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ORIGINAL RESEARCH

Atrial Arrhythmias in Clinically Manifest Cardiac Sarcoidosis: Incidence, Burden, Predictors, and Outcomes

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BACKGROUND: Recent data have suggested a substantial incidence of atrial arrhythmias (AAs) in cardiac sarcoidosis (CS). Our study aims were to first assess how often AAs are the presenting feature of previously undiagnosed CS. Second, we used prospective follow-up data from implanted devices to investigate AA incidence, burden, predictors, and response to immunosuppression.

METHODS AND RESULTS: This project is a substudy of the CHASM-CS (Cardiac Sarcoidosis Multicenter Prospective Cohort Study; NCT01477359). Inclusion criteria were presentation with clinically manifest cardiac sarcoidosis, treatment-naive status, and implanted with a device that reported accurate AA burden. Data were collected at each device interrogation visit for all patients and all potential episodes of AA were adjudicated. For each intervisit period, the total AA burden was obtained. A total of 33 patients met the inclusion criteria (aged 56.1±7.7 years, 45.5% women). Only 1 patient had important AAs as a part of the initial CS presentation. During a median follow-up of 49.1 months, 11 of 33 patients (33.3%) had device-detected AAs, and only 2 (6.1%) had a clinically significant AA burden. Both patients had reduced burden after CS was successfully treated and there was no residual fluorodeoxyglucose uptake on positron emission tomography scan.

CONCLUSIONS: First, we found that AAs are a rare presenting feature of clinically manifest cardiac sarcoidosis. Second, AAs occurred in a minority of patients at follow-up; the burden was very low in most patients. Only 2 patients had clinically significant AA burden, and both had a reduction after CS was treated.

REGISTRATION: URL: https://www.clinicaltrials.gov; unique identifier NCT01477359.

Key Words: atrial arrhythmia ■ atrial fibrillation ■ cardiac sarcoidosis

Sarcoidosis is a multisystem, inflammatory granulomatous disease of unknown cause. It is characterized by systemic infiltration with noncaseating granulomas occurring in any organ in the body including the heart, liver, spleen, eyes, and kidneys.[1] Autopsy analysis and cardiovascular magnetic resonance imaging studies have demonstrated a 20% to 47% rate of clinically silent cardiac involvement of patients with sarcoidosis;[2–4] 3% to 5% showed clinically manifest involvement.[1]

Cardiac sarcoidosis (CS) most often manifests with ventricular arrhythmias, conduction abnormalities, and heart failure, and most research has focused on these clinical issues. Atrial arrhythmias (AAs) have received less attention, but recent

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CLINICAL PERSPECTIVE

What is New?
- This is the first prospective study examining patients presenting with clinically manifest cardiac sarcoidosis (CS), using implanted device diagnostics; only 1 patient had important atrial arrhythmias (AAs) as a part of the initial CS presentation.
- During a median follow-up of 49.1 months, 11 of 33 patients had device-detected AAs; however, only 2 had a clinically significant AA burden.
- Both patients had reduced burden after CS was successfully treated, and there was no residual fluorodeoxyglucose uptake on positron emission tomography scan.

What are the Clinical Implications?
- AAs are a rare presenting feature of CS.
- At follow-up, only a minority of patients with CS developed AAs, and the burden was low.
- Our findings suggest that immunosuppression may suppress AAs in CS; however, this requires further investigation in larger populations.

Nonstandard Abbreviations and Acronyms

AA	atrial arrhythmia
CHASM-CS	Cardiac Sarcoidosis Multicenter Prospective Cohort Study
CS	cardiac sarcoidosis
LA	left atrial
PET	positron emission tomography

retrospective studies have suggested a substantial incidence in CS.[5] AAs have also been described as the presenting manifestation of CS[6–8]; however, this phenomenon has not been systematically examined. Finally, although there is evidence that immunosuppression is useful for the treatment of AAs in CS, it is limited to case reports.[8–10]

Our study sought to: (1) examine how often AAs are the presenting feature of previously undiagnosed CS; and (2) prospectively examine AA incidence, burden, predictors, and response to immunosuppression using follow-up data from implanted devices.

