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Original Article

Incidence of Atrial Fibrillation as the Initial Manifestation of Cardiac Sarcoidosis: Insights From a Catheter Ablation Registry

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ABSTRACT

Background: Cardiac sarcoidosis (CS) is a rare form of arrhythmogenic cardiomyopathy; a delayed diagnosis can lead to significant consequences. Patients with clinically manifest CS often have minimal extracardiac involvement and thus frequently present initially to cardiology. Indeed, certain specific arrhythmic scenarios should trigger investigations for undiagnosed CS. Atrial fibrillation (AF) has been described as one of the presenting features of CS; however, the incidence of this presentation is not known.

RÉSUMÉ

Contexte : La sarcoïdose cardiaque (SC) est une forme rare de cardiomyopathie arythmogène; un retard dans le diagnostic peut entraîner d'importantes conséquences. Les patients qui présentent une SC cliniquement manifeste ont souvent une atteinte extracardiaque minime, et consultent donc souvent d'abord en cardiologie. En effet, certains scénarios arythmiques précis devraient déclencher la recherche de signes d'une SC non diagnostiquée. La fibrillation auriculaire (FA) a été décrite comme un signe indicateur de SC; on ne

Sarcoidosis is a chronic inflammatory condition of unclear origin, characterized by organ infiltration with non-necrotizing granulomas. The lungs and lymph nodes are predilection sites, being involved in about 90% of cases.[1-5] In a small proportion of patients, the inflammatory process may affect the heart, leading to the development of clinically manifest cardiac sarcoidosis (CS). This rare form of cardiomyopathy usually manifests in middle-aged individuals; typical presentations include atrioventricular conduction disturbances, ventricular arrhythmias (VAs), and impaired ventricular function.[2,6,7] An early diagnosis is paramount to reducing the risk for adverse events.

Recognition is increasing that patients with clinically manifest CS often have minimal extracardiac involvement and thus frequently present to the cardiology department.[6] Guidelines suggest that certain specific clinical scenarios should trigger investigations for undiagnosed sarcoidosis.[1,4,8,9] For example, unexplained high-degree atrioventricular (AV) block in individuals age < 60 years, or idiopathic VA, may be caused by underlying CS in up to 47% and 29% of cases, respectively.[6,7] Atrial tachyarrhythmias, including atrial fibrillation (AF), have been reported to affect 29%-33% of CS patients, and they can occur at any time during the course of the disease. They also have been described as the initial manifestation of CS.[10-16] Previous research has focused predominantly on the most threatening presentations; little is known about the incidence of AF as the initial manifestation of CS and whether further workup should be warranted to rule out this condition.

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Methods: At our institution, cardiac computerized tomography is routinely performed prior to catheter ablation for AF. Noncardiac incidental findings are described by radiologists and are followed-up by interval investigations. We systematically reviewed noncardiac reports from 1574 consecutive patients in our prospective AF ablation registry. Specifically, we used text-scraping techniques to search on the following keywords: "adenopathy" and "sarcoidosis." Detailed chart review of identified cases was then performed to evaluate results of interval investigations and assess long-term outcomes.

Results: Twenty of 1574 patients (1.3%) had noncardiac reports containing "adenopathy" and/or "sarcoidosis." After interval imaging and a follow-up period averaging 60 $\pm$ 35 months, only 2 patients of 1574 (0.13%) were diagnosed with CS. Four of 20 (20%) had a previous history of extracardiac sarcoidosis, and another 1 of 20 (5%) was subsequently diagnosed with extracardiac sarcoidosis. However, none of these 5 patients had evidence of cardiac involvement.

Conclusions: CS is a rare finding among patients undergoing a first-time AF ablation. Our findings suggest that AF is an uncommon initial presentation of CS. Thus, investigations for CS in patients with AF are not warranted routinely, unless additional suggestive clinical features are present.

Méthodologie : Dans notre établissement, la tomodensitométrie cardiaque est souvent réalisée avant une ablation par cathéter de la FA. Les découvertes non cardiaques fortuites sont décrites par les radiologues, puis font l'objet d'un suivi par des examens d'imagerie réalisés à intervalles déterminés. Nous avons systématiquement évalué les éléments non cardiaques signalés chez 1 574 patients consécutifs dans notre registre prospectif sur l'ablation de la FA. Nous avons utilisé des techniques de dépouillement du texte pour trouver les mots-clés suivants : « adenopathy » (adénopathie) et « sarcoidosis » (sarcoïdose). Un examen du dossier médical complet des cas retenus a été réalisé pour évaluer les résultats des examens de suivi et évaluer les résultats à long terme.

