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CASE REPORT
Cardiac imaging

Natural evolution of cardiac sarcoidosis in an asymptomatic patient: a case report

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Background Sarcoidosis is a multi-organ granulomatous disease of unknown aetiology. Adverse outcome related with cardiac involvement, makes early diagnosis of cardiac sarcoidosis crucial.

Case summary In a 55-year-old man presenting with recurrent pulmonary infections, computed tomography (CT) showed several enlarged mediastinal lymph nodes and no lung pathology. Subsequent mediastinoscopy revealed the diagnosis of sarcoidosis. Further screening for organ involvement showed multifocal cardiac involvement both on cardiac magnetic resonance (CMR) and 18-F-fluorodeoxyglucose-positron emission tomography-computed tomography (^{18}F-FDG PET-CT). Because of the lack of functional deterioration and clinical symptoms, no steroid treatment was initiated and regular follow-up of cardiac abnormalities was performed by CMR. Unremarkable progression of cardiac involvement during the first 2 years of follow-up turned into a dramatic involvement after 4 years, with the increase in the number and size of lesions at late gadolinium enhancement (LGE) CMR. Late gadolinium enhancement areas matched the regions of strongly increased ^{18}F-FDG uptake. For the first time, the patient started complaining on shortness of breath, electrocardiography showed an atrioventricular block Grade 1. Cardiac biomarkers and cardiac function were still preserved. Steroid treatment was started. Although an electrophysiology study was negative, Holter monitoring showed ventricular arrhythmia. Cardioverter-defibrillator was implanted.

Discussion This case shows the progression of cardiac sarcoidosis on CMR in an asymptomatic untreated patient over a 4-year period, and rises the awareness of possible severe cardiac damage even in the absence of clinical signs of cardiac involvement. Combination of PET and CMR is appealing to better understand the evolution of cardiac sarcoidosis and may help in the management of such patients.

Keywords Case report • Cardiac sarcoidosis • CMR • PET-CT • ^{18}F-FDG

Learning points

- To show the natural evolution of cardiac sarcoidosis in an asymptomatic patient.
- To highlight the role of cardiac magnetic resonance and 18-F-fluorodeoxyglucose-positron emission tomography to depict and to follow the progression of cardiac sarcoidosis.

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Introduction

Sarcoidosis is a multi-organ granulomatous disease of unknown aetiology. The incidence of cardiac involvement varies between 5% and 10%, however, these percentages likely underestimate the true prevalence, as the disease course is often subclinical.[1,2] As cardiac involvement is related with adverse outcome, early diagnosis of cardiac sarcoidosis is crucial. We present a case of a dramatic progression of cardiac sarcoidosis in an asymptomatic patient over a period of 4 years.

Timeline

November 2014	Computed tomography (CT) for assessment of recurrent chest infection revealed mediastinal lymphadenopathy
	Mediastinoscopy revealed non-caseating granulomas
December 2014	Evidence of cardiac sarcoidosis at 18-F-fluorodeoxyglucose-positron emission tomography-computed tomography (^{18}F-FDG PET-CT) and cardiac magnetic resonance (CMR)
	Observation and clinical follow-up
2015	Follow-up visit + CMR: no disease progression
2016	Follow-up visit + CMR: mild disease progression
2017	Follow-up visit + transthoracic echocardiogram: no disease progression
2018	Follow-up visit + CMR + ^{18}F-FDG PET-CT: significant disease progression
	Steroid treatment initiated, ICD implanted

Case presentation

A 55-year-old male patient, with a history of arterial hypertension and recurrent pulmonary infections, presented with symptoms of a bronchopulmonary infection. Chest X-ray did not reveal a pulmonary infection but was suspicious for a small retro-cardiac nodule. Chest computed tomography (CT) showed several enlarged mediastinal lymph nodes. Subsequent mediastinoscopy revealed the diagnosis of sarcoidosis. Transthoracic echocardiogram (TTE) showed mild concentric left ventricular (LV) hypertrophy, preserved systolic and diastolic function, and absence of valvular abnormalities and pulmonary hypertension. ^{18}F-fluorodeoxyglucose-positron emission tomography-computed tomography (^{18}F-FDG-PET-CT) revealed several foci of increased myocardial FDG uptake. Cardiac magnetic resonance (CMR) showed normovolaemic and normokinetic ventricles with borderline increased septal wall thickness. At late gadolinium enhancement (LGE)-CMR, multifocal subepicardial enhancement was present in the basal anterior/inferolateral and mid to apical lateral LV wall (*Figure 1A*). As LGE-lesions spatially correlated with PET lesions, they were considered to represent active inflammation. Electrocardiography (ECG) findings were not specific, exercise stress test did not induce any chest pain or ECG changes, Holter monitoring, and cardiac biomarkers were also unremarkable (*Figure 2*, *Table 1*). On initial examination: blood pressure (BP)-140/80 mmHg, heart rate (HR)-66/min, oxygen saturation-98%, normal heart and lung auscultation, no ankle oedema, and no lymphadenopathy. Bronchoscopy, spirometry, and neurologic and ophthalmologic investigations were negative. Because of the lack of clinical symptoms and cardiac dysfunction, no treatment was initiated, but it was decided to closely follow-up the patient. Although a first follow-up CMR (2015) showed comparable findings, the 2016 CMR revealed new myocardial lesions in the RV outflow tract and inferior wall (*Figure 1B, C*). The ventricular function was normal, and the patient did not experience cardiac complaints and tolerated physical exercise well. In 2017, patient was still asymptomatic, there was no evidence of disease progression and CMR was substituted with TTE.