METHODS

Primary Study Population

This project is a single-center substudy of the CHASM-CS (Cardiac Sarcoidosis Multicenter Prospective Cohort Study; NCT01477349). This substudy was prespecified in the main protocol. Consecutive patients in CHASM-CS from a single center (University of Ottawa Heart Institute, Ottawa, ON, Canada) were assessed for inclusion. The protocol was approved by the local institutional ethics committee and all patients signed informed consent. Patients who met all of the following criteria were included in the substudy:

1. Active clinically manifest CS, defined as ≥1 of the following clinical features:
   - Advanced conduction system disease (sustained Mobitz II atrioventricular block or third-degree atrioventricular block).
   - Sustained ventricular tachycardia of unknown cause.
   - Ventricular dysfunction (left ventricular ejection fraction <50% and/or right ventricular ejection fraction <40%).

2. CS diagnosed based on Heart Rhythm Society criteria.[11]
3. Abnormal myocardial fluorodeoxyglucose (FDG) uptake on positron emission tomography (PET) scan in a pattern consistent with active CS.
4. No previous treatment for sarcoidosis.
5. Patient with an implanted device that reports accurate AA burden.

AA Definition

AA was defined as an episode of rapid atrial rate (≥190 beats per minute).[12]

AA Burden Data

Patients were reviewed every 6 months in the device clinic at the University of Ottawa Heart Institute. All data were stored in the device clinic database (Paceart, Medtronic). All visits with AA detected were reviewed in detail; in particular, ECGs were reviewed by 2 blinded observers to determine whether these were truly episodes of AA, with a third reviewer to adjudicate as necessary. The date of the clinic visits and AA burden were recorded.

Patients with AAs were classified according to burden as either having none, very low, low, or more than low burden.

- Very low burden was defined as all episodes lasting <6 minutes.
- Low burden was defined as at least 1 episode lasting >6 minutes but no episodes >24 hours.[12]
- More than low burden was defined as ≥1 episode lasting >24 hours.[13]

FDG-PET Scans

All patients had FDG positron emission tomography (PET) scans performed before initiation of corticosteroids. Full details on the imaging protocol and image interpretation methods have been previously published.[14] In brief, the imaging protocol included a whole-body acquisition (from the base of the cranium to the mid-thighs), 60 minutes after the intravenous injection of 5 MBq/kg of FDG, followed immediately by a dedicated cardiac acquisition with ECG gating for evaluation of left ventricular function. To achieve adequate suppression of physiological myocardial FDG uptake, all patients were instructed to follow a low-carbohydrate, fat-rich, protein-permitted diet the day before the examination, followed by a fast of at least 12 hours immediately before the examination. Unless contraindicated, patients also received a low dose (15 IU/kg) of intravenous unfractionated heparin before FDG injection. All patients also underwent rest myocardial perfusion imaging studies using PET-computed tomography with either rubidium-82 or ^{13}N-ammonia on the same day.

Additional FDG-PET Scan Analysis

All images were interpreted by an experienced nuclear cardiologist/medicine specialist with significant experience in reporting CS scans. Sites of disease involvement were defined as "active" when abnormal FDG uptake in a pattern consistent with sarcoidosis was present.[15] The number of discrete areas with increased FDG uptake was counted. Maximum standardized uptake value of the left ventricle was measured on axial images, while left ventricular mean standardized uptake value and its coefficient of variation and summed rest score were calculated using FlowQuant automated software (University of Ottawa Heart Institute). Right ventricular FDG uptake was recorded as present or absent.

FDG-PET Scan Analysis: Atrial FDG Uptake

All scans were interpreted independently by 2 blinded experienced nuclear cardiologist/medicine specialists. Each reader classified atrial FDG uptake as none, less than liver uptake, more than liver uptake, and markedly more than liver uptake. Only the latter 2 were considered as abnormal. Reviewers also scored atrial uptake as diffuse, focal, or focal on diffuse. The left and right atria and interatrial septum uptake were reported separately. In cases of disagreement, a third independent reader also reviewed the scans.

Statistical Analysis

Categorical variables are presented using percentages or frequencies, and continuous variables using mean (±SD) or median (25th, 75th percentiles), when appropriate. We compared categorical variables using chi-square test (or Fisher exact test when appropriate), and continuous variables using 1-way ANOVA or Kruskal-Wallis test for normally and nonnormally distributed variables, respectively. Statistical analysis was performed using IBM SPSS version 25. Statistical significance was defined as $P<0.05$.

