CARDIOLOGIE TUNISIENNE

CASE REPORT

Risque de mort subite pour la sarcoidose cardiaque

Sudden cardiac death in cardiac sarcoidosis: A narrative for a challenge

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RÉSUMÉ

Nous présentons le cas d'une femme de 59 ans, ayant des antécédents connus de sarcoïdose, adressée pour l'évaluation de palpitations récidivantes au repos. L'évaluation multimodale a confirmé une atteinte cardiaque sarcoïdosique ; toutefois, aucune arythmie définitive n'a été identifiée pour expliquer ses palpitations. Les facteurs de risque justifiant une prévention primaire de la mort subite étaient non concluants, soulignant la difficulté centrale d'apprécier la précision et la pertinence des outils diagnostiques actuels pour la stratification du risque.

MOTS-CLÉS

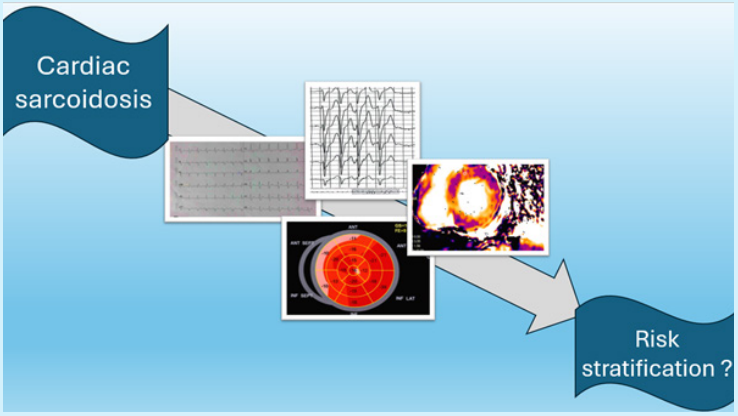
Sarcoidose; mort subite; stratification du risque

SUMMARY

We present the case of a 59-year-old woman with a known history of sarcoidosis who was referred for evaluation of recurrent palpitations at rest. Multimodal assessment confirmed cardiac sarcoidosis; however, no definitive arrhythmia was identified to explain her palpitations. Risk factors for primary prevention of sudden cardiac death were inconclusive, highlighting the central challenge of determining the accuracy and sufficiency of current diagnostic tools for risk stratification.

KEYWORDS

Sarcoidosis; sudden cardiac death; risk stratification



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INTRODUCTION

Sarcoidosis results from an interplay between environmental exposures and genetic susceptibility [1]. It is a multisystemic inflammatory disease that commonly involves the lungs, followed by the skin, liver, and gastrointestinal tract [2]. Clinical cardiac involvement is diagnosed in only about 5% of patients; however, autopsy studies have reported myocardial involvement in up to 25% of cases, highlighting the frequently subclinical nature of cardiac sarcoidosis (CS) [3]. Cardiac involvement in sarcoidosis represents a serious and potentially life-threatening manifestation of the disease [1,4].

The clinical presentation of CS is highly variable, ranging from asymptomatic or nonspecific symptoms such as chest pain and dyspnea to malignant ventricular arrhythmias (VA), heart failure (HF), conduction disturbances with presyncope, syncope or sudden cardiac arrest (SCD) [5]. Management relies primarly on immunosuppressive therapy in adjunction to guidelines-directed medical therapy for associated cardiomyopathy. Yet the main challenge remains in stratifying the risk of life-threatening arrhythmias as illustrated by the following case.

CASE PRESENTATION

We report the case of a 59-year-old woman with type 1 diabetes mellitus since the age of 26 years old. She has been diagnostic with mediastino-pulmonary sarcoidosis in 2021 already under immunosuppressive treatment. First referral for a cardiology evaluation was adressed after the patient reporting palpitations at rest over a 3-month period. Palpitations were classified as EHRA III, mostly during the night, without any other associated symptoms like syncope or chest pain. They were of very short duration, starting and ending abruptly.

