lumbar spine had classic changes of ankylosing spondylitis.

The electrocardiogram showed left ventricular

hypertrophy grade III. The echocardiogram showed an enlarged left ventricle with diastolic fluttering of the anterior mitral cusp. Cardiac catheterisation disclosed no evidence of aortic stenosis and no end-diastolic gradient across the mitral valve. Angiography showed severe aortic regurgitation, a tricuspid aortic valve and patent coronary arteries.

At operation the left ventricle was grossly enlarged and hypertrophied and the left atrium was of normal size. The aortic valve was tricuspid with fibrosis extending from the base of the cusp, there was no evidence of calcification or commissure fusion, and there was no evidence of aortic root disease. A satisfactory aortic valve replacement with a Hancock prosthesis was performed.

PILOT STUDY

To examine the possibility that lone aortic regurgitation without overt spondylitis may occur with HLA B27, 20 patients, 12 men and 8 women, were studied. All these patients had lone aortic regurgitation but no past history suggestive of rheumatic fever. Patients were questioned for a history of backache and examined for evidence of spondylitis; *x*-ray films of the lumbar spine and sacroiliac joints were taken and they were tissue typed. Though there was often a history of backache there was no limitation of spinal movement. In none was there radiological evidence of sacroiliitis though degenerative changes were common.

TISSUE TYPING

The technique for tissue typing was as follows.

Peripheral lymphocytes were separated on a Ficoll-sodium metrizoate density gradient, and typed on glass plates employing a two-stage, two-

Table HLA antigen frequencies in lone aortic regurgitation

Antigen	Per cent	Antigen	(n=20) Per cent
A1	35	B5	—
A2	65	B7	15
A3	15	B8	30
A9	10	B12	40
AW23	5	B13	—
AW24	5	B14	15
A10	—	B15	20
A25	5	BW16	5
A26	—	B17	15
A11	10	B18	15
AW19	—	BW21	—
AW30	—	BW22	—
AW31/33	5	B27	—
AW32	5	BW35	5
A28	10	BW37	5
A29	15	B40	15
		BW41	—
Blank + 1AG	15	Blank + 1AG	20

colour fluorochromatic microcytotoxicity technique based on the procedure of Bodmer *et al.* (1967).

A panel of 98 HLA antisera, kindly supplied by the National Tissue Typing Reference Laboratory, Bristol, was used to define a total of 16 A-locus and 17 B-locus specificities. Five potent, well-characterised antisera to B27 were included.

The distribution of phenotypes found in the patient group is listed in the Table. HLA B27 was found to be absent from this group. There was no evidence of disturbance in antigen frequency, and analysis using a control group of 417 healthy random Bristol blood donors (C. Entwistle, personal communication) confirmed that there was no significant deviation.

Discussion

With the decline of rheumatic fever, aortic regurgitation now represents a more heterogeneous group but the association with ankylosing spondylitis is not frequent. Moreover, death from aortic regurgitation complicating this condition is rare, for though deaths from all circulatory diseases were in excess in men suffering from ankylosing spondylitis the difference from the expected was of only borderline significance statistically (Radford *et al.*, 1977).

Various studies report the incidence of HLA B27 in ankylosing spondylitis as greater than 88 per cent (Whitfield, 1976). Of these patients 2 per cent will develop aortic regurgitation which is far in excess of that expected. This implies a relation

between HLA B27 and aortic regurgitation in these cases. HLA B27 is associated not only with ankylosing spondylitis but also with acute anterior uveitis alone. That this triad is even more closely linked has been shown by the demonstration of abnormal radioisotope scans of the sacroiliac joint in 19 of 30 patients with acute anterior uveitis, none of whom had clinical or radiographic evidence of sacroiliitis. Of these 19, 11 carried HLA B27 (Russell *et al.*, 1976). The association between this allele and acute anterior uveitis in the absence of clinical or radiographic evidence of sacroiliitis leads to speculation on an association between HLA B27 and aortic regurgitation occurring without overt sacroiliitis or spondylitis. Though the numbers are small, it is evident from our figures that there can be no strong correlation.

Whitfield (1976) reports that cardiac manifestations of ankylosing spondylitis tend to be seen in the most severe forms of the disease as judged by degree of disability and peripheral joint involvement. This could explain the negative correlation of our findings. The association of aortic regurgitation with more severe ankylosing spondylitis implies that the aortic valve and root are less susceptible than the articular structures to the disease process, and that the development of aortic regurgitation in these cases may be associated with the virulence of a putative exciting agent or with the immune response genes.

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