RESULTS

Study Population

A total of 33 patients met the inclusion criteria. Baseline demographics are shown in Table 1. The median follow-up after device implantation was 49.1 months (interquartile range, 24.7–66.4 months).

Patients With AAs Before the Diagnosis of CS

Three patients had a history of AAs before the diagnosis of CS (see Table 2 for details). Patient 1 presented with acute onset of symptomatic atrial tachycardia that was refractory to medical management, including calcium channel blockers and class I antiarrhythmic agents, and subsequently underwent an ablation. The atrial tachycardia was determined to arise from the crista terminalis. There was recurrence of the atrial tachycardia, and a second ablation

Table 1. Baseline Demographics of the Cohort Included in the Study*

Characteristics	Total (N=33)
Age at presentation of CS, y	56.1±7.7
White race	31 (93.9)
Women	15 (45.5)
History of extracardiac sarcoidosis	6 (18.2)
Hypertension	12 (36.4)
Diabetes mellitus	4 (12.1)
History of AA	3 (9.1)
Presenting cardiac feature	
• Sustained Mobitz II and/or third-degree atrioventricular block	28 (84.8)
• VT or cardiac arrest	5 (15.2)
• Sustained Mobitz II and/or third-degree atrioventricular block and VT	2 (6.1)
Type of device	
• CRT-D	4 (12.1)
• Dual-chamber ICD	29 (87.9)

Values are expressed as mean±SD or number (percentage). CRT-D indicates cardiac resynchronization therapy device; CS, cardiac sarcoidosis; ICD, implantable cardioverter-defibrillator; and VT, ventricular tachycardia.

*All patients had fluorodeoxyglucose-positron emission tomography scans and an implanted device capable of recording atrial arrhythmias (AAs).

Table 2. Patient-Level Data on AA Burden

Patient No.	AA Before or After CS Diagnosis	Sex (Age at Presentation, y)	Clinical Presentation	LV and RV Function at Diagnosis	LA FDG Uptake* (SUV$_{max}$)	RA FDG Uptake* (SUV$_{max}$)	Septal FDG Uptake* (SUV$_{max}$)
1	Before	Women (48.5)	Atrial tachycardia then CHB 6 mo later	Normal	Yes (6.45)	Yes (5.91)	No
2	Before	Men (57.1)	Atrial flutter then VT and RV dysfunction	Mild LV dysfunction, moderate RV dysfunction	No	No	No
3	Before	Women (64.0)	CHB in 2005 AA+VT in 2011 Nonischemic cardiomyopathy and CS diagnosed in 2014	Severe LV dysfunction (LV ejection fraction 25%)	Yes (4.65)	No	No
4	After	Women (56.6)	CHB	Mild LV dysfunction	No	No	No
5	After	Women (56.0)	CHB and VT	Normal	Yes (2.83)	No	Yes (6.29)

AA indicates atrial arrhythmia; CHB, complete heart block; FDG, fluorodeoxyglucose; LA, left atrial; LV, left ventricular; RA, right atrial; RV, right ventricular; SUV, standardized uptake value; and VT, ventricular tachycardia.

*At time of diagnosis of cardiac sarcoidosis (CS).

was performed 1 month later. Four months later the patient developed complete heart block unrelated to ablation and this led to investigation for and a subsequent diagnosis of CS. The atrial tachycardia was considered to be secondary to CS. Patient 2 presented with a stroke at age 56 years. Investigations found atrial flutter on ECG, and cardiovascular magnetic resonance imaging showed a dilated and dysfunctional left ventricle with a pattern of late gadolinium enhancement suggestive of CS. FDG-PET and then biopsy confirmed CS. Following implantable cardioverter-defibrillator placement, and initiation of amiodarone for ventricular tachycardia, there were no further episodes of AA. The patient had a cardiac transplant 2 years later.

Patient 3 originally presented at age 64 years with complete heart block, which was not worked up, but was likely caused by CS. Six years later she presented with severe nonischemic cardiomyopathy, ventricular tachycardia, and a single episode of atrial fibrillation, and was started on amiodarone. Three years later CS was diagnosed, and she has had no recurrent AA.