Physical examination was unremarkable. The 12-lead ECG revealed a normal sinus rhythm, a bifascicular block (Right bundle branch block and a posterior fascicular block), and normal repolarisation pattern (Figure 1).

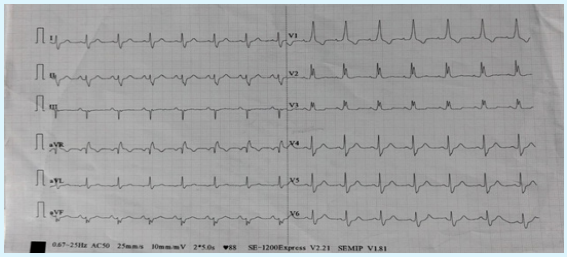

Figure 1. 12-lead ECG

The laboratory findings were in the normal range with no positive inflammatory markers. Glycaemic control was suboptimal, with an HbA1c of 8%.

A Holter monitoring was performed for 48h-duration. Only three asymptomatic nocturnal episode of nonsustained ventricular tachycardia (NSVT) with a maximum heart rate of 150 beats and maximum number of beats of 4 were documented (Figure 2).

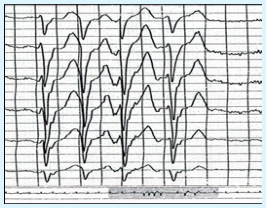

Figure 2. NSVT documented on 48-hour Holter monitoring

The transthoracic echocardiography (TTE) demonstrated a LV with normal geometry and homogeneous wall motion. LV systolic function was preserved, with a biplane left ventricular ejection fraction (LVEF) of 51%. LV global longitudinal strain (GLS) was mildly reduced at –16% (Figure 3). No significant valvular heart disease was identified. Right-sided cardiac chambers were not dilated, and right ventricular systolic function was preserved, with a right ventricular (RV) free-wall longitudinal strain of –26%. Estimated pulmonary artery systolic pressure was within the normal range. The inferior vena cava was not dilated and showed normal respiratory variation. No pericardial effusion was observed.

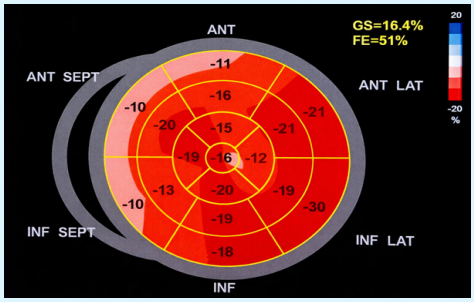

Figure 3. LV GLS assessed by speckle-tracking echocardiography

The cardiac magnetic resonance (CMR) imaging was suggestive of an infiltrative process. Late gadolinium enhancement (LGE) showed patchy pseudo-nodular intramyocardial involvement affecting septal wall (Figure 4). T1 mapping demonstrated normal native T1 values in the mid and apical LV, with an increased native T1 value at the basal septum (1200 ms) (Figure 5). Biventricular systolic function was preserved, with a LVEF of 52%.

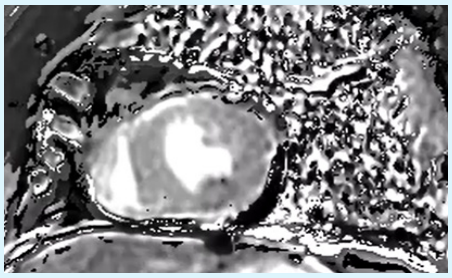

Figure 4. Short-axis LGE CMR demonstrating septal non-ischemic fibrosis

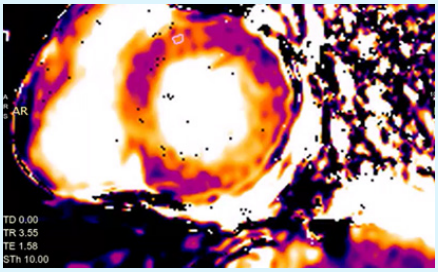

Figure 5. Myocardial tissue characterization by T1 mapping

An electrophysiology study was done. The baseline the HV interval was normal (< 70ms). No sustained ventricular tachycardia was induced with the programmed ventricular stimulation.

