Cardiovascular manifestations of ankylosing spondylitis

T. Douglas Kinsella,* M.D., F.R.C.P.[C], Louis G. Johnson,† M.D., F.R.C.P.[C] and R. Ian Sutherland,‡ M.D., F.R.C.P.[C], *Montreal*

Summary: The incidence of cardiovascular lesions in 97 patients with ankylosing spondylitis (AS) was found to be 14%; 8 patients had isolated aortic insufficiency (AI), 3 had isolated heart block, 2 had combined AI and heart block, and 1 had mitral insufficiency. In comparison with control groups of 81 patients with rheumatoid arthritis and 99 random hospital patients there was no increased incidence of isolated heart block in patients with AS. Clinical and postmortem findings indicated that the cardiovascular lesions of some patients with AS may antedate articular disease and may regress spontaneously. In addition, the unusual occurrence of AI in two patients with psoriatic spondylitis and in one with AS and regional enteritis is documented.

Résumé: *Les manifestations cardiovasculaires de la spondylite ankylopoïétique*

Nous avons constaté que l'incidence des lésions cardiovasculaires chez 97 malades souffrant de spondylite ankylopoïétique (SA) était de 14%. Chez 8 malades on trouvait une insuffisance aortique isolée (IA), chez 3 malades un blocage de coeur isolé, chez 2 malades une association de IA et de blocage du coeur et, chez un malade, une insuffisance mitrale. Par contre, chez un groupe-témoin de 81 malades souffrant d'arthrite rhumatoïde et 99 malades hospitalisés pris au hasard on ne notait aucune augmentation de l'incidence de blocage du coeur isolé chez les malades souffrant de SA. Les observations cliniques et les trouvailles postmortem indiquaient que les lésions cardiovasculaires chez certains malades souffrant de SA peuvent avoir existé antérieurement à la pathologie articulaire et peuvent régresser spontanément. En outre, nous signalons la présence exceptionnelle de IA chez deux malades souffrant de spondylite psoriasique et chez un autre souffrant de SA et d'une entérite régionale.

From the department of medicine, Queen Mary Veterans Hospital, Montreal

*Formerly consultant in rheumatology, Queen Mary Veterans Hospital; currently director, rheumatic diseases unit and associate professor of experimental medicine, McGill University, Montreal
†Formerly senior consultant in rheumatology, Queen Mary Veterans Hospital; currently senior physician, Royal Victoria Hospital and associate professor of medicine, McGill University, Montreal
‡Fellow of the Canadian Arthritis and Rheumatism Society

Reprint requests to: Dr. T. Douglas Kinsella, McGill University Rheumatic Diseases Unit, Royal Victoria Hospital, 687 Pine Ave. W., Montreal, Que. H3A 1A1

Ankylosing spondylitis (AS), a relatively common disease of unknown etiology, which primarily affects young men, may be associated with both extravertebral and extra-articular manifestations. Among the former, involvement of peripheral joints and of periosteal structures has been described.[1,2] Well documented extra-articular manifestations include anterior uveitis,[2,3] aortitis and cardiac conduction defects,[1-4] but there is considerable disparity in the recorded incidence of the cardiovascular manifestations.[1-5] The present study, based on a previously reported AS patient population,[1] was designed to provide long-term follow-up of the cardiovascular manifestations of AS.

Methods

Study groups consisted of 97 patients with AS and, for electrocardiographic (ECG) comparison, 81 patients with rheumatoid arthritis (RA) and 99 randomly selected hospital patients. Ninety-two of the AS patients have previously been reported in detail[1] and all met diagnostic criteria for "definite" disease;[6] four also had psoriasis and one had regional enteritis. All patients with RA met the diagnostic criteria of the American Rheumatism Association.[6]

Each surviving patient with AS (75 men and 1 woman) was examined on at least three occasions by one or more of the authors during a period of at least two years. Of the total series 21 had died; postmortem tissues of 4 with cardiovascular lesions were available for review. The majority of patients with RA (76 men and 5 women) were examined on at least one occasion by one or more of the authors; the ECG records of all were reviewed retrospectively. The majority of patients in the "hospital control" group (98 men and 1 woman) were not examined clinically by the authors but all of their ECG records were reviewed retrospectively and correlated with available clinical data; none were known to be afflicted with AS or RA and none were receiving cardiac glycosides.

Diagnoses of aortic insufficiency (AI) and mitral insufficiency (MI) were made by clinical examination; patients with a known history of rheumatic fever or with serologic evidence of syphilis were excluded from comparison. Atrioventricular conduction defects were sought by measurement of the PR interval on conventional ECGs; only PR intervals longer than 0.24 seconds were considered significant. In each group all ECGs obtained in the eight years before the study's completion were reviewed, the total numbers being AS, 593; RA, 451; hospital controls, 546.