Résultats : Parmi les 1 574 patients, 20 (1,3 %) présentaient des notes non cardiaques contenant les termes « adenopahy » (adénopathie) ou « sarcoidosis » (sarcoïdose). Après l'examen d'imagerie et une période de suivi d'une durée moyenne de 60 $\pm$35 mois, seuls deux patients (0,13 %) ont reçu un diagnostic de SC. Quatre des 20 patients visés (20 %) présentaient des antécédents de sarcoïdose extracardiaque, et un patient sur 20 (5 %) a reçu un diagnostic de sarcoïdose extracardiaque à la suite de l'intervention. Toutefois, aucun de ces cinq patients ne montrait de signes d'atteinte cardiaque.

Conclusions : La SC est une occurrence rare chez les patients qui subissent une première ablation de la FA. Nos constats indiquent que la FA est une présentation initiale peu commune de la SC. Aussi, la recherche de la SC chez les patients atteints de FA n'est pas justifiée dans une procédure de routine, à moins que d'autres caractéristiques cliniques pointant vers cette affection ne soient présentes.

In this study, we sought to investigate the incidence of undiagnosed CS in a population of patients investigated with advanced cardiac imaging (computerized tomography [CT] or cardiac magnetic resonance [CMR]) in preparation for catheter ablation for symptomatic AF. A secondary aim was to describe the ablation findings in the patients with sarcoidosis.

Material and Methods

Patients

We evaluated a population of consecutive patients, from our prospective AF catheter ablation registry, accepted for their first ablation. Patients scheduled for AF ablation routinely undergo a preoperative cardiac CT scan at 1-6 months prior to the procedure, to assess pulmonary vein anatomy and exclude thrombus in the left atrial appendage. Occasionally, at physician discretion, and/or patient preference, pre-ablation imaging is performed using CMR. Noncardiac structures included in the scanned field (usually from the carina to the lung bases) are evaluated separately by thorax radiologists. Incidental, noncardiac findings are disclosed to clinicians in dedicated supplemental reports and are followed up by interval investigations, if needed.

A comprehensive prospective database containing all AF ablations performed at our institution was interrogated, to generate a list of consecutive patients between January 1, 2003 (opening of our AF ablation program) and May 31, 2021 (in order to allow for appropriate follow-up).

Chest imaging and cohort creation

A system analyst retrieved supplemental reports from all cardiac CT scans within the period of interest and plotted them in a dedicated database (Excel for Windows, Microsoft Corp., Redmond, WA). Using the text scraping function, we identified reports containing the keywords "adenopathy" and/or "sarcoid." Each matching report was individually reviewed to assess the presence of significant lymphadenopathy (defined as lymph nodes with a diameter exceeding 1 cm) or findings compatible with sarcoidosis. Reports that fulfilled these criteria were noted, along with their corresponding case-sensitive identification numbers (medical record number [MRN] codes). The list that was generated was subsequently cross-matched with the one obtained from the AF ablation database, using case-sensitive MRN codes. In this way, we could identify those patients scheduled for AF ablation with incidental findings suggestive of sarcoidosis, our final study population. Those patients without a preoperative cardiac CT scan, but with CMR imaging, were reviewed on an individual basis and included in the analysis.

Lastly, we reviewed medical charts for each patient in detail, looking particularly for further workup to address incidental preoperative findings. All available sources of records were consulted, including referral letters, imaging

reports, and consultation notes from other institutions. When appropriate, we reviewed procedural reports and electroanatomic maps sampled during the ablation procedures. CS diagnosis was defined according to the 2014 Heart Rhythm Society and/or the 2016 Japanese Circulation Society diagnostic criteria.[1,4]

Data management and ethics

Data were managed according to the requirements dictated by our local data protection authority. The study was approved by our institutional board and performed in accordance with the principles stated in the Declaration of Helsinki.

Statistical analysis

Continuous variables are presented as mean and standard deviation, whereas categorical variables are presented as count and percentage. Statistical analysis was performed using IBM SPSS version 28 (IBM Corp., Armonk NY).

