

Cardiac Sarcoidosis Presented With Hiccups: A Case Report and Literature Review

Review began 06/01/2023

Review ended 06/04/2023

Published 06/07/2023

© Copyright 2023

Ghallab et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Muhammad Ghallab¹, Ivan Cancarevic¹, Nicole C. Noff¹, Daniel Miller¹, Allison Foster¹, Zakaria Alagha², Ashraf Sliem³, Sanjiv Bakshi⁴

1. Internal Medicine, Icahn School of Medicine at Mount Sinai, New York City (NYC) Health and Hospitals, New York, USA 2. Internal Medicine, Marshall University Joan C. Edwards School of Medicine, Huntington, USA 3. Internal Medicine, Flushing Hospital Medical Center, New York, USA 4. Cardiology, Icahn School of Medicine at Mount Sinai, New York City (NYC) Health and Hospitals, New York, USA

Corresponding author: Daniel Miller, ddmiller999@gmail.com

Abstract

Sarcoidosis is a multisystem disorder of unknown etiology commonly associated with hilar lymphadenopathy and granulomas. Cardiac involvement is less common; however, sarcoidosis is a known cause of restrictive cardiomyopathy. It typically presents as new-onset arrhythmias or heart failure, although cases of sudden cardiac death have been reported. We present a case of a 56-year-old male with a known history of pulmonary sarcoidosis, not on active treatment, who presented to the emergency department with a week of continuous hiccups every few seconds associated with non-exertional dyspnea. An initial computed tomography (CT) scan of the chest showed multiple stellate-like ground-glass opacities and the progression of bronchiectasis. Troponins were negative. On the initial electrocardiogram (ECG), he was found to be in atrial flutter and was admitted to the medical floor. Cardiology was consulted for suspected cardiac sarcoidosis, and they recommended transfer to the tertiary care center for further evaluation.

Upon arrival, the patient underwent catheter ablation for atrial flutter and returned to sinus rhythm after the procedure. The initial nuclear scan with gallium was not suggestive of cardiac sarcoidosis. However, subsequent cardiac magnetic resonance imaging (MRI) showed cardiac involvement.

Due to the high risk of arrhythmias, the patient was scheduled for implantable cardioverter defibrillator placement before discharge. The patient was given oral prednisone. The patient was discharged in stable condition, and interrogation of the device found it well functioning, and no significant arrhythmias were noted.

Presentation of cardiac sarcoidosis can be variable, and any should be considered in any patient with a known history of sarcoidosis who presents with atypical symptoms above the diaphragm, such as hiccups or with new-onset arrhythmias.

Categories: Cardiology, Internal Medicine

Keywords: cardiac imaging, adult cardiac disease, cardiology, hiccups, sarcoidosis

Introduction

Sarcoidosis is an idiopathic, diverse systemic illness that most frequently affects the lungs and lymph nodes or any organ and is characterized by non-necrotizing granulomatous inflammation [1]. About 20-30% of patients with systemic sarcoidosis will have cardiac involvement in the United States, which suggests a worse prognosis. In the United States and Europe, African Americans have a 3.8 times higher frequency of sarcoidosis than Caucasians; while in Japanese patients, cardiac sarcoidosis may be as common as 58% [2,3]. The diagnosis of cardiac sarcoidosis is challenging and can occur alone or in conjunction with multisystem symptoms. The manifestation can range from asymptomatic to high-grade atrioventricular block, ventricular arrhythmia, heart failure, atrial arrhythmias, or sudden cardiac death [1,4]. Hiccups are usually caused by an overly stretched stomach, excessive alcohol drinking or smoking, or rapid emotional changes [5]. Here we present a case of cardiac sarcoidosis that presents with persistent hiccups and then is found to have atrial flutter and newly diagnosed cardiomyopathy.

Case Presentation

A 56-year-old male with a past medical history of pulmonary sarcoidosis, sickle cell trait, pre-diabetes, Vitamin D deficiency, and leukopenia presented with ongoing intractable hiccups for one week with associated dyspnea without exertion for one day. The patient was treated for the hiccups three days earlier with chlorpromazine with relief, but ultimately the symptoms returned. The patient was then admitted for chest discomfort as well as abdominal pain. Electrocardiogram (ECG) revealed atrial flutter (Figure 1).