AA Burden Data

All patients had complete data for all visits. Eleven patients had AAs during follow-up. Three patients had very low burden, 6 patients had low burden, and 2 patients had more than low burden. Table 2 and Figure 1 show further clinical details for these patients.

The first of the 2 patients with more than low burden (patient 4) was diagnosed at age 56 years with CS after presenting with complete heart block. She had no history of AAs before her diagnosis and there was no atrial FDG uptake on her baseline PET. Her monthly AA burden, while her disease was active, based on serial PET scans, was 7.3%±5.5%. After therapy with steroids, her disease was suppressed and there was no disease relapse after stopping her second course. Her monthly AA burden, while her disease was inactive, was 2.2%±1.7% (*P*<0.001, compared with burden during active disease).

The second patient with more than low burden (patient 5) presented with monomorphic ventricular tachycardia at age 56 years and CS was diagnosed based on cardiac MRI, FDG-PET scan, and a cardiac biopsy. She had biatrial FDG uptake on her baseline scan. Her disease was difficult to suppress, and she had several changes of therapy (Figure 1). Disease was still active and she developed paroxysmal AA with an average monthly burden of 2.4%±2.9%, as well as an episode of persistent AA requiring cardioversion. On her most recent PET scan in October 2018, her disease was fully suppressed, and her device detected only 2 discrete episodes of atrial fibrillation between 2014 and 2019
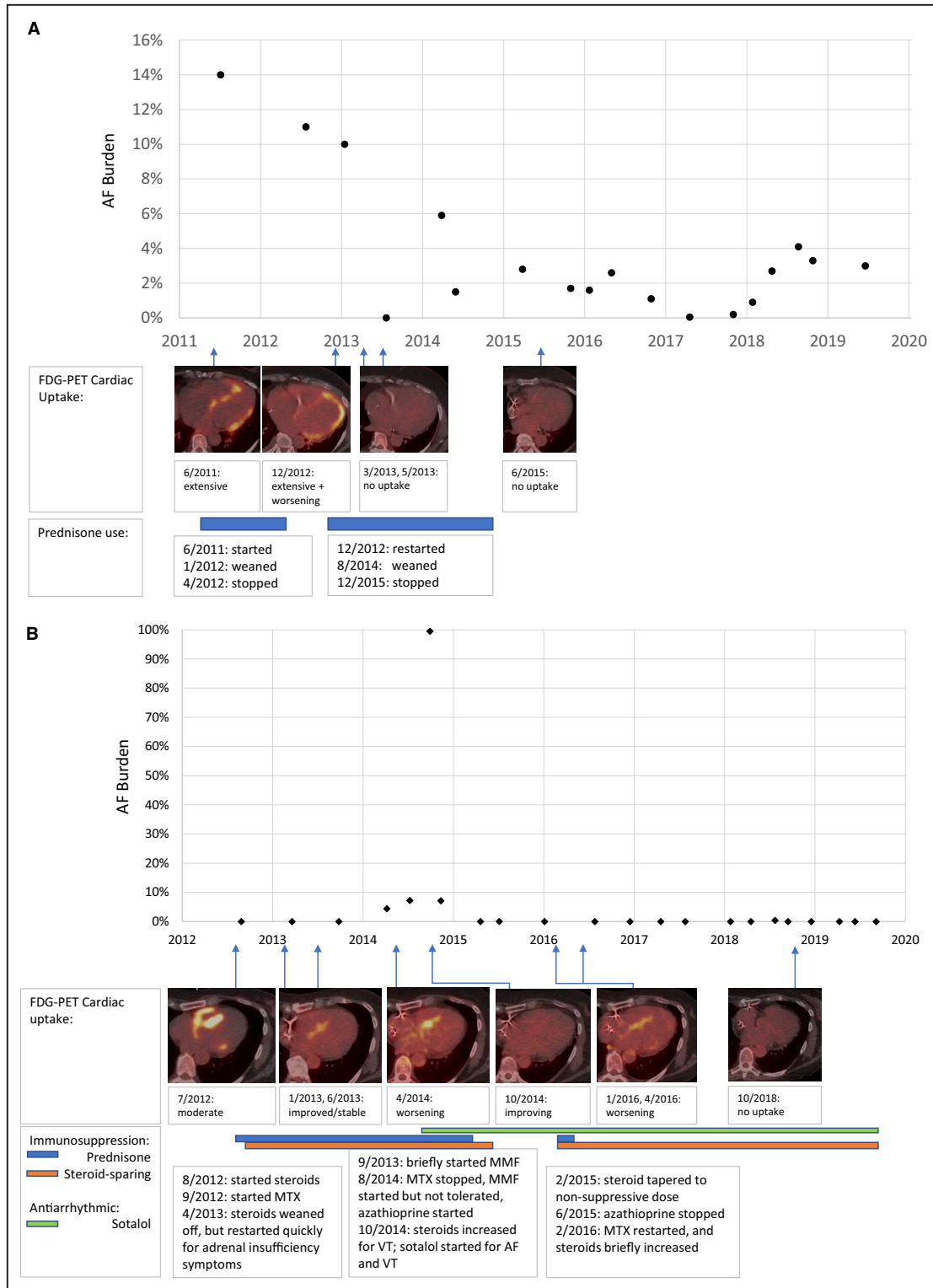
Figure 1. Clinical course of the 2 patients with more than low burden atrial arrhythmia (AA) at follow-up after initial diagnosis of cardiac sarcoidosis (CS).
Device-detected AA burden is shown on top, along with a summary of CS treatment and fluorodeoxyglucose (FDG)-positron emission tomography (PET) activity below. **A**, A 56-year-old woman (patient 4) with a diagnosis of CS after presenting with complete heart block. There was no history of AA before her diagnosis and no atrial FDG uptake on her pretreatment PET scan. B, A 56-year-old woman (patient 5) with a diagnosis of CS after presenting with monomorphic ventricular tachycardia (VT). There was no history of arrhythmia before her diagnosis and there was biatrial FDG uptake on her pretreatment PET scan. AF indicates atrial fibrillation; MMF, mycophenolate mofetil; and MTX, methotrexate.