Results

Study population

A total of 1583 patients underwent first-time AF ablation in the investigated time interval. Of these, 1568 underwent a preoperative cardiac CT, 6 received CMR imaging alternatively, and 9 did not undergo any form of cardiac imaging. Our study cohort consisted therefore of 1574 AF ablation patients, whose baseline data are shown in Table 1.

Supplemental reports, including incidental, noncardiac findings from a total of 22,920 cardiac CT scans, were reviewed. A keyword search returned 175 individual patients. The keywords "sarcoid" and "adenopathy" retrieved 109 and 98 hits, respectively, whereas both keywords were included in 32 reports. Cross-matching the list generated by keyword search and our AF ablation cohort resulted in a final population of 20 patients with one or both keywords (Fig. 1).

Of note, 4 of 20 patients (20%) had a previous history of extracardiac sarcoidosis: the diagnosis was histologically verified in 3, whereas 1 had a remote (> 40 years earlier) diagnosis without additional details. None of these 4 patients ever received immunosuppressive treatment, nor did they ever meet the criteria for a diagnosis of CS. Demographic data of patients with radiologic findings compatible with sarcoidosis are presented in Table 2.

Workup for incidental findings

Interval chest imaging was performed in 19 of 20 patients after a mean 11 ± 18 months, with one or a combination of the following modalities: chest CT (14 patients) or conventional chest radiograph (13 patients). Interval imaging showed improvement in 7 of 19 patients, whereas findings in the remaining 12 patients either progressed (3 patients) or remained unchanged (9 patients). Supplemental advanced cardiac imaging was performed in 7 patients, either with CMR alone (6 patients) or in combination with fluorodeoxyglucose positron emission tomography (FDG-PET; 3). One patient underwent exclusively FDG-PET scanning, due to a non-CMR conditional pacemaker. Workup for the incidental CT findings led to the diagnoses shown in Table 3.

Notably, only 2 of 20 patients (10%) were diagnosed with CS. After a follow-up consisting of 60 ± 35 months, none of the remaining 18 patients developed other manifestations that might suggest CS (ie, no patient developed high-grade AV block or VAs, or experienced worsening of their ventricular function). Hence, the incidence of undiagnosed CS in this cohort was 2 of 1574 patients (0.13%).

Table 1. Baseline characteristics of patients in the AF ablation database with chest imaging

Characteristic	n = 1574
Female sex	459 (29)
Age at the index procedure, y	60 ± 10
< 50	256 (16)
< 60	782 (50)
< 70	1459 (93)
Persistent AF	467 (30)
Coronary artery disease	204 (13)
Diabetes mellitus	158 (10)
Hypertension	626 (40)
Significant lung disease	84 (5)
Obstructive sleep apnea	329 (21)
Previous cardiac surgery	74 (5)
Cardiomyopathy	178 (11)
Tachycardia-mediated cardiomyopathy	132
Idiopathic dilated cardiomyopathy	18
Hypertrophic cardiomyopathy	11
Ischemic cardiomyopathy	17
Implanted cardiac device	42 (3)
Pacemaker	31
Defibrillator	11

Values are n (%), unless otherwise indicated.
AF, atrial fibrillation; SD, standard deviation.

History of the patients diagnosed with CS

Case 1. A 55-year-old gentleman underwent a previous catheter ablation for symptomatic typical atrial flutter. He also had a history of nonischemic cardiomyopathy with a lowest recorded left ventricular ejection fraction (LVEF) of 29%. He was later considered for catheter ablation of persistent AF. At that time, an electrocardiogram showed sinus bradycardia of 51 beats/minute, left-axis deviation, left bundle branch block (a QRS duration of 158 ms), and first-degree AV block (PR duration of 222 ms). Preoperative cardiac CT revealed mild bilateral hilar and subcarinal lymphadenopathy, suggesting sarcoidosis as a possible cause. Supplementary CMR revealed severe biventricular hypokinesia, a LVEF of 26%, and a right ventricular ejection fraction of 20%. Subendocardial and mesocardial late gadolinium enhancement involving the basal, mid, anteroseptal, and septal walls of the left ventricle was highly suggestive of sarcoid infiltration (Fig. 2). A baseline FDG-PET study did not show any active FDG uptake. However, a repeat study 2 years later showed intense focal uptake in the anterolateral wall, suggesting active inflammation (Fig. 3A, B). A rest perfusion scan showed mild reduction in tracer uptake across multiple segments of the left ventricle (Fig. 3C). After AF ablation, he was administered guideline-directed heart failure medical therapy and was implanted with a cardiac resynchronization therapy pacemaker-defibrillator. His symptoms and his LVEF improved significantly,