In October 2018, the patient presented with onset of dyspnoea and dry cough. At physical examination: BP-145/95 mmHg, HR-74/min, low-pitched breath sound, the rest was comparable to the examination at initial presentation. Electrocardiography showed an atrioventricular (AV) block Grade 1 (*Figure 2*). A new CMR showed important disease progression with increase in myocardial wall thickness, increase in size of the LGE regions, and presence of several new lesions (i.e. anterolateral/anteroseptal LV wall, anterior RV wall, and left atrium). Total LGE volume (37% of LV-mass) corresponded to a nearly three-fold increase compared to 2014 CMR. The LGE regions showed prolonged T1-relaxation time (range 1060–1090 ms; normal values at 1.5 T 997 ± 19ms) and increased extracellular volume values (range 30–60%; normal values 22–28%; *Figure 1E*). Remarkably, the global ventricular function was still low normal (ejection fraction (EF) 50%) and cardiac biomarkers remained within normal limits (*Table 1*). ^{18}F-FDG PET-CT scan showed multifocal areas with increased FDG uptake, nicely matching with the LGE areas (*Figure 3*). Moreover, strongly increased FDG uptake was present in abdominal and thoracic lymphadenopathies and to a lesser extent in the pulmonary parenchyma as well, consistent with nodal and pulmonary involvement. Subsequent spirometry revealed decreased pulmonary diffusion capacity. Holter monitoring as well as electrophysiology (EPI) study could not reveal (inducible) ventricular arrhythmias. It was decided to initiate steroid treatment (start dose: 32 mg/day), which was reduced to 24 mg/day at the latest (4-month) follow-up. Although the patient still complained of dyspnoea, physical examination and laboratory investigations (NT-proBNP-201 ng/L, hs troponine-0, 007 mcg/L) were not remarkable. Echocardiography showed decreased systolic LV function (EF 45%). Although a new EPI study could not induce ventricular arrhythmias, Holter monitoring showed frequent polymorphic ventricular extrasystoles and non-sustained ventricular tachycardia. Because of the increased risk of malignant ventricular arrhythmias the patient received implantation of cardioverter-defibrillator.

Discussion

Correct decision making in patients with cardiac sarcoidosis is crucial but often challenging, as shown in this case. As our patient had no cardiac symptoms, no evidence of ventricular arrhythmia or conduction disturbances and a preserved cardiac function during the first 3 years,