So according to the societal guidelines, the patient is to be considered at low risk for sudden cardiac death. The decision was then a close follow-up with periodic Holter monitoring and CMR imaging.

But the main discussion during the heartteam meeting was about the accuracy of our stratification. After all, palpitations were still not correlated to any diagnosis.

DISCUSSION

Cardiac manifestations of sarcoidosis are present in at least 25% of patients with systemic sarcoidosis, and can include Mobitz II, second-degree AV block, LBBB, RBBB or CHB (~30%), ventricular tachyarrhythmias, intracardiac masses, ventricular aneurysms, and dilated cardiomyopathy [1, 6].

For the clinician, the challenge is anchored in three core pillars. First the diagnosis, then the risk stratification for sudden cardiac death and last but not the least, management. Our case illustrate the dilemma for the second pilllar which is risk stratification. According to expert opinions, the stratification is related to the risk of life-threatening ventricular arrhythmias. The appraoch is ought to be multimodal and dynamic, integrating imaging, electrophysiological findings, and clinical presentation rather than relying on a single parameter [7,8,9].

A large population-based study evaluated the burden of VA among patients with sarcoidosis. Compared with individuals without sarcoidosis, patients with sarcoidosis exhibited significantly higher rates of VT, VF, and cardiac arrest, although they also had a higher prevalence of cardiovascular comorbidities. These findings highlight the increased arrhythmic burden associated with sarcoidosis, while underscoring the limitations of clinical findings in establishing causality or confirming cardiac involvement [10].

According to the 2022 ESC guidelines for the management of patients with VA and the prevention of SCD and the 2024 AHA scientific statement, the risk of VA in CS is increased in the presence of three major factors: LVEF ≤ 35%, high-degree atrioventricular block, and myocardial scarring involving the left or right ventricle on cardiac magnetic resonance imaging. However, no universally accepted definition of significant LGE exists. Bur extensive myocardial involvement such as LGE affecting ≥9 ventricular segments or ≥22% of LV mass has been associated with ventricular arrhythmic events [9,10]. Our patient did have LGE but only in a limited portion.

Importantly, LGE on CMR has emerged as one of the strongest independent predictors of VA and death, even in patients with preserved or mildly reduced ejection fraction. But the the LGE characterisation is a moving target. The question is not only about how much LGE is present but also about how it is distrubuted.

Extensive LGE (≥20% of LV mass) has been reported as an independent risk factor for adverse outcomes unlike limited LGE that predicts reverse remodeling and improvement in ejection fraction [11].

Specific diagnostic patterns were identified, including ring-like LGE defined as sub-epicardial or mid-myocardial LGE involving at least three contiguous segments in the same short-axis slice and the hook (or hug) sign, characterized by septal LGE extending into the RV free wall. Pathology-frequent LGE distribution was defined by the presence of sub-epicardial (including RV–sided septal), septal, multifocal LV, or RV free-wall involvement, with a cumulative score (0–4) recorded for each patient [12]. Pathology-frequent LGE patterns are associated with a markedly increased arrhythmic risk, independent of LVEF or LGE extent. Conversely, the absence of these high-risk patterns identifies patients at low arrhythmic risk.

In a nationwide registry study published in Circulation in 2024 including 305 patients with definite or probable CS and a median follow-up of 4 years, both the extent of myocardial LGE and the number of involved LV segments strongly predicted

SCD and ventricular arrhythmia. Thresholds of LGE ≥9.9% of LV mass or involvement of ≥6 LV segments identified patients at markedly higher arrhythmic risk, including those without conventional ICD indications. These findings suggest that quantitative assessment of LGE may refine risk stratification in CS, although prospective validation is required [14].