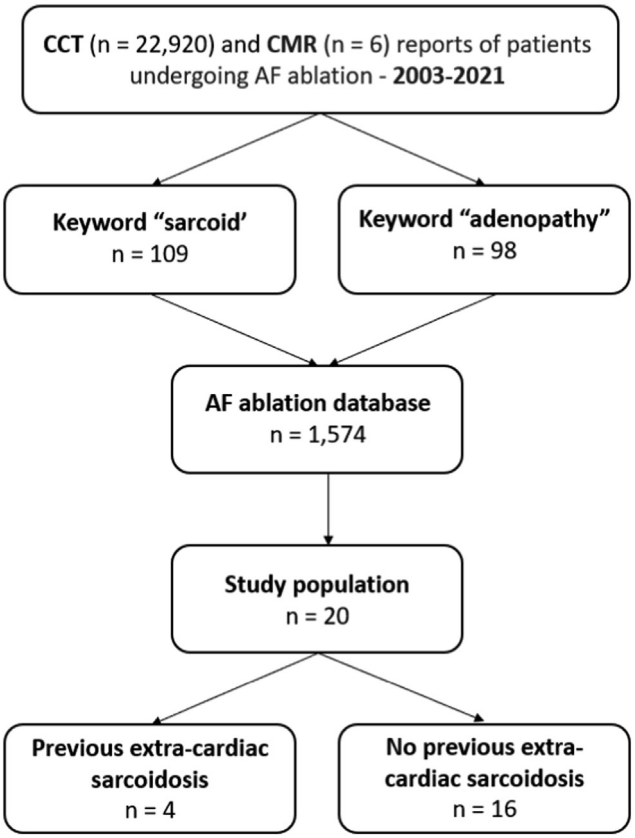

Figure 1. Flowchart showing patients' inclusion process. AF, atrial fibrillation; CCT, chest computed tomography; CMR, chest magnetic resonance.

and systemic immunosuppression was felt to not be indicated. However, 8 years after baseline, he developed a significant worsening of his LVEF: a repeat FDG-PET scan showed focal uptake in basal to mid anteroseptal segments, suggestive of active inflammation. Immunosuppression with a combination of prednisone and methotrexate was started. Despite ablation and antiarrhythmic drugs, his AF was poorly controlled, and he recently underwent AV-node ablation. His last recorded LVEF was 45%. His defibrillator has never delivered any therapy.

Case 2. A 54-year-old gentleman with previous history of obesity and obstructive sleep apnea, developed recurrent, symptomatic AF requiring multiple cardioversions. Baseline echocardiography revealed a mildly reduced LVEF of 40%. A baseline electrocardiogram showed sinus rhythm with left-axis deviation and borderline first-degree AV block (PR duration of 200 ms). Cardiac CT prior to catheter ablation showed multiple enlarged mediastinal lymph nodes: these findings remained unchanged at an interval study, 9 months later. Despite being in sinus rhythm, his LVEF did not improve. After 3 years, he experienced recurrence of AF, and a repeat ablation procedure was performed. Supplementary CMR imaging revealed mild left ventricular dysfunction, and patchy, nonischemic late gadolinium enhancement involving the septum, and inferior and inferolateral segments. A recent FDG-PET scan showed focal tracer uptake, suggestive of active, albeit mild, myocardial inflammation. Although his symptoms have improved, he is currently being considered for a trial of immunosuppression.

Findings from the ablation procedures

We reviewed procedural reports, as well as electroanatomic maps, for those patients with a previous sarcoidosis diagnosis (4) and those that received a sarcoidosis diagnosis following additional interval imaging (4). Four of 8 of these patients were ablated before the era of multipolar voltage mapping. Among the 4 with detailed left atrial voltage mapping (CARTO Confidense, Biosense Webster, Irvine, CA), only one patient (who ultimately received a CS diagnosis) had significant areas of low voltage in the posterior wall of the left atrium (Fig. 4).