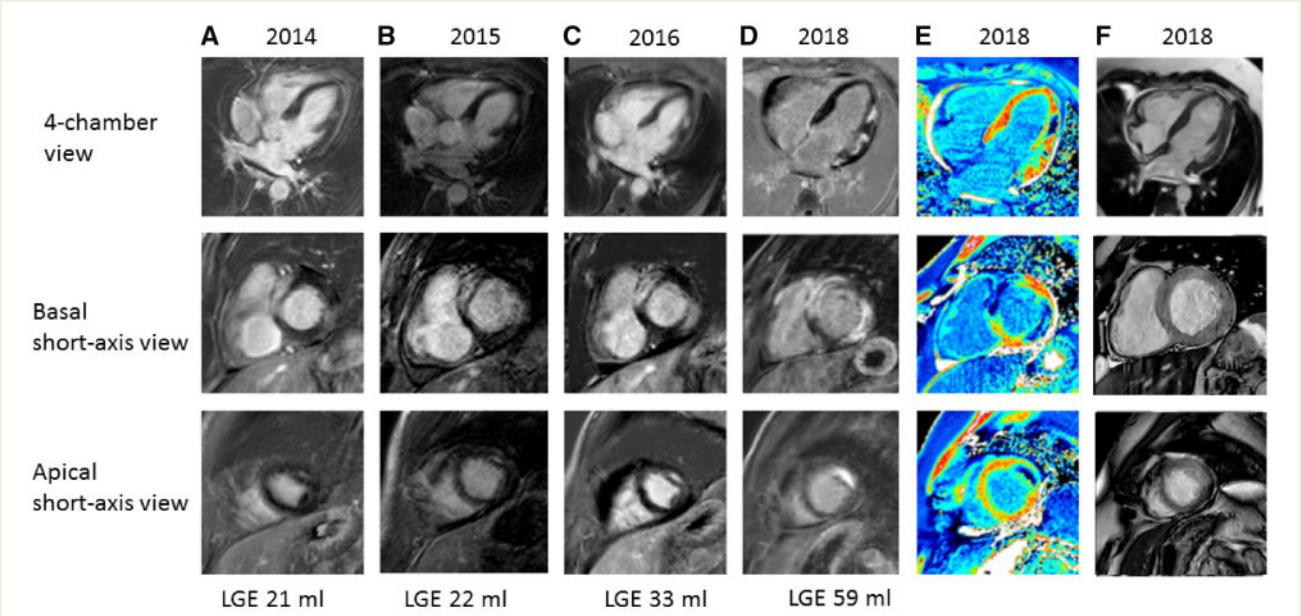

Figure 1 Progression of cardiac sarcoidosis at cardiac magnetic resonance. Late gadolinium enhancement-cardiac magnetic resonance (*A*–*D*) shows progressive increase in number and extent of myocardial lesions between 2014 and 2018. 2018 late gadolinium enhancement-cardiac magnetic resonance (*D*) matches well with post-contrast T1-maps (*E*). Cine images (*F*) show small pericardial effusion and increased myocardial wall thickness mainly in the lateral left ventricular wall.

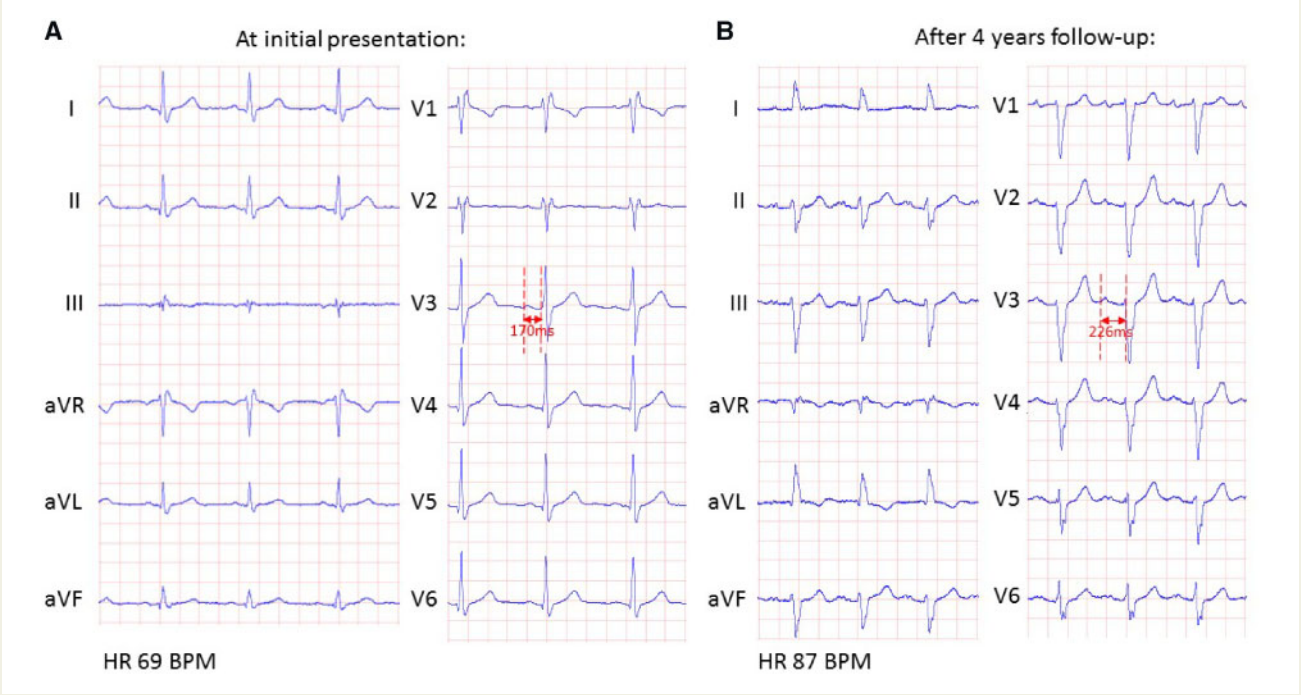

Figure 2 Electrocardiography findings at initial presentation (*A*) and after 4 years of follow-up (*B*).