Results

AS group

Table I lists the cardiovascular manifestations detected in 14 (14%) of the 97 patients with AS. Ten (10%) of the 97 patients had AI and 5 (5%) heart block, as either isolated or combined lesions. Of the five patients with heart block four had persistent first-degree lesions, and one (J.P.) had third-degree block (complete atrioventricular dissociation) that reverted spontaneously to sinus rhythm eight months after implantation of a pacemaker (Table II).

Postmortem findings in four patients with cardiovascular manifestations of AS, all of whom died cardiac deaths, are summarized in Table I. One patient (L.S.) with isolated heart block displayed extensive myocardial fibrosis but neither vascular lesions nor cellular infiltrates. Of two patients with isolated AI one (H.B.) had typical active aortitis and the other (W.G.), "healed" aortitis with extensive fibrosis in the aortic root (Figs. 1 and 2) and calcification in aortic valve cusps. One patient (K.C.) with combined aortic insufficiency and heart block had active aortitis. In both patients with active aortitis the inflammatory reaction was primarily localized in the root and proximal ascending aorta and was characterized by endarteritis obliterans and perivascular infiltration of lymphocytes and plasma cells.

Other manifestations of AS preceded the cardiovascular lesions in all but one patient (J.J.), who developed AI 13 years prior to the onset of sacroiliitis (he later developed typical AS and psoriasis). Two patients with AI (H.B. and J.J.) were noted to have psoriasis and another (R.C.) regional enteritis in association with AS. Peripheral arthritis was present in 64% of the 14 patients but in only 34% of the 83 patients without cardiovascular lesions (Table III). This difference is statistically significant by chi-square analysis.

Patients excluded from comparison included one with an antecedent history of rheumatic fever who had mitral stenosis and two with antecedent syphilis who had aortic insufficiency (one of the latter also had the murmur of aortic stenosis and persistent second-degree heart block).

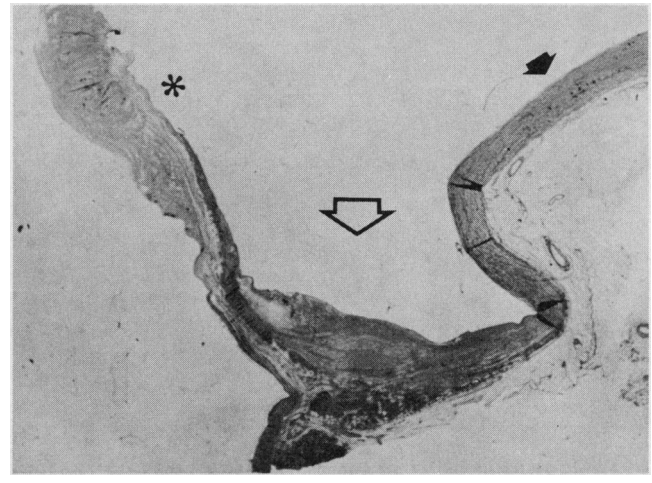

FIG. 1—Longitudinal section through aortic valve cusp and root of aorta of a patient with AS-associated aortic insufficiency. Note thickening and calcification of valve cusp and extensive fibrosis at root of aorta and in the media. Asterisk indicates aortic valve cusp, large open arrow the sinus of Valsalva and small closed arrow the proximal ascending aorta. Hematoxylin-eosin. Original magnification x60.

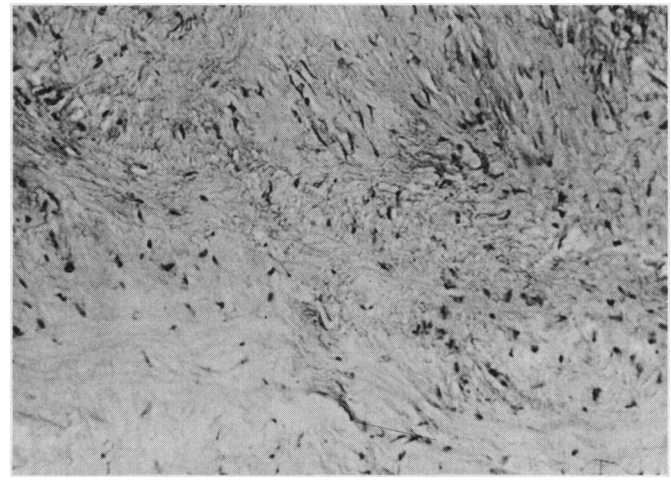

FIG. 2—Higher magnification of aortic root in Fig. 1. Note extensive fibrosis in the media and absence of vascular or cellular proliferation. Hematoxylin-eosin. Original magnification x160.