In a large multicentre study including 1,514 patients with histology-supported sarcoidosis and suspected cardiac involvement, CMR imaging phenotyping outperformed societal guidelines in predicting fatal or life-threatening VA [15]. During a median follow-up of 4.5 years, a high-risk CMR phenotype was associated with markedly higher 5- and 10-year arrhythmic event rates (24% and 35%), whereas low-risk phenotypes showed very low event rates. The authors argued about a CMR phenotyping rather than a LGE threshold evaluation.

Additional risk factors are to be considered by the 2024 scientific statement related to the programmed electrical stimulation to induce sustained monomorphic ventricular tachycardia, the myocardial scarring on the FDG-PET/CT [10].

Although, FDG uptake is not disease-specific for CS, but combined with resting myocardial perfusion imaging allows detection of metabolically active myocardial inflammation and scar. Unfortunatly, for logistic reasons, our patient was unable to follow the correct diet to get the FDG.

Characteristic perfusion–metabolism mismatch patterns, multifocal FDG uptake, and RV involvement are highly suggestive of CS and carry important prognostic implications, being associated with an increased risk of adverse cardiac events [1–3].

For our patient, who presented with palpitations but nothing found on the Holter monitoring and nothing induced with the programmed ventricular stimmulation. And the cardiac imaging did not reveal any extensive involvement of the sarcoidosis. So, how confident can we truly be for our risk stratification for sudden cardiac death?

Clinical uncertainty persists because the underlying cause of the palpitations remains unidentified. The short Holter recording did not capture any significant arrhythmic events, yet the patient was asymptomatic during that period. A longer duration of ECG monitoring might increase diagnostic yield, but only if symptoms occur concurrently.

Initiating an anti arrhythmic drug is another option, but the patient already has an intraventricular conduction delay and an underlying cardiac condition that may progress to more advanced conduction block. This raises a difficult question: how do we balance the potential benefits of therapy against the risk of exacerbating conduction disturbances?

This naturally leads to the next question: how closely should we monitor this patient, and which tools are appropriate within the constraints of our national health care resources?

CONCLUSION

CS represents a complex and heterogeneous condition, with a highly variable clinical course and a substantial risk of malignant VA and SCD. Definitive clinical data are not available to stratify risk of sudden cardiac death among patients with cardiac sarcoidosis. Thus decisions regarding ICD implantation must be individualized. A multidisciplinary approach, integrating clinical evaluation, electrophysiological assessment, and advanced cardiac imaging is essential. Yet the most crucial element remains the need for dynamic risk evaluation. The disease itself is inherently progressive, and although diagnostic and therapeutic innovations continue to evolve, our current tools still leave important gaps in risk prediction.

As research advances, emerging technologies may offer new pathways. In particular, computational modelling, combining patient-specific anatomy, electrophysiology, and longitudinal data, holds promise as a future solution for more precise, individualized risk stratification.

REFERENCES

1. Vereckei A, Besenyi Z, Nagy V, Radics B, Vágó H, Jenei Z, et al. Cardiac Sarcoidosis: A Comprehensive Clinical Review. Rev Cardiovasc Med 2024;25. https://doi.org/10.31083/j.rcm2502037.
2. Sallam S, Shahrori Z, Rana M, Sullivan C, Sallam S, Shahrori Z, et al. A Case of Burnt-Out Cardiac Sarcoidosis Presenting With Sustained Ventricular Tachycardia. Cureus 2022;14. https://doi.org/10.7759/cureus.28931.
3. Iwai K, Takemura T, Kitaici M, Kawabata Y, Matsui Y. Pathological studies on sarcoidosis autopsy. II. Early change, mode of progression and death pattern. Acta Pathol Jpn 1993;43:377–85. https://doi.org/10.1111/j.1440-1827.1993.tb01149.x.
4. Pattnaik B, Pb S, Verma M, Kumar S, Arava S, Mittal S, et al. Patient profile and comparison of three diagnostic criteria for cardiac sarcoidosis in a tuberculosis endemic population. Sarcoidosis Vasc Diffuse Lung Dis 2021;38:e2021040–e2021040. https://doi.org/10.36141/svdld.v38i4.10977.