(mean monthly burden, 0.023%±0.089%; *P*<0.005, compared with burden during active disease).

FDG-PET Scan Analysis: Atrial FDG Uptake

In brief, there were 16 patients with atrial FDG uptake (Table 3). Fifteen patients had focal uptake and 1 had focal on diffuse uptake. A representative case is shown in Figure 2.

Predictors of AA

Univariate analysis is shown in Table 4. Only left atrial (LA) FDG uptake approached significance, occurring more commonly in patients with subsequent AAs (3/11, 27.2%) compared with those without AAs (1/22, 4.5%, *P*=0.06).

DISCUSSION

We believe that this is the first study to prospectively evaluate the frequency of AAs as a presenting feature of

Table 3. FDG-PET Results at the Time of Diagnosis of CS (N=33)

Ventricular data	
Focal/focal on diffuse LV pattern	28/5
Discrete LV areas with increased FDG uptake	5.00±3.30
LV SUV$_{max}$	9.66±4.21
LV SUV$_{mean}$	3.74±2.51
RV FDG uptake	16/33 (48.5)
SRS	5.27±6.13
Atrial FDG uptake	
Any atrial uptake	16/33 (48.4)
Focal/focal on diffuse atrial pattern	15/1
LA uptake only	4/16 (25.0)
RA uptake only	3/16 (18.8)
Septal uptake only	3/16 (18.8)
Biatrial uptake	6/16 (37.5)
Whole-body FDG uptake	
Lymph nodes	28/33 (84.8)
Lungs	17/33 (51.5)
Spleen	7/33 (21.2)
Liver	6/33 (18.2)
Bone	9/33 (27.3)
Neurological	1/33 (3.0)
Skin/subcutaneous (PET findings)	1/33 (3.0)
No. of extracardiac organ involvement, mean	2.09

Values are expressed as number/number, mean±SD, or number (percentage). CS indicates cardiac sarcoidosis; FDG, fluorodeoxyglucose; LA, left atrial; LV, left ventricular; PET, positron emission tomography; RA, right atrial; RV, right ventricular; SRS, summed rest score; and SUV, standardized uptake value.

clinically manifest CS, and to examine AA incidence in follow-up after the diagnosis of CS. Our study has 2 main findings: first, AAs are a rare presenting feature of clinically manifest CS, with only 1 of 33 patients (3.0%) diagnosed with CS presenting with AAs. This patient also had evidence of atrioventricular block. Second, using device diagnostics, we found that AAs occurred in a minority of patients at follow-up after diagnosis of CS. In addition, the burden of AA was very low in most patients. Only 2 patients (6.1%) had an episode that lasted >24 hours.