Control groups

In the group with RA, cardiac conduction defects were found in 3 (3.7%) of 81 patients — persistent first-degree

Table I—Clinical characteristics of patients with spondylitic heart disease

Patient	Age*	Duration* of AS	Cardiovascular lesion		Other lesions
			Type	Duration*	
J.O.	32	17	AI	5	Raynaud's phenomenon
H.B.†	35	10	AI	?	Iritis, psoriasis. Portmortem: aortitis‡
J.J.	44	3	AI	16	Psoriasis
C.V.	48	23	AI	2	—
S.I.	53	22	AI	2	—
J.V.	54	10	AI	7	—
W.G.†	73	47	AI	23	Postmortem: fibrosis of aortic root and aortic valve cusps‡
R.C.	49	17	AI	2	Regional enteritis
K.C.†	37	8	AI-HB	4	Postmortem: aortitis, valvulitis‡
A.V.	73	41	AI-HB	?	Iritis
L.S.†	42	14	HB	5	Iritis. Postmortem: myocardial fibrosis‡
J.P.	46	21	HB	1	—
H.S.	57	23	HB	1	—
A.C.	76	> 24	MI	> 10	—

*All values in years.
†Deceased
‡Aortitis and valvulitis refer to active inflammatory lesions. Fibrosis indicates an absence of active inflammation, with healing by fibrous proliferation.
AI = aortic insufficiency; MI = mitral insufficiency; HB = heart block

heart block in 2 patients and third-degree block in 1. Similarly, 3 (3%) of 99 patients in the hospital control group were found to have persistent first-degree heart block; none had second- or third-degree block (Table II).

Discussion

Our results demonstrate that aortic insufficiency and cardiac conduction defects may be encountered with relative frequency in patients with ankylosing spondylitis. Although the association of AS with valvular disease has been well documented in contemporary medical literature there exist discrepancies with respect to the frequency of this association.[1-10] Not surprisingly, greater awareness of the association has resulted in a progressively increasing reported incidence of AS-associated AI, from 1.7% in a study by Bernstein[11] in 1951 to approximately 10.0% (the figure we obtained in this study) in the definitive report by Graham and Smythe[7] in 1958. A recent report has re-emphasized the occurrence of mitral valve involvement in the form of mitral insufficiency in AS.[5]

In contrast to previous studies[5,12] the present investigation has failed to ascertain a significant difference in the incidence of isolated heart block between AS patients and RA and hospital control subjects. Although the overall incidence of heart block was increased in AS patients when those with and without AI were considered, the numbers involved were small and should be interpreted with some reservation. The findings in larger series reported in the literature,[5,12] as well as in histopathologic studies,[9,10,13] suggest that an increased incidence of heart block might be expected to occur in patients with AS.

We have documented several unusual features of AS-associated cardiovascular disease: first, AI can antedate clinically recognizable articular lesions (patient J.J.); second, AI can occur with the spondylitis associated with psoriasis and regional enteritis; and third, the inflammatory reaction in cardiovascular tissues in AS is not necessarily persistent and progressive.

Evidence that AI may antedate articular disease is also provided in the recent report of Bulkley and Roberts.[13] Indirect support for such a possibility can be derived inferentially from the well documented observation that anterior uveitis and extraspinal disease[3,4] may also precede the articular lesions of AS by months or years. Hence the discovery of isolated AI in young or middle-aged men should not be ascribed to "previously unrecognized rheumatic fever" until AS has been definitively ruled out by appropriate serial clinical and radiologic observations.

The association of cardiovascular lesions with the "secondary" forms of AS, such as the spondylitis associated with psoriasis and regional enteritis, is not well documented in contemporary medical literature.[14-16] Indeed, we have been unable to locate a previous reference to an association between the spondylitis of regional enteritis and AI. Therefore the present report, which documents such an association in two AS patients with psoriasis and one with regional enteritis, may serve to emphasize pathogenetic similarities between the primary and secondary forms of AS.

Our observation that the inflammatory reaction in cardiovascular tissues in AS need not be persistent and progressive is supported by histologic descriptions in the literature.[10,13] In the present study no cases of progressive heart block were encountered; indeed, in one patient with third-degree block there was spontaneous conversion to sinus rhythm eight months after implantation of a cardiac pacemaker, which suggests resolution of an acute inflammatory lesion in the cardiac conduction tissues. Furthermore, postmortem histologic studies in four cases demonstrated that cardiovascular lesions in AS, whether in the aorta or cardiac conduction tissues, may be either "acute", with cellular and vascular proliferation, or "chronic", with noninflammatory fibrosis. Therefore AS-associated conduction defects should be observed with appropriate deliberation before implementation of surgical therapeutic measures.

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Table II—Cardiac conduction defects in patients with AS and RA and in hospital controls

Diagnostic group	No. of patients	No. of ECGs*	Conduction defect (degree)		
			First	Second	Third
Ankylosing spondylitis	97	593	4	0	1†
Rheumatoid arthritis	81	451	2	0	1
Hospital controls	99	546	3	0	0

*All ECGs recorded during eight years before completion of study.
†Converted spontaneously to sinus rhythm.

Table III—Prevalence of peripheral arthritis in AS patients with and without cardiovascular lesions

	Peripheral arthritis	
	No.	%
With cardiovascular lesions (N = 14)	9	64
Without cardiovascular lesions (N = 83)	28	34

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