How to cite this article

Ghallab M, Cancarevic I, Noff N C, et al. (June 07, 2023) Cardiac Sarcoidosis Presented With Hiccups: A Case Report and Literature Review. Cureus 15(6): e40078. DOI 10.7759/cureus.40078

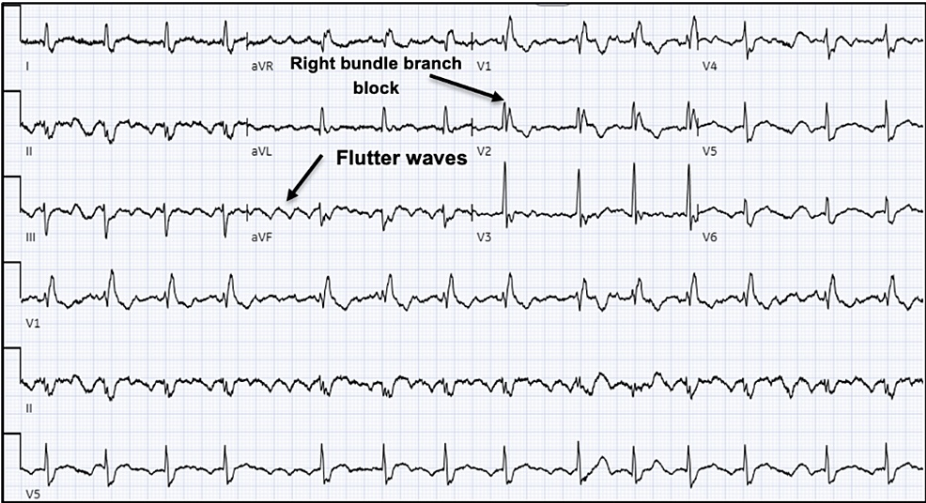


FIGURE 1: 12-leads EKG shows the right bundle branch block and atrial flutter.

EKG: electrocardiogram

The differential diagnosis list included diaphragmatic irritation from respiratory issues, phrenic nerve injury, and worsening pulmonary sarcoidosis.

A complete blood picture revealed leukopenia and microcytic anemia. The basic metabolic panel and liver function tests were unremarkable. Troponins were negative. Computed tomography angiogram chest with contrast (Figure 2) revealed no pulmonary emboli but did show multiple small stellate-like ground glass opacities with some bronchiectasis.

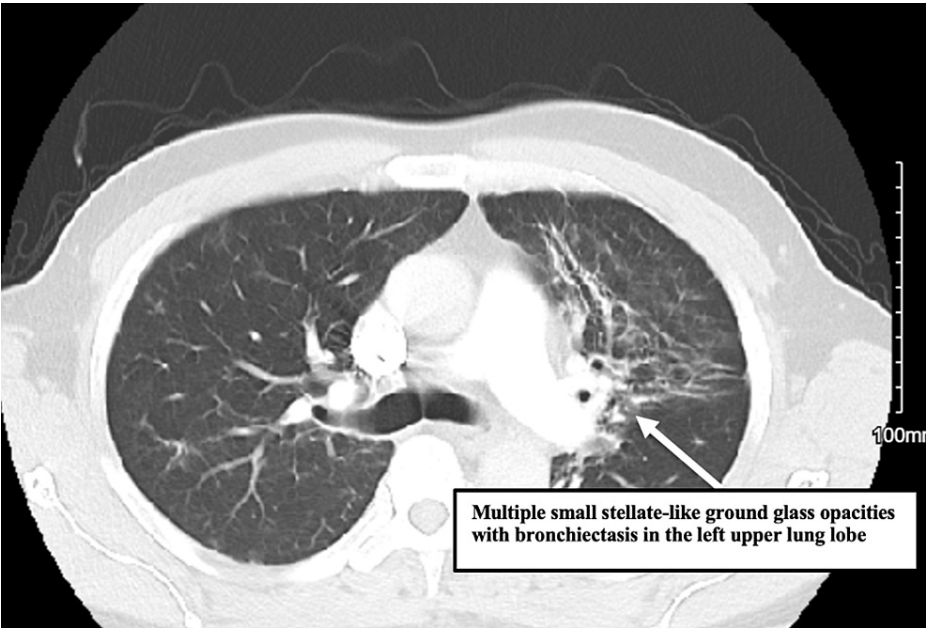
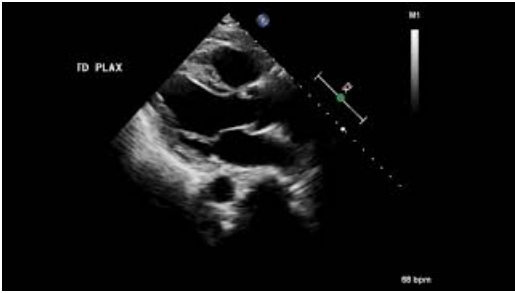


FIGURE 2: CT pulmonary angiography showing multiple small stellate-like ground glass opacities with bronchiectasis in the left upper lung lobe.

