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# A fearsome evolution of presumed cardiac sarcoidosis: The sarcoid-lymphoma syndrome

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In November 2014, a 69-year-old Caucasian man with multiple cardiovascular risk factors and without a history of dyspnea or angina came to our attention after multiple emergency department evaluations for dizziness with pre-syncope. Laboratory analysis revealed elevated C-reactive protein and leukocytosis. The patient underwent a brain computed tomography (CT) scan and a brain magnetic resonance imaging (MRI) scan that showed chronic cerebral small vessel disease without specific findings that could explain the reported symptoms. The EKG showed negative T waves in the lateral precordial leads. The echocardiogram revealed an inferolateral wall hypokinesia. The exercise stress test showed a slight worsening of the repolarization abnormalities without symptoms. He underwent coronary angiography, and angioplasty of a critical stenosis of the left anterior descending artery was performed. A cardiac MRI (CMRI) study was performed to investigate the cause of inferolateral wall hypokinesia. The CMRI showed hypertrophy (17 mm, Fig. 1**A**, and Video 1 and Video 2), positive T2 weighted short tau inversion recovery (STIR) images, and subepicardial late gadolinium enhancement (LGE) of the inferolateral left ventricular segments. These findings were compatible with myocardial inflammation of uncertain origin, possibly due to acute myocarditis or cardiac sarcoidosis or potentially due to another cardiac infiltrative disease. He remained paucisymptomatic during the subsequent follow-up. Meanwhile, further medical evaluations were performed, including a chest CT scan that revealed multiple lung micronodules not suggestive of extracardiac sarcoidosis. These micronodules were not suitable for histologic characterization by CT-scan-guided biopsy. An abdominal ultrasound scan revealed hepatic steatosis without evidence of any mass. Further laboratory exams showed a normal white blood count with beta-2 microglobulin of 2.2 mg/L (normal values [nv]: 1.5–3 mg/L). Angiotensin enzyme converter (ACE) enzyme levels and urinary calcium (124 mg/24 h – nv of 25–300 mg/24 h for males) were also in the normal ranges. Chest CT and abdominal ultrasound scans did not suggest systemic sarcoidosis or other hematologic lymphoproliferative disorders like lymphoma. Initially, after the abovementioned diagnostic tests, a total body fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT scan with suppression of physiological uptake of FDG uptake was not performed. He repeated a CMRI in October 2015 that confirmed the hypertrophy (Fig. 1**B**) and hypokinesia of the left ventricular inferolateral wall with persistent positive STIR and homogeneous enhancement. Later, the patient reported palpitations, and prolonged EKG monitoring showed episodes of sustained ventricular tachycardia. He repeated coronary angiography without evidence of progression of the coronary disease and right ventricular endomyocardial biopsies (EMB) that demonstrated normal myocardium. At that time, a left ventricular EMB of the lateral wall with electroanatomic mapping was not attempted because, in our institution, there were no skills to perform such a diagnostic exam that could be useful to reach a histologic diagnosis [1]. Even if the risk of major complications in performing EMB of the inferolateral wall, such as acute severe mitral valve regurgitation due to chordal rupture or perforation of the left ventricular lateral wall and sudden tamponade, must be considered. An implantable cardiac defibrillator (ICD) MRI-conditional was implanted, and the patient was discharged with oral prednisone based on presumed cardiac sarcoidosis [2]. The suggested criteria for presumed cardiac sarcoidosis are unexplained high-grade atrioventricular block or ventricular arrhythmia and findings suggestive of cardiac sarcoidosis on either CMRI or PET without any histologic evidence of sarcoidosis [2]. He repeated a CMRI in September 2016. The scan was performed in an ICD-protection mode, and a progression of the inferolateral wall hypertrophy (34 mm) with a homogeneous LGE pattern was demonstrated (Fig. 1**C,** Video 3 and Video 4). STIR images, suggestive of edema, have been positive since 2014 (Fig. 1**D, 1E**). In September 2016, a total body FDG-PET/CT scan with a carbohydrate-free diet revealed a left adrenal mass (8x6 cm) with multiple abdominal nodules and adenopathy and multifocal cardiac uptake (Fig. 1**F, 1G**). The adrenal mass biopsy documented a high-grade B cell Burkitt-like lymphoma. A Follow-up CT scan in February 2017 showed a significant reduction of both the abdominal bulk and the cardiac mass after etoposide, vincristine, doxorubicin, and cyclophosphamide (EPOCH) chemotherapy (Fig. 1**H**, compared with pre-chemotherapy CT and CMRI in Fig. 1**I, 1 J**). Nevertheless, a few months later, the patients developed severe leucopenia and died of septic shock. No post-mortem examination was requested. The overall long history of disease and the response to chemotherapy supported the final diagnosis of transition from presumed cardiac sarcoidosis to sarcoid-lymphoma syndrome with cardiac localization. In conclusion, even if some cases have described the association between sarcoidosis

