A Rare Case Report of Cardiac Sarcoidosis with Pulmonary Hypertension

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Abstract

Introduction: *Cardiac sarcoidosis (CS) is a rare granulomatous disorder in which white blood cells form clusters on the myocardium. The clinical presentations of CS are varied, as is its etiology. Multiple diagnostic approaches to determine the cause of persistent dyspnea may fail, as cardiac sarcoidosis can mimic many other diseases.*
Case: *A 47-year-old woman presented with a sudden onset of dyspnea and a history of chronic thrombo-embolic pulmonary hypertension (CTEPH). Multiple diagnostic approaches were employed, including a CT scan of the thorax with contrast, CT pulmonary angiography, CT coronary angiography, and a Ventilation/Perfusion test, but the results were inconclusive. A Cardiac MRI was ultimately performed, which led to a diagnosis of cardiac sarcoidosis..*
Case Discussion: *The patient had been stable and asymptomatic over the years, despite her history of CTEPH, until she developed a sudden onset of dyspnea. The presence of pitting edema, ECG results, and echocardiography data initially suggested a diagnosis of congestive heart failure. However, tests from the pulmonary system and cardiac coronary were normal. This highlights the elusive nature of cardiac sarcoidosis, which can often go unnoticed and be frequently misdiagnosed. Given the inconclusive results from previous tests, a Cardiac MRI was performed to further characterize the pathology. This led to the findings of Late Gadolinium Enhancement (LGE) and the diagnosis of CS.*
Conclusion: *Cardiac sarcoidosis is a master imitator of many diseases, with patients sometimes presenting with only dyspnea. In such cases, Cardiac MRI plays a pivotal role as a diagnostic test, especially when results from other diagnostic workups are nonspecific.*

Keywords: *Cardiac Sarcoidosis, Cardiac MRI, Pulmonary Hypertension*

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Laporan Kasus Langka Sarkoidosis Jantung dengan Hipertensi Pulmonal

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Abstrak

***Pendahuluan**: Sarkoidosis Jantung atau Cardiac Sarcoidosis (CS) adalah penyakit granulomatosa langka dengan terjadinya penumpukan kluster sel darah putih pada miokardium. Presentasi klinis dan etiologi CS sangat beragam. Berbagai pendekatan diagnostik untuk mencari penyebab sesak nafas persisten seringkali gagal karena sarkoidosis jantung dapat meniru banyak penyakit.*
***Laporan Kasus**: Seorang wanita berusia 47 tahun datang dengan keluhan utama sesak napas yang mendadak dan riwayat hipertensi pulmonal trombo-emboli kronis (CTEPH). Beberapa pendekatan diagnostik telah dilakukan, seperti CT scan toraks dengan kontras, CT angiografi paru, CT angiografi koroner, dan tes Ventilasi/Perfusi, namun hasilnya tidak memberikan petunjuk jelas. MRI Jantung akhirnya dilakukan dan menemukan indikasi sarkoidosis jantung.*
***Diskusi kasus**: Pasien ini telah stabil dan asimptomatik selama bertahun-tahun, meski memiliki riwayat CTEPH, hingga ia mengalami sesak napas mendadak. Keberadaan edema pitting, hasil EKG, dan data ekokardiografi awalnya mengarah pada diagnosis gagal jantung kongestif. Namun, hasil pemeriksaan dari sistem paru dan koroner jantung adalah normal. Hal ini menunjukkan sifat elusive dari sarkoidosis jantung, yang bisa sering kali tidak terdeteksi dan salah didiagnosis. Mengingat hasil pemeriksaan sebelumnya yang tidak konsisten, dilakukanlah MRI Jantung untuk memahami lebih lanjut mengenai patologinya. Hal ini mengarah pada temuan LGE dan diagnosis CS.*
***Kesimpulan**: Sarkoidosis jantung adalah peniru yang lihai dari banyak penyakit, sehingga pasien sering kali hanya mengalami keluhan sesak napas. MRI Jantung memegang peran penting sebagai alat tes diagnostik pada pasien dengan keluhan sesak napas, terutama ketika hasil pemeriksaan diagnostik lainnya tidak spesifik.*