Discussion

In this study, we were able to show that undiagnosed CS is an exceedingly rare finding (only 2 in 1574 patients) among patients undergoing first-time catheter ablation for AF. These results suggest that AF is an uncommon initial manifestation of CS.

Incidence of atrial arrhythmias as initial presentation of CS

A previous study from our group found that only 1 of 33 patients (3%) with clinically manifest CS presented with atrial arrhythmias.[12] Other evidence describing AF as initial manifestation of CS is limited to case reports.[14-16] Hussain and colleagues described the case of a young male patient who had undergone several catheter ablation procedures for symptomatic AF and had normal ventricular function.[14] Three years after his initial ablation procedure, chest pain workup with cardiac CT revealed incidental findings suggestive of sarcoidosis. Transbronchial biopsy confirmed the diagnosis, and additional FDG-PET scan showed hypermetabolic lesions

Table 2. Demographic characteristics of patients with incidental findings possibly suggestive of sarcoidosis

Characteristic	Previous history of extracardiac sarcoidosis n = 4	No previous history of extracardiac sarcoidosis n = 16
Female sex	1 (25)	3 (19)
Age at baseline, y	65 ± 1	64 ± 10
Body mass index, kg/m^2	27 ± 5	30 ± 6
Persistent AF	1 (25)	6 (38)
Hypertension	1 (25)	8 (50)
Obstructive sleep apnea	2 (50)	5 (31)
Coronary artery disease	1 (25)	4 (25)
History of cardiomyopathy	0	3 (19)
History of sustained ventricular arrhythmias	0	0
History of sustained high-degree AV block	0	0
History of any AV conduction disturbances	1 (25)	5 (31)
First-degree AV block	1 (25)	5 (31)
Hemiblock (R axis < −30° or > +90°)	1 (25)	4 (25)
Bundle branch block (QRS > 120 ms)	0	1 (6)

Values are n (%) or mean ± standard deviation.
AF, atrial fibrillation; AV, atrioventricular.

Table 3. List of interval investigations performed to follow up on incidental findings, and final diagnoses emerging from follow-up

Patient	Interval CT scan	Interval CR	Change in incidental findings	CMR scan	FDG-PET scan	Follow-up (mo)	Final diagnosis
1	**Yes**	**Yes**	**Resolution**	**Yes**	**Yes**	**111**	**CS**
2	No	Yes	Unchanged	Yes	Yes	17	Extracardiac sarcoidosis
3*	Yes	No	Resolution	Yes	No	60	Reactive adenopathy
4	Yes	No	Resolution	Yes	No	96	Reactive adenopathy
5*	Yes	Yes	Unchanged	Yes	No	110	Extracardiac sarcoidosis
6	Yes	Yes	Unchanged	No	No	99	Interstitial lung disease
7*	No	No	—	No	No	100	Reactive adenopathy
8†	No	Yes	Unchanged	No	No	73	Reactive adenopathy
9	No	Yes	Unchanged	No	No	102	Hematologic malignancy
10‡	Yes	Yes	Unchanged	No	No	89	Interstitial lung disease
11‡	Yes	Yes	Progression	No	No	50	Primary lung cancer
12	Yes	No	Resolution	No	No	66	Reactive adenopathy
13‡	Yes	Yes	Unchanged	No	No	17	Hematologic malignancy
14	**Yes**	**No**	**Unchanged**	**Yes**	**Yes**	**51**	**CS**
15	Yes	No	Resolution	No	No	39	Reactive adenopathy
16	Yes	No	Progression	No	No	25	Interstitial lung disease
17	No	Yes	Resolution	No	No	20	Reactive adenopathy
18*	No	Yes	Unchanged	No	Yes	25	Extracardiac sarcoidosis
19	Yes	Yes	Resolution	No	No	17	Reactive adenopathy
20	Yes	Yes	Progression	No	No	25	Hematologic malignancy

Bold indicates patients that ultimately received a diagnosis of cardiac sarcoidosis.

CMR, cardiac magnetic resonance; CR, chest radiograph; CS, cardiac sarcoidosis; CT, computed tomography; FDG-PET, fluorodeoxyglucose positron emission tomography.