CT: computed tomography

A transthoracic echocardiogram (Video 1) revealed a reduced left ventricular ejection fraction of 45%, representing newly diagnosed cardiomyopathy, as his baseline ventricular contractility was normal.



VIDEO 1: A transthoracic echocardiogram revealing a reduced left ventricular ejection fraction.

View video here: <https://youtu.be/RWcX5aM0mvo>

The patient had a cardiac ablation of atrial flutter. The ablation eliminated the cavotricuspid isthmus-dependent flutter waves without complications, with a follow-up EKG (Figure 3) showing normal sinus rhythm.

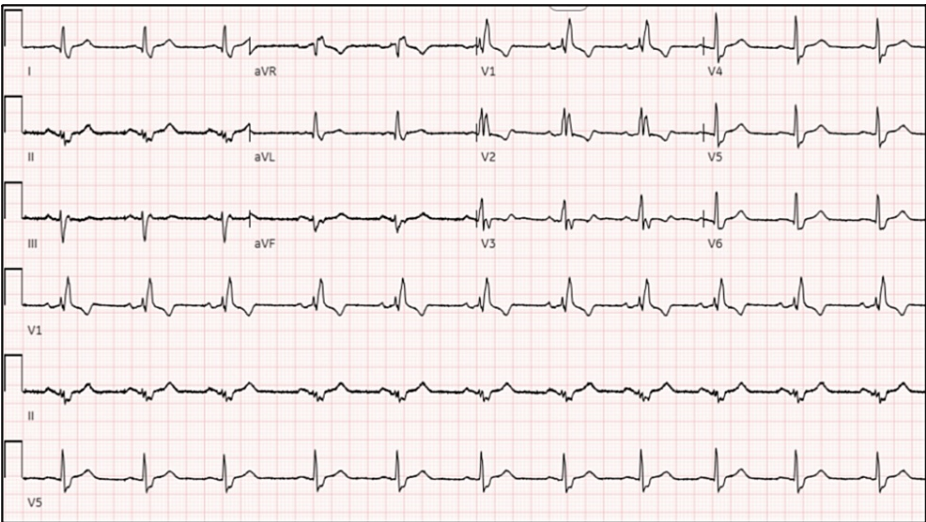


FIGURE 3: 12-leads EKG after the catheter ablation showing right bundle branch block and normal sinus rhythm.

EKG: electrocardiogram

A gallium scan revealed no myocardial uptake. It also showed mild left upper lung lobe uptake, likely due to parenchymal pulmonary sarcoid. Cardiac magnetic resonance imaging (MRI) revealed patchy subepicardial late gadolinium enhancement of the mid-anterolateral wall, apical lateral, inferior walls, and apex, compatible with cardiac sarcoidosis (Figures 4, 5).



FIGURE 4: Cardiac MRI - four chambers view showing patchy subepicardial late gadolinium enhancement in the apex, apical lateral, and mid-anterolateral walls. Subendocardial late gadolinium enhancement is evident in the apex as well.

