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Complete heart block in HLA B27 associated disease
Electrophysiological and clinical characteristics

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SUMMARY A genetic predisposition associated with HLA B27 for developing complete heart block with or without clinical or radiological signs of associated rheumatic disease has recently been found. In this electrophysiological study of 12 patients with spontaneous complete heart block and HLA B27 associated disease, of whom eight had ankylosing spondylitis, 10 had suprahisian second or third degree atrioventricular block (eight spontaneously and two during atrial pacing at rates below 90 impulses per minute) and one infrahisian block. One patient with narrow QRS complexes during complete heart block three months earlier had normal findings. Three patients also had sinus node malfunction and six had fascicular or bundle branch block.

In HLA B27 associated disease the atrioventricular block seems to be preferentially located in the atrioventricular node, although the conduction system may be widely affected. The findings in this study indicate a further cause of high degree atrioventricular block with a predominantly suprahisian location in addition to acute inferior myocardial infarction, digitalis intoxication, and "congenital" heart block.

The HLA B27 associated diseases—seronegative spondarthritides—are closely related rheumatic disorders characterised by a strong but variable association with the immunogenetically important cell surface protein HLA B27, a high frequency of radiological sacroiliitis, and the absence of rheumatoid factor. Ankylosing spondylitis and Reiter's disease are the main disease entities in this group. Acute anterior uveitis/iritis may occur both in association with these diseases or as an isolated disease manifestation.[1 2]

HLA B27 associated syndromes have recently been detected in 13% of a group of 223 Swedish men undergoing permanent pacemaker treatment.[3 4] In addition, the prevalence of B27 was also found to be significantly increased in patients with complete heart block and pacemaker treatment without radiological or clinical evidence of a seronegative spondarthritis.[5] It thus seems likely that in about 15% to 20% of men with permanently paced complete heart block a B27 associated disease process may lead to the development of conduction disturbances. The importance of this group of rheumatic disorders and the HLA B27 associated disease process in the development of severe bradyarrhythmias requiring pacemaker treatment thus seems to have been underestimated previously.

Previous reports of five cases of ankylosing spondylitis/Reiter's disease and complete heart block, studied electrophysiologically, suggest a predominantly proximal localisation of the atrioventricular block.[6–8] Pathoanatomical studies have also indicated that the typical inflammatory changes are located in the aortic root and upper part of the myocardial septum.[9]

The purpose of the present study was to determine whether proximal localisation was a characteristic feature of high degree atrioventricular block in patients with ankylosing spondylitis and other HLA B27 associated disorders in agreement with pathoanatomical studies.

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Patients and methods

STUDY POPULATION

The study population was selected from patients referred to our department for evaluation of the indications for pacemaker treatment. The following three

Table 1 *Clinical data in 12 men with complete heart block and HLA B27 associated disease*

Case No	Age	Sacroiliitis	Spondylitis	Uveitis	Peripheral arthritis	Ankylosing spondylitis*	Syncope	CHF (or DPC)	Aortic regurgitation	Surface ECG at complete heart block		Pacemaker
										HR (beats/min)	QRS	
1	65	+	−	+	+	−	−	+	+	45	RBBB	+
2	83	+	+	−	−	+	−	+	+	30	N	+
3	33	+	−	−	+	−	+	−	−	35–40	N	+‡
4	77	+	+	+	−	+	−	+	−	35–60	N	+
5	34	+	+	+	+	+	+	−	+	<57	RBBB LAFB	+
6	67	−	+	−	−	−	−	+	+	38	LBBB	+
7	73	+	+	−	+	+	−	+	+	40–49	LBBB	+
8	68	+	−	−	+	+	−	−	+	35–40	LBBB	−
9	75	−	−	+	−	−	−	−	+	38–45	LAFB	−
10	50	+	+	−	+	+	+?	+	+	56	N	+
11	60	+	+	+	+	+	+	−	+	36–49	N	+
12	69	+	−	+	+	+	−	+	+	35	N	+
Total		10	7	6	8	8	3(+1?)	7	10†			10

*Diagnosis according to modified American Rheumatism Association criteria.[3 10]
†No valve prosthesis.
‡Terminated because of technical problems and restoration of atrioventricular conduction.
CHF, congestive heart failure (DPC, decreased physical capacity due mainly to bradycardia); HR, heart rate; QRS, configuration of ventricular complexes; N, narrow (<0·12 s) with normal axis; RBBB/LBBB, right/left bundle branch block; LAFB, left anterior fascicular block; +, present; −, absent.

criteria were used: (*a*) recorded evidence of complete heart block; (*b*) HLA B27 at tissue typing; and (*c*) typical HLA B27 associated disease manifestations such as specific radiological changes of the spine or sacroiliac joints or acute anterior uveitis. Twelve men (mean age 63 (range 33–83) years) fulfilled these criteria. Table 1 summarises the clinical data. No patient was being treated with drugs known to affect the cardiac conduction system at the time the complete heart block was recorded or during the electrophysiological investigation. Other possible alternative causes of heart disease were identified in one patient (case 7)—namely, hypertension and diabetes mellitus. At necropsy, however, cardiac histological changes consistent with ankylosing spondylitis were found (unpublished observation).