*Patient with previous diagnosis of extracardiac sarcoidosis.

†Lost to follow-up.

‡Deceased.

in both atria, suggestive of active inflammation.[14] Golwala and Dernaika[15] described a 45-year-old, previously healthy man, who made multiple visits to the emergency department due to paroxysmal atrial tachycardia/AF. Further workup, including a chest CT showing marked lymphadenopathy, led to a diagnosis of CS.[15] Finally, Lau et al.[16] presented the case of a 55-year-old Caucasian male patient who was referred to catheter ablation for symptomatic persistent AF. Enlarged lymph nodes were detected on the preoperative cardiac CT scan, and advanced cardiac imaging with CMR and FDG-PET imaging confirmed CS.[16]

In this study, we sought to investigate this issue from the other direction—that is, instead of studying a population with CS, we reviewed a large cohort of patients who had AF that was sufficiently symptomatic to warrant ablation. Pulmonary findings and/or thoracic lymphadenopathy are found in the majority of patients (> 90%) with sarcoidosis, making chest CT a reasonable screening modality (sensitivity of 94%; specificity of 86%) for sarcoidosis.[2,3,5] Indeed, chest CT is recommended as the initial screening method to look for possible underlying sarcoidosis in a number of clinical scenarios, including in patients aged < 60 years who have unexplained AV block, patients with idiopathic ventricular tachycardia, and patients with new-onset uveitis of unknown origin.[1,3,8,9] The diagnostic yield in these subgroups is substantial, potentially unveiling undiagnosed CS in 11%-35% of patients.[2,9]

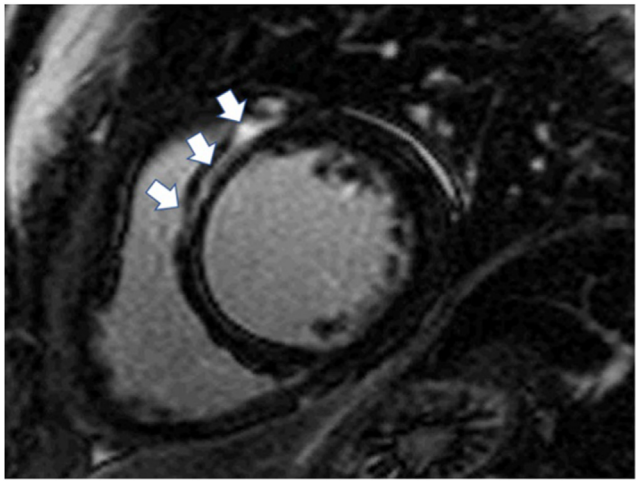

Figure 2. Cardiac magnetic resonance imaging showing short-axis view with mid-myocardial late gadolinium enhancement with the mid-anteroseptal segment (**white arrows**).

After reviewing radiologic findings in 1574 patients, we found only 2 patients with undiagnosed CS. A very important point to note is that both these patients had concomitant evidence of conduction system disease and impaired ventricular function. Hence, given the enormous burden of AF and the results of the present study, we argue that, in the absence of other cardiac manifestations, AF alone does not justify further workup aimed at excluding CS.

Incidence of AF in patients with sarcoidosis and CS

Patients with sarcoidosis are at increased risk for AF.[17-19] A recent investigation among over 20 million California residents showed that patients with sarcoidosis had a 10-fold higher risk of developing incidental AF, compared to the risk in a healthy population.[18] The presence of pulmonary hypertension secondary to lung involvement, chronic activated inflammatory response, and treatment with high-dose corticosteroids may all contribute to the development of AF in this population.[10,20] Additionally, AF may be caused by