Previously published information regarding CS presenting with AAs is limited to case reports.[6–8] Golwala et al[6] reported a 45-year-old Black patient who presented with paroxysmal atrial tachycardia and atrial fibrillation, and was found to have underlying CS. Enzan et al[7] reported a 61-year-old woman who presented with paroxysmal atrial tachycardia and was found to have CS. Of interest, the authors also described focal FDG uptake in the LA wall.

Eleven of 33 (33.3%) patients had AAs during follow-up. Of the 11 patients, 3 had very low burden, 6 had low burden, and the remaining 2 had more than low burden. Two previous retrospective studies reported on the incidence of AAs and CS. Viles-Gonzalez et al[16] investigated 100 patients with biopsy-proven systemic sarcoidosis and evidence of cardiac involvement by performing cardiovascular magnetic resonance imaging, PET, or endomyocardial biopsy, and followed them for a mean of 5.8 years. After reviewing ECGs, device interrogation data, and ambulatory telemetry monitoring, they found a 32% incidence of supraventricular arrhythmias. Atrial fibrillation was the most common supraventricular arrhythmia in 18% of patients, followed by atrial tachycardia in 7%, atrial flutter in 5%, and atrioventricular nodal reentry tachycardia in 2%.[16] LA enlargement was the only independent predictor of AAs (risk ratio, 6.12; 95% CI, 2.19–17.11). Cain et al[17] studied 44 patients with biopsy-proven extracardiac sarcoidosis and a diagnosis of cardiac involvement based on late gadolinium enhancement on cardiovascular magnetic resonance imaging. AAs were documented in 16 of 44 patients (36.3%) during a median follow-up of 25 months; there were no significant independent predictors of AAs. [17] There were no data presented on AA burden or duration of episodes in either study.

Our observation that 33% of patients had AAs at follow-up is similar to the rates previously reported (32%[16] and 36.3% [17]). However, a closer comparison of the studies would suggest that the AA burden in our patients was likely substantially less than in the 2 prior studies. The first important consideration is the different methods of monitoring for AAs. In our study, burden was assessed by continuous monitoring via the atrial lead of implantable cardioverter-defibrillators. In the other 2 studies, monitoring was intermittent; full details are not available, but a mixture of Holter monitoring,
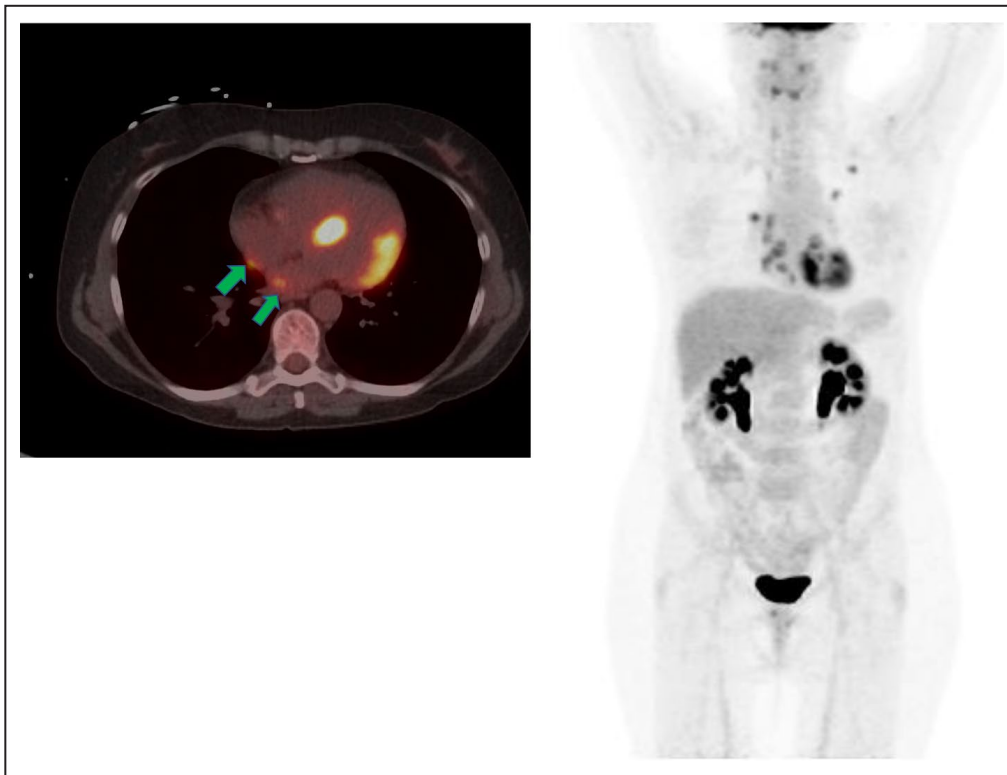
Figure 2. Fusion (left) and whole-body fluorodeoxyglucose-positron emission tomography (right) images of a 59-year-old patient who presented with complete heart block.
Note: focal uptake in the left atrium (maximum standardized uptake value, 4.43) and right atrium (maximum standardized uptake value, 5.54), shown by the green arrows. This patient has had no atrial arrhythmias in the 9 years since diagnosis.