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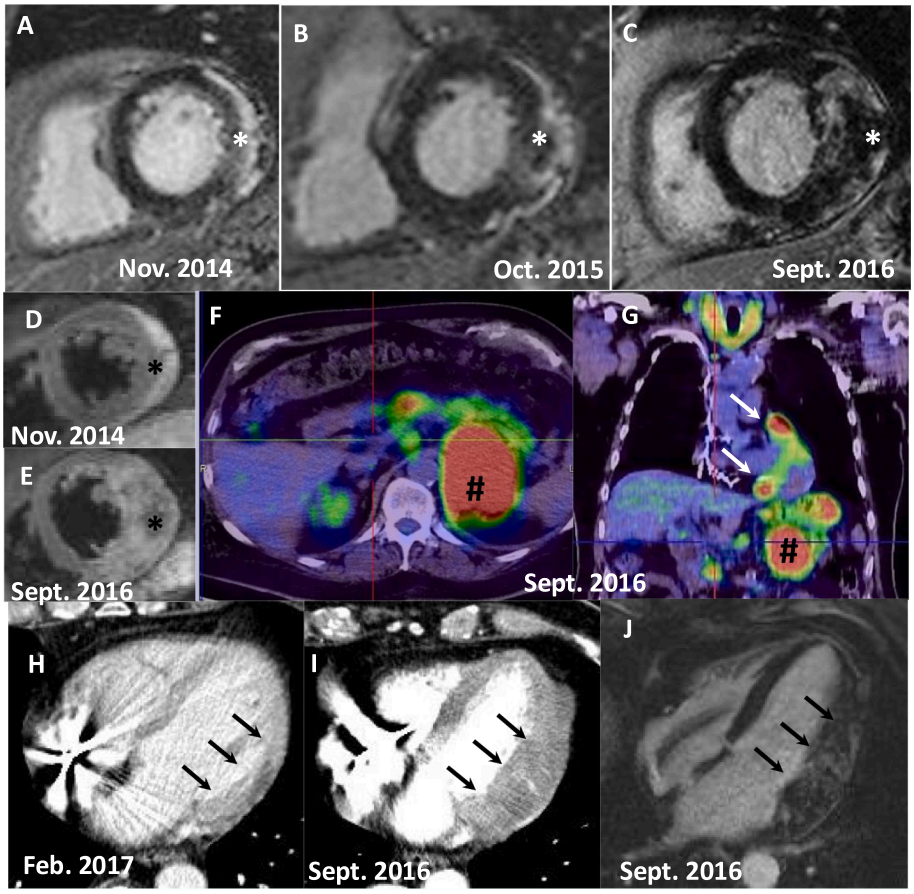


**Fig. 1.** Cardiac magnetic resonance images (CMRI) and fluorodeoxyglucose (FDG)-positron emission tomography (PET)/ computed tomography (CT) of the evolution from presumed cardiac sarcoidosis to lymphoma. **(A)** CMRI showed lateral wall hypertrophy (17 mm) with sub-epicardial late gadolinium enhancement (LGE, *) which was performed in November 2014 and suspected of cardiac sarcoidosis. **(B)** A second CMRI in October 2015 showed a further focal thickening of the left ventricle (LV, *). **(C)** In September 2016, CMRI showed a further progression of lateral wall hypertrophy (34 mm) with a nonhomogeneous LGE pattern (*). **(D-E)** Short tau inversion recovery (STIR) images on CMRI have been suggestive of edema since 2014 (*). **(F-G)** FDG-PET/CT scan with suppression of physiological uptake of FDG uptake revealed a left adrenal mass (8x6 cm, #) with abdominal lymphadenopathy and multifocal cardiac uptake (**arrows**). The adrenal mass biopsy diagnosed a B-cell Burkitt-like lymphoma. **(H)** In February 2017, a CT scan showed a significant reduction of both the cardiac and adrenal masses after chemotherapy compared with (I-J) pre-chemotherapy CT and CMRI scans.