Table 1 Imaging, ECG and laboratory findings during follow-up period

	2014	2015	2016	2018
CMR findings				
Left ventricle				
EDV, ml	221	200	191	243
Ejection fraction, %	53	58	61	50
Mass, g	129	127	144	158
EDD/ESD, mm	54/42	52/40	52/40	57/49
Septum, mm	12	13	14	18
Lateral wall, mm	10	9	10	13
MAPSE, %	16	17	16	15
Right ventricle				
EDV ml	230	229	229	227
Ejection fraction, %	50	50	53	51
TAPSE, %	25	29	21	25
Atrium				
Left atrium (cm^2/m^2)	13	13	14	14
Right atrium (cm^2/m^2)	10	11	12	11
Pericardial effusion	+	+	+	+
LGE (ml)	21	22	33	59
ECG findings				
Rhythm	Sinus	Sinus	Sinus	Sinus
Heart rate, BPM	69	73	75	87
PR interval, ms	176	176	154	226
Findings	Non-specific changes	Non-specific changes	Non-specific changes	IVCD, AVblock, 1 grade
Cardiac biomarkers				
hsTroponine, µg/L (normal values ≤0.013)	0.005	0.003	0.009	0.012
NTproBNP, ng/L (normal values ≤263)	57	53	13	66

AVblock, atrioventricular block; EDD, end-diastolic diameter; EDV, end-diastolic volume; ESD, end-systolic diameter; IVCD, interventricular conduction delay; LGE, late gadolinium enhancement.

no steroid treatment was initiated. On the other hand, LGE-CMR showed important disease progression, in particular in the last 2 years. This raises the key question, whether and when to initiate treatment to prevent or slow-down disease progression and to reduce the risk of malignant ventricular arrhythmias.

While in some studies presence of LGE and FDG-active lesions in cardiac sarcoidosis patients was associated with adverse events, other studies showed a more favourable outcome.[3,4] Furthermore, several small studies demonstrated that patients with (relatively) preserved LV function may benefit from early corticosteroid therapy. However, all these patients presented with either AV block or ventricular arrhythmia.[5,6] Decision making is further complicated by the lack of evidence-based studies. According to the Japanese guidelines, cardiac sarcoidosis patients with evidence of active lesions are candidates for steroid treatment.[7] According to HRS Expert Consensus Group, treatment should be started at the presence of heart block or ventricular ectopy.[1]

As LGE-CMR is able to depict focal myocardial fibrosis, it is increasingly used to image sarcoidosis patients and is considered by some members of the HRS Expert Consensus Group as a prognostic criterion.[1,8] However, it is important to emphasize, as shown in our patient, that LGE does not necessarily reflect scarring, but may also represent active, ongoing inflammation. Arguments in favour are the perfect match with the PET lesions (*Figure 3*). This underscores the need for complementary tissue characterization. Nowadays besides T2-weighted imaging, novel quantitative techniques such as T1 and T2 mapping, or combined PET/CMR imaging are preferable.[9,10] Lesions with active inflammation typically have increased T1 and T2 values.

Use of CMR and PET-CT was of great help in our asymptomatic patient, not only to depict and to tissue characterize cardiac sarcoidosis, but also to monitor disease progression over time. However, as mentioned above, clinical decision making may be challenged if the extent of myocardial damage at imaging is out of proportion to the patient's clinical symptoms, exercise tolerance, preserved cardiac biomarkers, and lack of cardiac dysfunction. Therefore, further studies are needed to better understand how these imaging findings can be integrated in guidelines for cardiac sarcoidosis management.

Conclusions

Complementary value of CMR and FDG-PET is appealing to better understand the natural evolution of cardiac sarcoidosis as shown in this asymptomatic patient. A better understanding of disease progression may be helpful in the management of such patients.