***Kata kunci:** Sarkoidosis Jantung, MRI jantung, Hipertensi Pulmonal*

Introduction

Sarcoidosis is a rare, multisystem inflammatory granulomatous disease that can affect various organs, including the cardiac system. The prevalence of sarcoidosis in the American population is approximately 10-40 cases per 100,000 people, with cardiac sarcoidosis occurring in 20-30% of these cases.[1] Clinically, cardiac sarcoidosis can be diagnosed in about 5% of the population, but autopsy or cardiac imaging can identify up to 25% of cases.[2]

The clinical manifestations of cardiac sarcoidosis are varied, but the most common presentations include conduction abnormalities, fatal arrhythmias, sudden death, and heart failure.[3] A significant complication of cardiac sarcoidosis that clinicians need to be aware of is Sarcoidosis-Associated Pulmonary Hypertension (SAPH).[4] This condition results in higher oxygen consumption and functional abnormalities, leading to a worse prognosis than in patients with sarcoidosis without pulmonary hypertension.[5]

Diagnosing cardiac sarcoidosis (CS) can be difficult, as the symptoms are not specific and there is no gold standard criterion. Consequently, the diagnosis of cardiac sarcoidosis is often missed. This poses a challenge for clinicians, as an early diagnosis enables early treatment, which could signifi-

cantly reduce the risk of death. Therefore, non-invasive imaging techniques, such as Cardiac MRI and echocardiography, are crucial for initial screening or diagnostic tests.

In this case report, we describe the challenge of diagnosing a rare case of cardiac sarcoidosis, accompanied by pulmonary hypertension and pulmonary embolism.

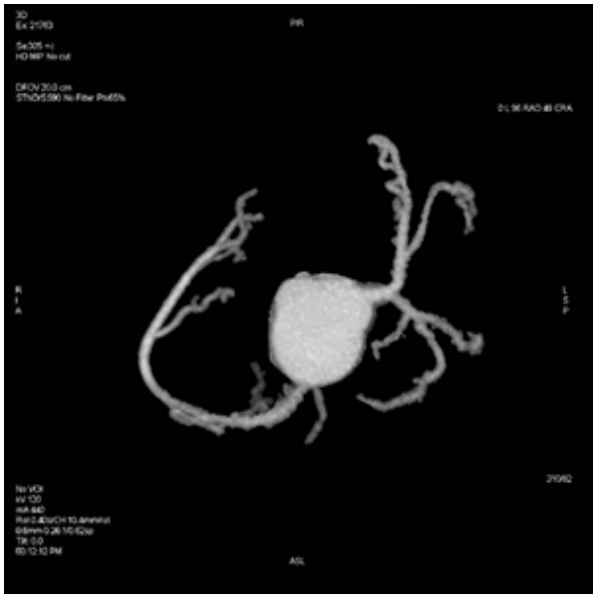
Case Report

A 47-year-old woman presented to the Emergency Department with sudden onset dyspnea. The difficulty in breathing was exacerbated by lying down and talking, but relieved by sitting. She was a non-smoker and did not complain of chest discomfort, shortness of breath during daily activities, paroxysmal nocturnal dyspnea, or orthopnea. She had no history of cardiac disease, diabetes, asthma, or hypertension but had a medical history of chronic thromboembolic pulmonary hypertension (CTEPH). Three years prior, at a different hospital, she experienced dyspnea and fatigue. A transthoracic echocardiography showed a normal systolic LVEF of 60% by Teichholz's method, concentric LVH with grade II diastolic dysfunction, mild mitral regurgitation (MR), a differential diagnosis of pulmonary embolism or pericardial fat, mild pericardial effusion with no signs of tamponade, and a PASP of 45-50 mmHg, suggesting a very high probability of pulmonary hypertension (PH). She remained stable over the years and adhered to her routine treatment but suddenly experienced shortness of breath and was admitted to our emergency room.

Physical examination showed a blood pressure of 130/90 mmHg, a heart rate of 58 bpm, respiratory rate of 26 breaths per minute, a temperature of 36.2 degrees Celsius, and an oxygen saturation of 99% on room air. No conjunctival anemia or icteric sclera was observed. The thorax, heart, and lungs were within normal limits. No premature beats or murmurs were detected on heart auscultation. The abdomen was soft but distended, with epigastric tenderness and ascites. The extremities were warm to the touch, but there was pitting edema on both legs. No increase in JVP or hepatojugular reflux was observed. The patient was obese, weighing 88 kg with a height of 155 cm, and a BMI of 33.3 kg/m^2.