ELECTROPHYSIOLOGICAL STUDY

Two or three pacing wires with a distance of 1 cm between the electrodes were introduced percutaneously under local anaesthesia via a femoral vein. One quadripolar catheter was positioned high in the right atrium against the lateral wall for stimulation and recording. A tripolar electrode catheter was placed across the tricuspid valve for recording of the His bundle potential, and in some patients a bipolar catheter was positioned in the right ventricular apex for safety reasons. The intracardiac electrogram and surface leads I, II, and V1 were recorded on a Mingograph (Siemens-Elema, Sweden) with frequency limits of 50–700 Hz at a paper speed of 100 mm/s. Pacing was performed with a stimulus duration of 2 ms and a voltage of about three times the stimulation threshold using a stimulator for programmed pacing (Devices Ltd, United Kingdom).

Terms and definitions relating to cardiac rhythm followed the recommendations by Hecht *et al*[11] and Robles de Medina *et al.*[12] Left anterior fascicular block was diagnosed in the presence of narrow (<0·12 s) QRS complexes with a frontal plane axis deviation to the left of −30° or more.

Sinus node function was studied by repeated atrial pacing at rates of 90 or 100 impulses per minute (i/min) and at 130 i/min for periods of 10 and 30 seconds with a pause of at least 20 seconds between each stimulation period. Sinus node recovery time was defined as the interval from the last stimulus artifact to the first P wave with a configuration and activation sequence consistent with sinus node origin. The corrected sinus node recovery time was obtained by subtracting the PP interval, determined as the mean of five sinus cycle lengths immediately before pacing, from the longest sinus node recovery time. The atrioventricular conduction intervals were determined as the mean of at least three beats and measured as follows: the PR interval in surface lead II, and the PA interval from the first atrial activity appearing in either surface or intracardiac leads to the beginning of the most rapid phase of the intrinsicoid deflection of the A wave recorded low in the right atrium. The AH interval was determined from the latter point to the first rapid phase of the H wave and the HV interval from this point to the earliest ventricular activity seen in any lead. The QS duration was measured in lead II. Table 2 gives the reference values of our laboratory.[13] Atrial pacing was in all cases performed in connection

Table 2 *Results of intracardiac electrophysiological investigation showing degree of block and conduction intervals in spontaneous rhythm and sinus node function*

Case No	AVB*	HR (beats/min)	Conduction intervals (ms)					Sinus node function (ms)	
			PP	PA	AH	HV	QS	SNRT	CSNRT
1	II	54	740	55	>280	55	140	1140	365
2	I–II	40	725	45	200	30	60	1535	800
3	SR	76	795	40	90	30	110	1220	420
4	I–II	70–85	755	35	295	35	100	1180	345
5	SR, III	70	860	40	100	70	150	1400	650
6	I	60	1000	35	275	50	195	1140	140
7	III	49	835	45	—	50	175	1240	345
8	III	35	825	30	—	45	145	1380	565
9	III	38	805	65	—	45	100	1295	480
10	I, III	98	615	60	(615)	35	70	930	300
11	I	51	1170	55	225	30	100	1555	295
12	I–II	36	1015	40	285	45	100	1480	395
Reference values[13]				30–65	55–110	30–55	<120	<1735	<545

*All suprahisian (except case 5).
AVB, atrioventricular block of first (I), second (II), and third (III) degree; SR, sinus rhythm; SNRT, sinus node recovery time; HR, heart rate (that is, ventricular rate either conducted or escape); CSNRT, corrected sinus node recovery time (SNRT−PP immediately before the pacing period).

with testing of sinus node function. In most cases it was also performed at successively decreasing cycle lengths to determine the rate at which atrioventricular block occurred and on which level in the conduction system.

The investigation procedure was approved by the ethical committee of the hospital and the patients gave informed consent.

Results

INITIAL SURFACE ELECTROCARDIOGRAPHY

Spontaneous intermittent complete heart block was recorded in all patients. The escape rhythm during complete heart block had the same QRS configuration as the conducted rhythm in all but one case. Case 1 had right bundle branch block configuration only during complete heart block. Case 5 with a right bundle branch block and left anterior fascicular block had spontaneous variations in sinus rate, and his intermittent complete heart block occurred at sinus cycle lengths corresponding to a rate less than 57 beats/min; thus the complete heart block depended on bradycardia dependent fascicular block. This intermittent complete heart block occurred without an escape rhythm for up to 5 s. Intraventricular conduction disturbances were present in six patients, five of whom had complete bundle branch block. Thus seven patients had narrow (<0·12 s) QRS complexes both during conducted rhythm and during second and third degree atrioventricular block, indicating suprahisian or intrahisian localisation of the block.

INTRACARDIAC ELECTROGRAPHY

One patient (case 3) showed entirely normal electrophysiological results (Table 2). Two patients with first degree atrioventricular block had impaired atrioventricular nodal conduction with a prolonged AH interval. Spontaneous second or third degree atrioventricular block was recorded in nine patients. The localisation was suprahisian=atrioventricular nodal in all patients but one (case 5) who had infrahisian block.

