



## Original article

## Recovery of atrioventricular block following steroid therapy in patients with cardiac sarcoidosis



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## ABSTRACT

**Background:** Atrioventricular (AV) block is one of the main clinical manifestations in patients with cardiac sarcoidosis (CS). Although steroid therapy is considered to be effective for AV block, the efficacy has not been demonstrated in detail.

**Methods and results:** Fifteen CS patients presenting with advanced or complete AV block were retrospectively investigated. All patients were treated with 30 mg/day of prednisone after device implantation, which was tapered to a maintenance dosage of 5–10 mg/day. During a mean follow-up of 7.1 years, AV block resolved to normal conduction or first-degree AV block in 7 patients (recovery group). The improvement was driven within the first week of steroid therapy in 4 patients, while 3 patients showed late recovery of AV conduction. The remaining 8 patients were classified as the non-recovery group. The recovery group showed a higher left ventricular ejection fraction ( $69.4 \pm 8.9\%$  versus  $44.1 \pm 19.3\%$ ,  $p = 0.029$ ) and higher prevalence of advanced AV block (87.5% versus 28.6%,  $p = 0.040$ ) compared with those of the non-recovery group. In patients with the recovery group, there was no late recurrence of AV block during the follow-up period.

**Conclusions:** Early initiation of steroid therapy may be effective for AV block, and steroid therapy before device implantation is a possible therapeutic strategy for some selected patients.

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## Introduction

Sarcoidosis is a common multisystem granulomatous disease of unknown etiology [1]. Cardiac sarcoidosis (CS) is relatively rare but sometimes life-threatening because of fatal arrhythmias or severe congestive heart failure. Atrioventricular (AV) block is one of the common manifestations of CS which could result in syncope, and possibly sudden cardiac death. Currently, pacemaker implantation is recommended for patients with advanced or complete AV block. Although steroid therapy is reported to be effective for AV block [2,3], the efficacy has not been demonstrated in detail. This study was performed to determine the prevalence and clinical implications for recovery of advanced AV block following steroid therapy.

## Methods

This study was retrospective with 15 CS patients (2 men and 13 women; mean age  $59.9 \pm 9.7$  years) presenting with advanced or complete AV block on electrocardiography (ECG). All patients were referred to Nippon Medical School Main Hospital or Nippon Medical School Chiba Hokusoh Hospital for treatment of AV block between June 1, 1995 and December 31, 2012. We applied the guidelines for the diagnosis of CS based on the report from the Japanese Society of Sarcoidosis and Other Granulomatous Disorders (Table 1) [4,5]. Significant coronary artery disease was excluded by angiography in all patients. Patients with known other cardiac diseases were also excluded from the present investigation. All of the patients were treated with steroid after device implantation, and the initial dosage was 30 mg/day of prednisone or its equivalent on alternate days, which was tapered over a period of 6 months to a maintenance dosage of 5–10 mg/day. Cardiac echocardiography, gallium-67 scintigraphy, serum angiotensin-converting enzyme (ACE) and plasma B-type natriuretic peptide (BNP) concentrations, electrophysiological study, cardiovascular magnetic resonance imaging

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**Table 1**

Clinical diagnosis group: extracardiac sarcoidosis is diagnosed histologically or clinically and satisfies the following conditions (more than 2 of 4 major criteria, or 1 in 4 major criteria and more than 2 in 5 minor criteria are satisfied) and more than 1 in 6 basic diagnostic criteria.

Major criteria
(a) Advanced AV block
(b) Basal thinning of the interventricular septum
(c) Positive cardiac 67Ga uptake
(d) Depressed ejection fraction of the left ventricle (LVEF < 50%)
Minor criteria
(a) Abnormal ECG findings: ventricular arrhythmias (VT, multifocal or frequent PVCs), CRBBB, axis deviation, or abnormal Q-wave
(b) Abnormal echocardiography: regional abnormal wall motion or morphological abnormality (ventricular aneurysm, wall thickening)
(c) Nuclear medicine: perfusion defect detected by 201Tl myocardial scintigraphy or 99Tc myocardial scintigraphy
(d) Gd-enhanced MRI: delayed enhancement of myocardium
(f) Endomyocardial biopsy: interstitial fibrosis or monocyte infiltration over moderate grade

AV, atrioventricular; LVEF, left ventricular ejection fraction; ECG, electrocardiogram; MRI, magnetic resonance imaging; PVC, premature ventricular contraction; cRBBB, complete right bundle branch block; VT, ventricular tachycardia.