5. Ramireddy S, Shakir A, Ramireddy S, Shakir A. Syncope and Sarcoidosis: A Criss-Cross of Diagnoses. Cureus 2021;13. https://doi.org/10.7759/cureus.16367.
6. Birnie DH, Sauer DH, Bogan F, et al: HRS Expert consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis. Heart Rhythm .2014;11:1304–1323, 2014.
7. Sharma R, Kouranos V, Cooper LT, Metra M, Ristic A, Heidecker B, et al. Management of cardiac sarcoidosis: A clinical consensus statement of the Heart Failure Association, the European Association of Cardiovascular Imaging, the ESC Working Group on Myocardial & Pericardial Diseases, and the European Heart Rhythm Association of the ESC. Eur Heart J 2024;45:2697–726. https://doi.org/10.1093/eurheartj/ehae356.
8. Patel R, Mistry AM, Mulukutla V, Prajapati K, Patel R, Mistry AM, et al. Cardiac Sarcoidosis: A Literature Review of Current Recommendations on Diagnosis and Management. Cureus 2023;15. https://doi.org/10.7759/cureus.41451.
9. Zeppenfeld K, Tfelt-Hansen J, de Riva M, Winkel BG, Behr ER, Blom NA, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Developed by the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC) Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2022;43:3997–4126. https://doi.org/10.1093/eurheartj/ehac262.
10. Cheng RK, Kittleson MM, Beavers CJ, Birnie DH, Blankstein R, Bravo PE, et al. Diagnosis and Management of Cardiac Sarcoidosis: A Scientific Statement From the American Heart Association. Circulation 2024;149:e1197–216. https://doi.org/10.1161/CIR.0000000000001240.
11. Ise T, Hasegawa T, Morita Y, Yamada N, Funada A, Takahama H, et al. Extensive late gadolinium enhancement on cardiovascular magnetic resonance predicts adverse outcomes and lack of improvement in LV function after steroid therapy in cardiac sarcoidosis 2014. https://doi.org/10.1136/heartjnl-2013-305187.
12. Pöyhönen P, Lehtonen J, Syväranta S, Velikanova D, Mälkönen H, Simonen P, et al. Magnetic Resonance Imaging in the Assessment of the Risk of Sudden Death in Cardiac Sarcoidosis: What Is Extensive or Significant Late Gadolinium Enhancement? Circ Arrhythm Electrophysiol 2025;18:e013239. https://doi.org/10.1161/CIRCEP.124.013239.
13. Mathijssen H, Bawaskar PH, Rochlani Y, Georgy I, Athwal PSS, Guo Y, et al. Prediction of ventricular arrhythmic outcomes in suspected cardiac sarcoidosis: a comparison of cardiovascular magnetic resonance phenotyping vs. societal recommendations for implantable cardioverter-defibrillator placement n.d.
14. Areekkara Poduvattil P, Hashim Z, Kumar S, Jain N, Ora M, Gambhir S, et al. Speckle-Tracking Echocardiography as an Effective Screening Tool for Cardiac Involvement Among Patients With Systemic Sarcoidosis in an Indian Cohort: A Prospective Observational Study. Echocardiography 2024;41:e15957. https://doi.org/10.1111/echo.15957.
15. Natarajan B, Huang-Tsang J, Janardhanan R. Screening Asymptomatic Cardiac Sarcoidosis: Role of Cardiac MRI. Am J Med 2016;129:e23–4. https://doi.org/10.1016/j.amjmed.2016.01.022.