During atrial pacing two patients with first degree atrioventricular block developed suprahisian second degree block both at very low rates (62 and 87 i/min). One patient with second degree block developed complete heart block and two with second degree block showed a higher proportion of blocked atrial impulses (3:1 and 4:1); all blocking occurred in the atrioventricular node. Altogether 10 patients showed suprahisian second or third degree block spontaneously or during atrial pacing at pathologically low rates, and one (case 5) infrahisian block. In three patients (cases 2, 5, and 8) sinus node malfunction, defined as a prolonged corrected sinus node recovery time, was found.

Discussion

The purpose of this study was to determine systematically whether proximal atrioventricular block reported previously in a few cases with ankylosing spondylitis/Reiter's disease and complete heart block was a characteristic feature of complete heart block in HLA B27 associated disease and thus if there is a correlation with pathoanatomical findings. The surface electrocardiogram showed intermittent complete heart block in all 12 patients and narrow QRS complexes suggesting a suprahisian or intrahisian localisa-

tion of the atrioventricular block in seven of them.

During the intracardiac investigation spontaneous suprahisian second or third degree atrioventricular block was recorded in eight patients and infrahisian in one. Atrial pacing at 62 and 87 i/min caused suprahisian second degree atrioventricular block in two other patients but did not provoke any intrahisian or infrahisian second or third degree atrioventricular block. These results, together with unchanged QRS configuration during varying degrees of atrioventricular block, support an atrioventricular nodal localisation of the previously recorded spontaneous complete heart block in all but one of the 12 patients. This result is therefore consistent with the findings of the five previously reported cases.[6-8] Acquired complete heart block is otherwise predominantly infrahisian (about 60%) or intrahisian (about 20%).[14] This study of 12 consecutive patients with HLA B27 associated disorders therefore identifies a further cause of predominant suprahisian second and third degree atrioventricular block in addition to acute inferior myocardial infarction, "congenital" heart block, and digitalis intoxication.[15-17]

Another feature of conduction disturbances associated with the HLA B27 associated diseases is their tendency to occur intermittently, as was evident in all our 12 cases and which has been previously reported.[4 18 19] Complete longlasting remission, on the other hand, rarely occurs in patients with acquired complete heart block. In this study one patient (case 3) showed no signs of conduction disturbances at the electrophysiological investigation three months after the onset of symptomatic complete heart block. He has had no relapse during three years' follow up. We have previously reported the case of a patient with ankylosing spondylitis followed up for 26 years, who within six months of the onset of complete heart block had only first degree atrioventricular block and over the past 18 years no signs or symptoms of heart disease.[19]

The common pathophysiological feature of both B27 associated aortic regurgitation and conduction disturbances is an inflammatory process in the aortic root and the adjacent myocardium, which may to a varying extent lead to fibrosis.[9 20] Both the conduction disturbance[18 19] and the aortitis due to this rheumatic cause may, however, resolve without leaving any clinically important sequelae.[20 21]

The reasons for the intermittent occurrence of the atrioventricular nodal block are probably complex. The composite organisation of the atrioventricular node both structurally and functionally, with its great number of cells involved in conduction, rich vascular supply, and important influence from the autonomous nervous system, provide the basis for different mechanisms of disturbed conduction. Furthermore, the acquired complete atrioventricular nodal block associated with HLA B27 may obviously be the result of the interaction of one or several of these factors—in addition to inflammatory activity—as suggested by the observed spontaneous momentary and long term variations in the conduction capacity.

Although the most important clinical manifestation of the conduction disturbances in our patients was predominantly localised to the atrioventricular node, disturbances were evident in all parts of the conduction system. Signs of widespread cardiac involvement have also been reported by Takkunen *et al*[22] and Morley *et al*[23] who found evidence of impaired myocardial function in some patients with ankylosing spondylitis and Reiter's disease without valve disease.

Ten of the patients in this study were treated with a permanent pacemaker. Of these, seven had a rate programmable pulse generator implanted because of the tendency for intermittent atrioventricular block and the association with aortic regurgitation which sometimes develops later than the atrioventricular block.[4] In two other patients (cases 8 and 9) the absence of serious symptoms led us to defer a decision regarding pacemaker treatment. During two and four and a half years' follow up neither patient has shown evidence of a need for pacemaker treatment despite the presence of second or third degree atrioventricular block at each follow up examination.

CONCLUSION

In this series of 12 consecutive patients the level of HLA B27 associated high degree atrioventricular block was found to be predominantly suprahisian which agrees with the results of pathoanatomical studies. Disturbances of other parts of the conduction system including the sinus node were also shown. The course of the disease is not necessarily progressive—as evident in this and other studies—but may be intermittent, arrest at any stage, or even resolve without leaving any important clinical sequelae.[18-21] A "wait and see" policy regarding pacemaker treatment sometimes seems to be appropriate when asymptomatic suprahisian complete heart block is present in patients with HLA B27 associated disorders.

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