(CMR), and endomyocardial biopsy were assessed before steroid therapy. Left ventricular (LV) end-diastolic and end-systolic dimensions were determined from cardiac echocardiography and LV ejection fraction (EF) was measured by the Modified Simpson's method. Serum ACE concentrations were measured by a colorimetric method (colorimetric assay kit; Fujirebio, Tokyo, Japan) with p-hydroxyhippuryl-L-histidyl-L-leucine as the substrate [6] and plasma BNP concentrations were determined with a specific immunoradiometric assay for human BNP with commercial kits

**Table 2**

Clinical characteristics of the study patients.

Patient no.	Age	Sex	Type of AV block	LVEF (%)	IVST (mm)	BNP (pg/ml)	ACE (U/L)	Ga uptake (heart)	Time to recovery of AV block	Other organ involvement	Device
1	56	F	Advanced	78	12	141.0	10.6	(+)	3 days	Lung, skin	PM
2	63	F	Advanced	68	8	21.7	30.0	(+)	7 days	Lung	PM
3	43	F	Complete	80	6	78.1	19.9	(+)	6 days	Lung	PM
4	61	F	Advanced	53	9	124.0	19.4	(-)	1 day	Eye, lung	ICD
5	65	F	Advanced	72	9	48.9	9.7	(-)	3 weeks	Skin	PM
6	58	F	Advanced	66	9	212.8	32.0	(-)	6 months	Lung	PM
7	65	F	Complete	69	7	54.3	25.6	(-)	14 months	Lung	PM
8	63	F	Complete	56	7	643.0	20.2	(-)	-	Lung,	PM
9	54	F	Complete	72	5	149.8	13.2	(-)	-	Lung	PM
10	60	F	Complete	19	6	244.4	14.8	(-)	-	Lung	ICD
11	73	F	Advanced	34	5	834.8	10.9	(-)	-	Lung	PM
12	73	F	Complete	32	6	75.6	16.2	(-)	-	Skin	PM
13	46	M	Complete	40	10	162.0	11.5	(-)	-	Lung,	ICD
14	57	M	Complete	69	10	74.1	31.4	(-)	-	Eye, lung, skin	PM
15	55	F	Complete	31	9	208.2	21.0	(-)	-	Skin	PM

AV, atrioventricular; LVEF, left ventricular ejection fraction; ACE, angiotensin converting enzyme; BNP, B-type natriuretic peptide; Ga, Gallium-67; PM, pacemaker; ICD, implantable cardioverter defibrillator; IVST, intraventricular septal thickness.

**Table 3**

Comparison of parameters between recovery group and non-recovery group.

	Recovery group (n = 7)	Non-recovery group (n = 8)	p Value
Age (years)	58.7 ± 7.7	60.1 ± 9.4	0.867
Male	0	2	0.475
BNP (pg/ml)	97.2 ± 66.1	299.0 ± 282.4	0.054
LVEF (%)	69.4 ± 8.9	44.1 ± 19.3	0.029
IVST (mm)	8.6 ± 1.9	7.3 ± 2.1	0.298
ACE (U/ml)	21.0 ± 8.8	17.4 ± 6.8	0.694
Ga uptake (heart)	3	1	0.282
Type of AVB (advanced/complete)	5/2	1/7	0.041

Data are presented as mean ± SD or no. of patients. BNP, B-type natriuretic peptide; LVEF, left ventricular ejection fraction; IVST, intraventricular septal thickness; ACE, angiotensin-converting enzyme; Ga, gallidium; AVB, atrioventricular block.

(Shionoria kit; Shionogi and Kyowa Medex, Tokyo, Japan). The study protocol was approved by the ethical committee of Nippon Medical School, and written informed consent was obtained from all patients.

**Statistical analysis**

Measurements are presented as mean value ± SD. Comparisons of measurements between two groups were analyzed by Mann–Whitney U-test. Fisher exact test was used for discrete variables. A p-value < 0.05 was considered statistically significant.

**Results**

During a mean follow-up of 7.1 ± 5.3 years, AV block resolved to normal conduction or first-degree AV block in 7 patients (recovery group). The improvement was driven within the first week of steroid therapy in 4 patients, while 3 patients showed late recovery of AV conduction (3 weeks, 6 months, and 14 months, respectively). The remaining 8 patients were classified as the non-recovery group. Clinical characteristics of the study patients are shown in Table 2. The recovery group showed a higher LVEF (69.4 ± 8.9% versus 44.1 ± 19.3%, p = 0.029) and higher prevalence of advanced AV block (87.5% versus 28.6%, p = 0.040) compared with those of the non-recovery group (Table 3). However, there were no significant differences in the other parameters. All patients were alive except one who died suddenly 17 months after pacemaker implantation (no. 11). In patients with the recovery group, there was no subsequent recurrence of AV block during the follow-up period.

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