Laboratory examination revealed leukocytosis of 13,400/uL, elevated levels of aspartate aminotransferase (AST) at 38 U/L, alanine aminotransferase (ALT) at 60 U/L, and hypoglycemia of 53 mg/dL. Electrolyte levels, creatine kinase myocardial band (CKMB), and Troponin T were all within normal limits.

The electrocardiogram (ECG) revealed sinus bradycardia with left ventricular hypertrophy and type I AV block. Echocardiography in our hospital showed normal left ventricle (LV) systolic function, LVEF by Teichholz's method of 60%, LV global normokinesis, concentric LVH with grade II diastolic dysfunction, normal RV contractility, mild MR, mild tricuspid regurgitation (TR) with a probability of PH, and mild pericardial effusion with no signs of cardiac tamponade. She subsequently underwent CT pulmonary angiography to investigate the cause of persistent dyspnea. The results showed enlargement of the pulmonary trunk, pulmonary hypertension, no signs of pulmonary thromboembolism, but the mosaic perfusion in the lungs suggested chronic pulmonary embolism. Subsequent CT coronary angiography showed no plaques in any of the coronary branches. An exercise stress test showed an inverted T wave in all leads, ST depression at the inferior leads, and the test was disrupted due to shortness of breath and poor tolerance to physical activity.



**Our documentation from patient's medical record*

Figure 1. CT Coronary Angiography Showed Normal Coronary Arteries

The CT thorax with and without contrast revealed a mosaic pattern in both lungs (with differential diagnoses including vascular occlusion disease, small airway obstruction, parenchymal disease), suspected pulmonary hypertension, and minimal fibrosis in the 5th segment of the left lung. The Ventilation/ Perfusion test indicated normal lung perfusion. The patient eventually underwent a cardiovascular MRI, which showed preserved

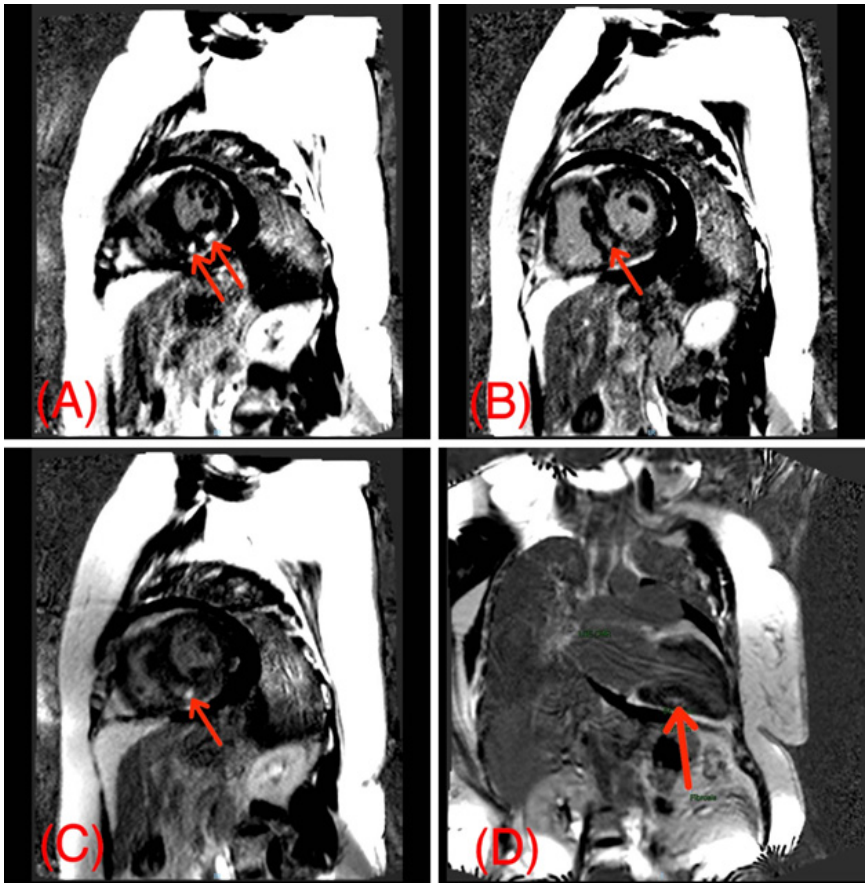
left ventricular systolic function (LVEF 63%) with global normokinesis, enlargement of the left atrium, normal systolic function of the right ventricle, right ventricle ejection fraction (RVEF) of 75% with LV global normokinesis, inflammation of the myocardium at the mid-inferior and apex, slow blood movement in the left atrium, and late gadolinium enhancement (LGE) in the inferior and infero-septal region. This was concluded as possible cardiac sarcoidosis (50-90%). The findings of increased PASP also indicated the presence of pulmonary hypertension, and so a diagnosis of Sarcoidosis-Associated Pulmonary Hypertension (SAPH) could also be considered in this patient.