ECGs, and implantable device assessments were used.[16,17] Hence, it follows that with our more complete monitoring strategy, perhaps a higher incidence of AAs might have been expected. The second consideration is the lower individual patient AA burden in our study. Only 2 of 33 (6.1%) patients had episodes >24 hours in our study. In the other 2 studies, although some details are lacking, almost all were symptomatic (100%[17] in one study, and 96%[16] in the second); additionally, a significant proportion in one study (28%) went on to ablation after failing antiarrhythmic drugs.[18] Thus, it would seem that almost all patients who had AAs detected, had clinically significant burden.

There are several possible explanations for the lower burden in our study. First, the other studies were retrospective in design with an important attendant risk of selection and/or referral bias. In contrast, our study was a prospective study of consecutively presenting patients. Second, our study only included patients with CS who were treatment-naive; in general, all were quickly treated following diagnosis. This is relevant given that AAs in CS are thought to be caused by a combination of atrial inflammation and scarring, and early diagnosis and prompt therapy likely minimized the amount of atrial scarring. There

are limited details on the time course of AA presentation and treatment of the underlying sarcoidosis available from the other publications (56% of patients received immunosuppression,[16] while data were not presented[17] in the second study). Third, our study focused on a different phenotype of patients with CS. Specifically, we focused on patients with acute presentations of severe clinically manifest cardiac sarcoid. In contrast, the prior studies investigated patients who initially presented with extracardiac sarcoid and then were subsequently evaluated for asymptomatic cardiac involvement.[16,17] A final possible explanation also relates to potentially different phenotypes between studies. We have previously described a specific phenotype of clinically manifest CS, mostly in patients of Northern European descent, with minimal or no pulmonary involvement and no pulmonary hypertension.[19] In contrast, most patients in the prior studies had pulmonary involvement (75%[17] and 82%[16]) and pulmonary hypertension (30% in one study[16], not reported in the second[17]). Hence, it is possible that some of those patients had AAs secondary to pulmonary hypertension.

We had limited power to look for predictors of development of AAs. Only 1 variable approached

Table 4. Patient Characteristics at the Time of CS Diagnosis, Stratified by Presence of AA at Follow-Up