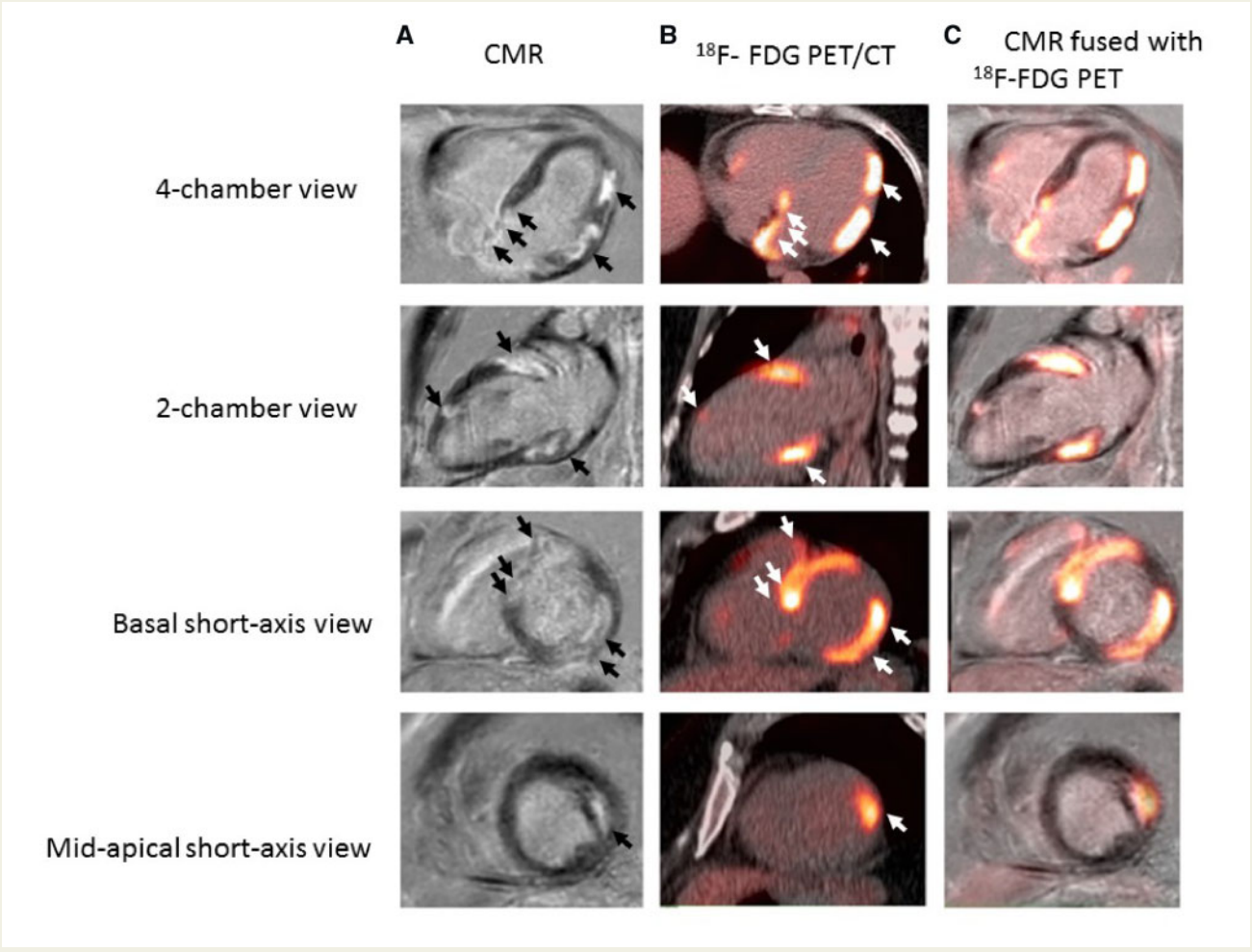

Figure 3 Late gadolinium enhancement-cardiac magnetic resonance (*A*), 18-F-fluorodeoxyglucose-positron emission tomography-computed tomography (*B*), and fused cardiac magnetic resonance/positron emission tomography (*C*). The abnormalities visualized at late gadolinium enhancement-cardiac magnetic resonance (*A*, arrows) and 18-F-fluorodeoxyglucose-positron emission tomography-computed tomography (*B*, arrows), show a perfect alignment at fused cardiac magnetic resonance/positron emission tomography, suggestive an acute inflammation rather than end-stage replacement fibrosis.

Lead author biography

Ganna Degtiarova was born in Donetsk, Ukraine, in 1989. She received the MD degree from M.Gorkiy Donetsk National Medical University, Donetsk, Ukraine in 2012 and afterwards got a specialization in cardiology. Since 2016, she has been enrolled in the PhD program of biomedical sciences at the Nuclear Medicine and Molecular Imaging unit (University Hospital, Leuven) and Department of Imaging and Pathology (KU Leuven), Leuven, Belgium. Her research interest is mainly focused on multimodal cardiac imaging, in particular in ischaemic heart diseases and heart failure.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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