The patient was treated with corticosteroids, calcium channel blockers, angiotensin receptor blockers, alpha-adrenergic agonists, phosphodiesterase inhibitors, and prostacyclin analogues during her hospitalization period, which lasted approximately one week. She was stable and her symptoms improved. She was discharged and continued her medications.

Discussion

Cardiac sarcoidosis is a rare disease with high morbidity and mortality. It was caused by the formation of non-caseating granulomas, which is the clusters of white blood cells in the myocardium.[3]

These sarcoid granulomas and scar tissue that infiltrate the myocardium caused ECG abnormalities such as AV block (Mobitz type II or complete heart block) (23-30%), bundle branch block (12-32%), ventricular arrhythmia (23%), heart failure (HF) (25–75%), and sudden cardiac death (25–65%).[3] Echocardiography abnormalities in patients with suspected CS are not specific, including thinning on the septal and interventricular wall, especially at the basal, left ventricular systolic and diastolic dysfunction, pericardial effusion, and valvular anomalies.[6] In some patients, CS



**Our documentation from patient's medical record*

Figure 2. Cardiac MRI showed multifocal Late Gadolinium Enhancement (LGE) of the inferior and infero-septal LV wall. Short Axis view: (A) apical wall, (B) basal wall, (C) mid septum wall. (D) Two chambers view

echocardiography could also show thickening of ventricular wall, mimicking hypertrophic cardiomyopathy.[7]

The non-specific signs and symptoms made the diagnosis of cardiac sarcoidosis to be difficult. Until now, there is no established diagnostic criteria for CS. The gold standard for CS diagnosis was endomyocardial biopsy (EMB), but it was invasive and has low sensitivity (10-20%). Therefore, imaging studies play a major role to diagnose CS. There are two non-invasive imaging modalities for CS, which are 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) and Cardiac MRI.[8]

The Heart Rhythm Society (HRS) has proposed criteria for the diagnosis of CS: confirmed of non-caseating granulomas in myocardium or extracardiac, exclusion of other causes of cardiac dysfunction, and clinical diagnosis or imaging consistent with CS.[9] In this patient, she had history of CTEPH that was first diagnosed in the previous hospitalized period. She was admitted to our ER with main problem of persistent dyspnea. She has AV block type I and echocardiography showed concentric LVH with preserved ejection fraction and high PASP of 45-50 mmHg. Subsequent imaging examinations of pulmonary system, including ventilation/perfusion lung scan, and cardiac coronary arteries are within normal results. This patient then underwent Cardiac MRI and found the presence of LGE in the inferior and infero-septal region, which are the pattern of multifocal and patchy lesions. These findings led to the diagnosis of suggestive Cardiac Sarcoidosis (50-90%) with SAPH.

The presence of PH in sarcoidosis was commonly caused by pulmonary fibrosis. The other possible mechanism of SAPH are intimal fibrosis, medial proliferation, and inflammatory changes. The development of SAPH in patients with sarcoidosis is an indicator for poor prognosis. The real prevalence of SAPH ranges between 5.7-28.3%.[10] Pulmonary hypertension should be suspected in any patients with sarcoidosis who has dyspnea, hypoxemia, or clinical manifestation suggesting right heart failure. The most common symptom is progressive dyspnea with activity. Other common symptoms are cough, chest pain, palpitations, and symptoms suggestive of right heart failure, such as lower extremities edema and syncope.[5] However, based on echocardiography, only 21% of patients with SAPH showed decreased systolic function (LVEF <50%), the others presented with preserved ejection fraction. Another study reported sudden death due to pulmonary artery compression. Left heart failure could also lead to PH, because of systolic and diastolic dysfunction of left ventricle. The gold standard for diagnosis of pulmonary hypertension is right heart catheterization (RHC).[10]

Our case is an interesting case, because our patient has unique characteristics. She was diagnosed with CTEPH from the previous hospital and was relatively stable for some years. It showed that cardiac sarcoidosis could be unnoticed and frequently misdiagnosed as other disease, because of its nature as a great imitator. Comprehensive examinations and Cardiac MRI play a significant role to diagnose cardiac sarcoidosis.