MRI: magnetic resonance imaging

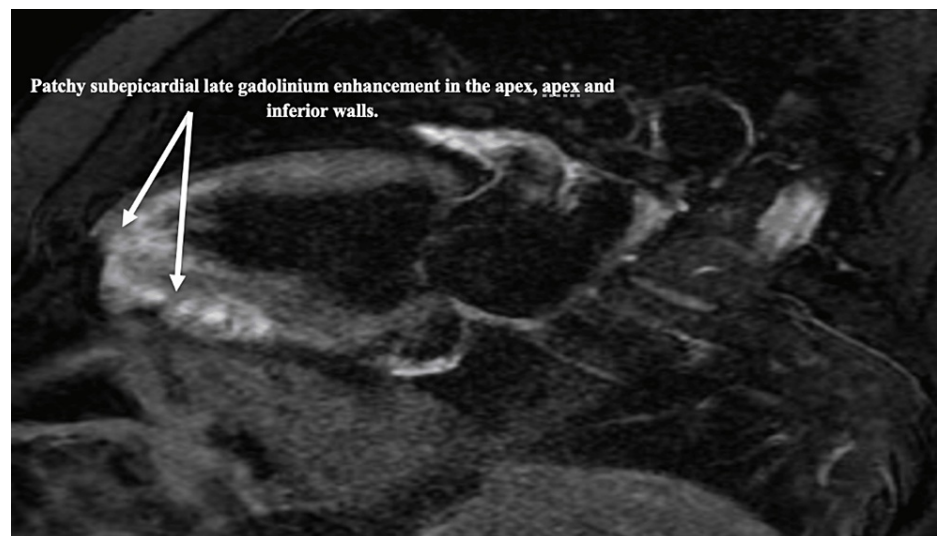


FIGURE 5: Cardiac MRI - two chambers view showing patchy subepicardial late gadolinium enhancement in the apex and inferior walls.

MRI: magnetic resonance imaging

Positron emission tomography-computed tomography-fluorodeoxyglucose (PET-CT-FDG) was used to confirm the diagnosis and revealed minimal FDG-avidity in the left ventricular myocardium, suggestive of myocardial inflammation/ sarcoidosis, along with bilateral peri-hilar ground glass and nodularity with FDG-avid hilar foci, likely related to sarcoidosis. The patient then underwent an implantable cardioverter defibrillator (ICD) placement for primary prevention of ventricular arrhythmias and was offered oral prednisone and follow-up in the sarcoidosis clinic.

Discussion

Sarcoidosis is a rare inflammatory disorder of unknown etiology that includes multiple organ systems, most commonly the lungs, eyes, lymphatic system, skin, and nervous system. However, it less commonly affects the cardiac system, including the atria, ventricles, papillary muscles, pericardium, conduction system, and coronary vessels [6]. Sarcoidosis is most common in young adults, especially African Americans [7]. Sarcoidosis exists in roughly 60 people per 100,000 in the United States, representing 200,000 people currently living with the disease. Of those diagnosed, approximately 5% have cardiac sarcoidosis. However, with advancements in cardiac imaging, cardiac manifestation is likely higher at around 30%.

The most common presentations of cardiac sarcoidosis are atrioventricular block, ventricular dysrhythmias, and heart failure. Less common presentations include bundle branch blocks, atrial dysrhythmias, valvular abnormalities, pericardial effusion, and sudden cardiac death [8]. However, hiccups are among the rarest presentations of sarcoidosis, specifically cardiac sarcoidosis.

A hiccup is an involuntary contraction of the diaphragm and intercostal muscles, causing sudden inspiration and abrupt closure of the glottis. The reflex arc of a hiccup comprises an afferent limb, including the vagus and phrenic nerves, sympathetic chain, central mediator, and an efferent limb, including the phrenic nerve, with accessory efferent neural connections to the glottis and inspiratory intercostal muscles [5]. Possible etiologies of hiccups in patients with sarcoidosis include a lesion along any area of the reflex arc, thoracic lymphadenopathy, and involvement of the central nervous system [5,7].

Treatments for cardiac sarcoidosis involve a multidisciplinary approach. Corticosteroids are the primary medical therapy; however, the precise dosage has yet to be thoroughly studied, given the lack of randomized control trials. The largest cohort study, including 95 Japanese patients treated with a high dose of prednisone (≥ 40 mg/d, mean 54 mg/d), was not correlated with increased survival compared to a lower dose (≤ 30 mg/d, mean 29 mg/d) [9]. Combining corticosteroids with additional immunosuppression therapies may improve outcomes [8]. A prospective cohort study from Japan, including 17 patients with cardiac sarcoidosis, was split into two groups, either treated exclusively with corticosteroids ($n=7$) or corticosteroids and low-dose methotrexate ($n=10$). Combination therapy revealed stable ejection fractions at five years versus the monotherapy group, which developed worsening values [10]. Patients with sarcoidosis and hiccups that were treated with corticosteroids had variable responses. In cases with predominant central nervous system sarcoidosis, more than half responded to steroids or combination therapy [7]. Concomitantly, a high-dose steroid invokes hiccups in its effect on synaptic transmission or neuroexcitatory properties [11]. Alternatively, other pharmacological hiccup treatments can be added concomitantly with sarcoidosis treatment, such as chlorpromazine, dopamine agonists, gabapentin, serotonin, and histamine agonists. Non-pharmacological therapies include phrenic nerve block, vagus nerve stimulator, acupuncture, and breath holding [7].