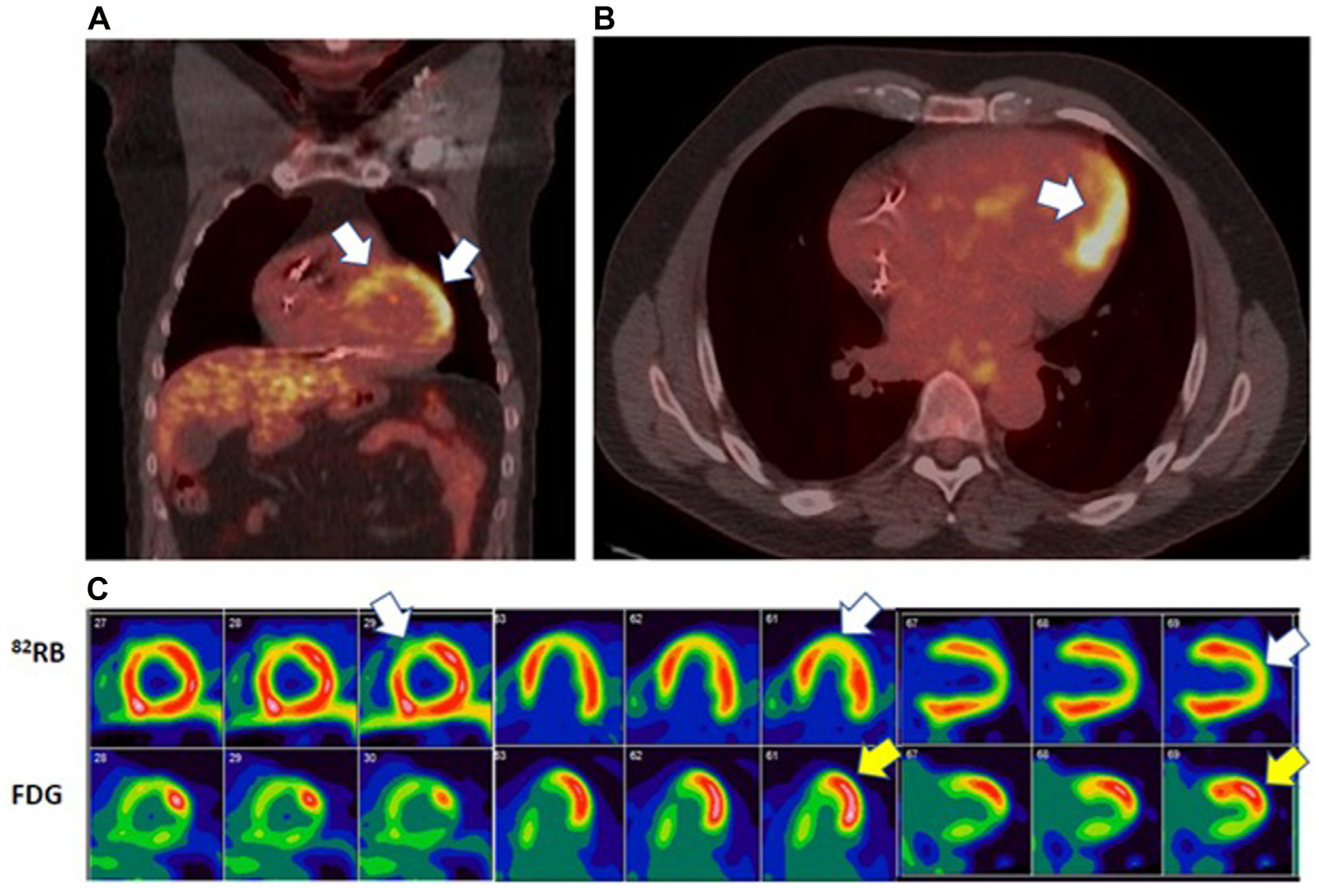

Figure 3. F-18 fluorodeoxyglucose positron emission tomography (^{18}FDG-PET) with (**A**) coronal and (**B**) axial computerized tomography of the thorax showing multiple areas of FDG uptake in the anteroseptal, anterior, and anterolateral segments (**white arrows**). (**C**) Rubidium-82 (^{82}RB) perfusion (**upper row**) and FDG (**lower row**) short axis, horizontal axis, and vertical long axis showing perfusions defects (**white arrows**) and myocardial FDG uptake (**yellow arrows**).

cardiac involvement of sarcoidosis, through either increased filling pressures in the presence of impaired ventricular function, or direct sarcoid infiltration in the atrial myocardium.[11,12,21,22] In the former scenario, one may expect AF to present later in the course of the disease, whereas in the latter, it may manifest early, even potentially as the initial manifestation of CS.