and lymphoma,[3–6] this is the first case showing a transition from isolated cardiac sarcoidosis to lymphoma with cardiac involvement, as depicted by the CMRI over 3 years in this case. As a major limitation of our case report, no histology confirming the diagnosis of cardiac sarcoidosis was available. Even if Burkitt-like lymphomas are usually aggressive, it might be a case of primary cardiac localization of lymphoma, growing over the years, instead of cardiac sarcoidosis. Nevertheless, initially, no extracardiac lesions were detected by chest CT scan or abdominal ultrasound scan, the patient reported no typical symptoms for lymphoma, and the laboratory exams did not suggest hematologic lymphoproliferative disorders. All these findings support the idea that an initial presumed isolated cardiac sarcoidosis evolved into a systemic lymphoma. In any case, this case further stresses the relevance of FDG-PET/CT scan in identifying sarcoidosis localizations, ruling out other potential differential diagnoses, and its usefulness in monitoring cardiac sarcoidosis. Finally, our case shows a potential fearsome evolution of isolated cardiac sarcoidosis that must be considered, and recent reviews and analyses on this subject have not underscored it [7–10]. In case we were wrong with the interpretation of available data, despite our best attempt to reach a final diagnosis, this case highlighted the relevance to consider primary cardiac lymphoma in the differential diagnosis of isolated cardiac sarcoidosis and primary cardiac lymp, further stressing the relevance to reaching a histologic diagnosis.

## Disclosures

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## CRediT authorship contribution statement

**Paola Sormani:** Writing – original draft, Data curation, Conceptualization. **Enrico Ammirati:** Writing – original draft, Conceptualization. **Cristina Giannattasio:** Writing – review & editing. **Andrea Garascia:** Writing – review & editing. **Patrizia Pedrotti:** Writing – review & editing, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2024.101496.

## References


[1] E. Ammirati, A. Buono, F. Moroni, et al., State-of-the-art of endomyocardial biopsy on acute myocarditis and chronic inflammatory cardiomyopathy, Curr Cardiol Rep 24 (2022) 597–609.

[2] A.N. Rosenbaum, N. Kolluri, M.Y. Elwazir, et al., Identification of a novel presumed cardiac sarcoidosis category for patients at high risk of disease, Int J Cardiol 335 (2021) 66–72.

[3] S.S. Taha-Mehlitz, I.I. Zschokke, J.J. Metzger, L.L. Fourie, Challenges in the management of life-threatening complications caused by a rare case of sarcoid-lymphoma syndrome, Int J Colorectal Dis 35 (2020) 343–346.

[4] A. Kumthekar, P.W. Raess, D. Ghetie, A missing link: Sarcoid-lymphoma syndrome, Am J Med 132 (2019) 48–51.

[5] A.H. Jbeli, A. Sunassee, A. Sanford, A. Elshami, J. Bleeker, A very rare case of sarcoid-lymphoma syndrome imposing an intriguing diagnostic challenge, S D Med 71 (2018) 108–111.

[6] T. Goswami, S. Siddique, P. Cohen, B.D. Cheson, The sarcoid-lymphoma syndrome, Clin Lymphoma Myeloma Leuk 10 (2010) 241–247.

[7] D.H. Birnie, R. Kandolin, P.B. Nery, M. Kupari, Cardiac manifestations of sarcoidosis: diagnosis and management, Eur Heart J 38 (2017) 2663–2670.

[8] H.K. Nordenswan, J. Lehtonen, K. Ekström, et al., Manifestations and outcome of cardiac sarcoidosis and idiopathic giant cell myocarditis by 25-year nationwide cohorts, J Am Heart Assoc 10 (2021) e019415.

[9] J. Lehtonen, V. Uusitalo, P. Poyhonen, M.I. Mayranpaa, M. Kupari, Cardiac sarcoidosis: phenotypes, diagnosis, treatment, and prognosis, Eur Heart J 44 (2023) 1495–1510.

[10] J.K. Malhi, C. Ibecheozor, J. Chrispin, N.A. Gilotra, Diagnostic and management strategies in cardiac sarcoidosis, Int J Cardiol 403 (2024) 131853.



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