Conclusion

Cardiac sarcoidosis is a rare disease and diagnostic workup is challenging. A 47-year-old patient with dyspnea, sinus bradycardia with AV block type I, pulmonary hypertension, and preserved ejection fraction is presented in this case report. The initial imaging tests such as echocardiography, exercise stress test, CT thorax, CT pulmonary angiography, and CT coronary angiography were failed to build a definitive diagnosis. Cardiac MRI is a crucial imaging modality regarding diagnosis of cardiac sarcoidosis. Unexplainable case of pulmonary hypertension could be an indication of doing Cardiac MRI and lead to definitive diagnosis.

Abbreviations

18F-FDG-PET	: 18F-fluorodeoxyglucose positron emission tomography
CS	: Cardiac sarcoidosis
CT	: Computed Tomography
CTEPH	: Chronic thromboembolic pulmonary hypertension
EMB	: Endomyocardial biopsy
LGE	: Late gadolinium enhancement
LVEF	: Left ventricular ejection fraction
LVH	: Left ventricular hypertrophy
MRI	: Magnetic Resonance Imaging
PASP	: Pulmonary artery systolic pressure
PE	: Pulmonary emboly
PH	: Pulmonary hypertension
RVEF	: Right ventricular ejection fraction
SAPH	: Sarcoidosis-associated pulmonary hypertension

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publications

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material

Not applicable

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Competing Interest

All of the authors have no competing interest

Author's contribution

Nathania Purnomo as first and corresponding author, reported the case and wrote the discussion. Vito Damay and Sony Hilal Wicaksono as co-authors and supervisors, assisted for data collection and documentation.

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References

1. Martusewicz-Boros M, Boros P, Wiatr E, Zych J, Piotrowska-Kownacka D, Roszkowski-Śliż K. Prevalence of cardiac sarcoidosis in white population. Medicine. 2016;95(32):e4518.
2. Hulten E, Aslam S, Osborne M, Abbasi S, Bittencourt MS, Blankstein R. Cardiac sarcoidosis-state of the art review. Cardiovasc Diagn Ther. 2016;6(1):50-63.
3. Sekhri V, Sanal S, DeLorenzo L, Aronow W, Maguire G. Cardiac sarcoidosis: a comprehensive review. Archives of Medical Science. 2011;4:546-54.
4. Duong H, Bonham CA. Sarcoidosis-associated Pulmonary Hypertension: Pathophysiology, Diagnosis, and Treatment. Clin Pulm Med. 2018;25(2):52-60.
5. Sulica R, Teirstein AS, Kakarla S, Nemani N, Behnegar A, Padilla ML. Distinctive clinical, radiographic, and functional characteristics of patients with sarcoidosis-related pulmonary hypertension. Chest. 2005;128(3):1483–9
6. Patel AR, Klein MR, Chandra S, Spencer KT, Decara JM, Lang RM, et al. Myocardial damage in patients with sarcoidosis and preserved left ventricular systolic function: an observational study. Eur J Heart Fail. 2011;13:1231-7.
7. Gilotra N, Okada D, Sharma A, Chrispin J. Management of Cardiac Sarcoidosis in 2020. Arrhythmia & Electrophysiology Review. 2020;9(4):182-8.
8. Skali H, Schulman AR, Dorbala S. 18F-FDG PET/CT for the assessment of myocardial sarcoidosis. Curr Cardiol Rep. 2013;15:352.
9. Birnie D, Nery P, Ha A, Beanlands R. Cardiac Sarcoidosis. Journal of the American College of Cardiology. 2016;68(4):411-21.
10. Maimon N, Salz L, Shershevsky Y, Matveychuk A, Guber A, Shitrit D. Sarcoidosis-associated pulmonary hypertension in patients with near-normal lung function. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 2013;17(3):406–11.