	Patients With AA (n=11)	Patients Without AA (n=22)	P Value
Age at presentation of CS, y	55.91±8.01	56.45±7.53	0.85
White race	10/11 (90.9)	21/22 (95.5)	0.61
Women	7/11 (63.6)	8/22 (36.4)	0.14
History of extracardiac sarcoidosis	2/11 (18.2)	4/22 (18.2)	1.00
Hypertension	5/11 (45.5)	7/22 (31.8)	0.44
Diabetes mellitus	2/11 (18.2)	2/22 (9.1)	0.45
Prior AA	1/11 (9.1)	2/22 (9.1)	1.00
Presenting cardiac feature:			
Sustained Mobitz II and/or third-degree atrioventricular block	10/11 (90.9)	18/22 (81.8)	0.49
VT or cardiac arrest	1/11 (9.1)	4/22 (18.2)	0.49
Sustained Mobitz II and/or third-degree atrioventricular block and VT	1/11 (9.1	1/22 (4.5)	0.61
LV ejection fraction on echocardiogram	50.97±11.2	51.18±12.03	0.96
LA volume index on echocardiogram	30.66±7.92	31.03±12.79	0.94
Type of device (dual-chamber versus CRT)	10/11 (90.9)	19/22 (86.4)	0.71
Discrete LV areas with increased FDG uptake	4.91±3.70	5.22±3.00	0.55
LV SUV$_{max}$	10.36±5.37	8.52±3.78	0.12
LV SUV$_{mean}$	3.39±2.21	3.85±2.63	0.57
RV FDG uptake	5/11 (45.4)	12/22 (54.5)	0.62
SRS	6.91±6.95	5.09±5.95	0.62
Any atrial uptake	3/11 (27.2)	4/22 (18.2)	0.085
LA uptake (±septal)	3/11 (27.2)	1/22 (4.5)	0.059
RA uptake (±septal)	0	3/22 (13.6)	
Septal uptake only	0	3/22 (13.6)	
Biatrial uptake	0	6/22(27.2)	

Values are expressed as mean±SD or number (percentage). AA indicates atrial arrhythmia; CRT, cardiac resynchronization therapy; CS, cardiac sarcoidosis; LA, left atrial; LV, left ventricular; RA, right atrial; RV, right ventricular; SRS, summed rest score; SUV, standardized uptake value; and VT, ventricular tachycardia.

statistical significance: LA FDG uptake occurred more commonly in patients with subsequent AAs (27.2% compared with 4.5%, P=0.06). In the study by Viles-Gonzalez et al,[16] LA enlargement was the only independent predictor of AAs (risk ratio, 6.12; 95% CI, 2.19–17.11). There were no independent predictors of AAs in the second study.[17]

Evidence that immunosuppression is useful for the treatment of AAs in patients with sarcoidosis is limited to case reports.[8,9] In our 2 patients with important AA burden, there was less AA after CS was treated and there was no FDG uptake on PET scan. The 2014

Heart Rhythm Society guidelines on the management of arrhythmias in patients with CS contain limited guidance, with the writing group voting on a recommendation that a trial of immunosuppression can be useful in patients with CS who have AAs.[11] Most of the writing group (8/14 [57.1%]) voted to include this recommendation but the vote did not reach the predefined threshold to become a formal recommendation. Other recommendations were to assess anticoagulation based on a standardized score, and to avoid class I antiarrhythmic drugs.[11] Data on catheter ablation of AAs in CS are scarce. Willner et al[18] reported on 9 patients (5 with AA, 2 with LA flutter, and 2 with typical flutter), and after ablation, over an average follow-up period of 1.8 years, 2 patients had recurrence (1 patient with atypical atrial flutter and another patient with AA).[18]

Limitations

The major limitation of our study is the small sample size. This is attributable to the strict inclusion criteria of the study. Also, it follows from the inclusion criteria that our observations are limited to that specific population and cannot be extrapolated to other subsets of CS, eg, patients who do not have an implanted device. However we believe our population is similar to most patients presenting with clinically manifest CS, who are typically recommended to receive an implantable cardioverter-defibrillator (usually with an atrial lead).[11] Our findings cannot be extended to patients with less severe forms of CS; specifically, patients with clinically silent disease.[1] Another limitation is the lower-than-expected rate of AAs, which limited our power to examine predictors. A final issue is that our observations are in a population that exhibits a specific phenotype of clinically manifest CS, which has been described mostly in patients of Northern European descent.[19]

Conclusions

Our study had 2 main findings: first, that AAs are a rare presenting feature of clinically manifest CS; and second, using implanted device diagnostics, AAs occurred in a minority of patients at follow-up after diagnosis of CS. In addition, most patients who developed AA had a very low burden. Only 2 patients had episodes >24 hours at follow-up, and both patients had a lesser burden after CS was successfully treated.

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