Viles-Gonzalez and colleagues[23] investigated the presence of supraventricular arrhythmias including AF, in a CS population. The authors found a prevalence of 18%: left atrial enlargement was found to be the only independent predictor, suggesting that AF may be a consequence of heart failure in these patients.[23] Other reports, including a prospective study that used arrhythmia monitoring from implanted cardiac devices, showed that atrial arrhythmias occur in roughly one third of CS patients.[12,21,22,24] These studies confirmed the role of left atrial enlargement as a predictor for the development of atrial arrhythmias but indicated the presence of atrial FDG uptake, a marker of atrial inflammation, as an additional prognostic parameter.[12,21,22,24] These findings indicate that atrial inflammation may be an important contributor to the development of AF. Furthermore, the work of Niemelä and colleagues showed that, in patients with atrial FDG uptake, AF occurs earlier and more often than in those without signs of atrial inflammation.[22]

Findings at ablation

In the ventricles, low electrogram voltage is commonly found in those areas with either active granulomatous inflammation or fibrosis.[2] Low voltage has also been associated with fibrosis in the atria. In this study, we found low voltage atrial electrograms in one patient with CS. One possibility is that myocardial inflammation had affected the left atrium, at some point in his clinical course. Nevertheless, the association between AF, low electrogram voltage, and atrial inflammation remains unclear and deserves further research.

Limitations

The intrinsic limitations of this single-centre investigation should be acknowledged.

Sarcoidosis was not the primary focus of the CT scans analyzed in this study, thus raising the possibility of pathologic findings being overlooked. This circumstance, however, is unlikely, as noncardiac structures were systematically evaluated by external thorax radiologists.

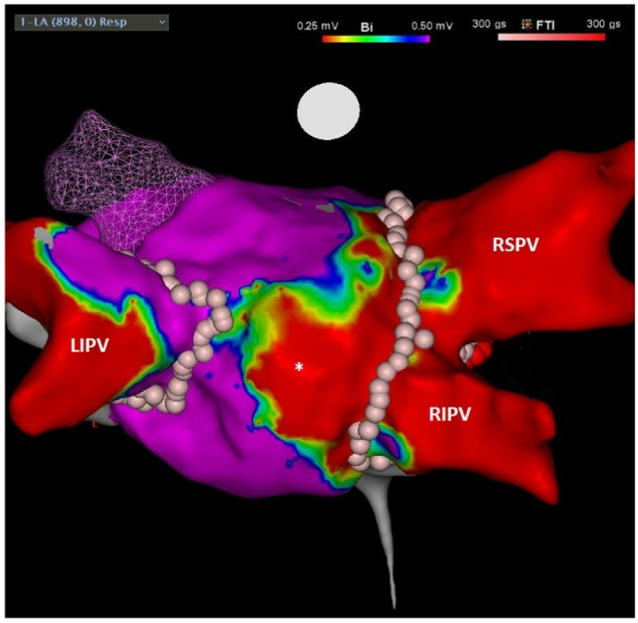

Figure 4. Electroanatomic map of a 55-year-old patient with a previous history of obesity, obstructive sleep apnea, and hypertension. Incidental pre-procedural findings led to a diagnosis of thoracic sarcoidosis. Supplemental cardiac magnetic resonance and positron-emission tomography were consistent with cardiac sarcoidosis. The electroanatomic map, sampled following pulmonary vein isolation, revealed a large low-voltage area in the posterior wall of the left atrium (**asterisk**). **Grey dots** represent ablation lesions. LIPV, left inferior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.

The mean age of patients (60 ± 10 years) was relatively higher than the age of a typical CS population (51 ± 9 years[7]); however, half of our cohort was aged < 60 years.

Six patients were further investigated by only interval chest radiograph, which is known to have lower sensitivity than chest CT in diagnosing sarcoidosis. Nevertheless, the long duration of our follow-up, averaging 60 months, without development of any typical manifestations, suggests that no patients with CS were missed.

Conclusion

Undiagnosed CS is an exceedingly rare finding among patients undergoing first-time catheter ablation for AF (only 2 in 1574 patients). Thus, screening investigations are not warranted routinely unless additional suggestive clinical features are present.

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Ethics Statement

Data were managed according to the requirements dictated by our local data protection authority. The study was approved by our institutional board and performed in accordance with the principles stated in the Declaration of Helsinki.

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Disclosures

D.H.B. has served on the advisory board for Star Therapeutics and Kinevant/Roivant Sciences, not pertinent to this work. The other authors have no conflicts of interest to disclose.

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