Nine reported cases of sarcoidosis are presenting with hiccups (Table 1). Of the nine cases, only one had cardiac sarcoidosis. The etiology of the hiccups was either due to central nervous system involvement or mediastinal lymphadenopathy. In five cases, pharmacological treatment failed, and hiccups persisted after corticosteroids were tapered off. Four cases were cured with either only corticosteroid treatment or in addition to clonazepam or methotrexate. In one case, invasive measures were taken and were successful.

Case Report	Age, Gender	Cardiac Involvement	Proposed Etiology	Treatment
Neuman et al., 2020 [7]	64, Male	No	Mediastinal lymphadenopathy	Mediastinoscopy and removal of lymph nodes
Kondo et al., 1989 [11]	67, Male	No	Central nervous system	Failed pharmacologic treatment
Chen et al., 2018 [12]	55, Female	Yes	Central nervous system and mediastinal lymphadenopathy	Corticosteroids
Hackworth et al., 2009 [13]	61, Male	No	Mediastinal lymphadenopathy and peritoneal lesions	Failed pharmacologic treatment
Lin et al., 2010 [5]	48, Male	No	Mediastinal lymphadenopathy	Failed pharmacologic treatment
Connolly et al., 1991 [14]	25, Male	No	Central nervous system	Corticosteroids
Douglas et al., 1973 [15]	38, Male	No	Central nervous system	Failed pharmacologic treatment
Miura et al., 2010 [16]	56, Male	No	Central nervous system	Corticosteroids and clonazepam
Seby et al., 2012 [17]	45, Male	No	Central nervous system and mediastinal lymphadenopathy	Corticosteroids and methotrexate

TABLE 1: Characteristics of sarcoidosis patients presenting with hiccups.

The case presented will be the 10th reported case of sarcoidosis presenting with hiccups and the second with cardiac involvement. The patient was treated with corticosteroids concurrently with metoclopramide with complete resolution of hiccups. Our review of sarcoid patients with hiccups on presentation identifies the common treatments utilized. Although steroids have variable responses, according to the literature, they should still be used first line if there are no contraindications. In conjunction, supporting pharmacologic therapy should be utilized prior to invasive measures. However, even with the treatments available, hiccups may persist long-term.

Conclusions

Sarcoidosis is a multi-system disease that can affect any organ in the body. We should consider cardiac involvement in patients with a history of sarcoidosis who presents with new cardiac symptoms, including recent onset heart failure, new onset reduction in cardiac contractility, and new onset ventricular and/or supra ventricular arrhythmias. We should also think of other atypical presentations in those patients. Our patient presented with an atypical presentation in the form of hiccups. This led us to further diagnosis of new-onset atrial flutter and new-onset heart failure. Despite the gallium scan being normal, other more sensitive investigations as cardiac MRI and PET-CT confirmed the diagnosis of cardiac sarcoidosis. He underwent ablation of atrial flutter and placement of ICD and was discharged on oral prednisone.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Giblin GT, Murphy L, Stewart GC, et al.: Cardiac sarcoidosis: when and how to treat inflammation . Card Fail Rev. 2021, 7:e17. [10.15420/cfr.2021.16](#)

2. Hulten E, Aslam S, Osborne M, Abbasi S, Bittencourt MS, Blankstein R: Cardiac sarcoidosis-state of the art review. Cardiovasc Diagn Ther. 2016, 6:50-63. [10.3978/j.issn.2223-3652.2015.12.13](#)

3. Sekhri V, Sanal S, Delorenzo LJ, Aronow WS, Maguire GP: Cardiac sarcoidosis: a comprehensive review. *Arch Med Sci*. 2011, 7:546-54. [10.5114/aoms.2011.24118](#)
4. Hu X, Carmona EM, Yi ES, Pellikka PA, Ryu J: Causes of death in patients with chronic sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2016, 33:275-80.
5. Lin LF, Huang PT: An uncommon cause of hiccups: sarcoidosis presenting solely as hiccups. *J Chin Med Assoc*. 2010, 73:647-50. [10.1016/s1726-4901\(10\)70141-6](#)
6. Tan JL, Fong HK, Birati EY, Han Y: Cardiac sarcoidosis. *Am J Cardiol*. 2019, 123:513-22. [10.1016/j.amjcard.2018.10.021](#)
7. Neumann M, Lazo KG, Stover D: Sarcoidosis presenting as hiccups. *Respirol Case Rep*. 2020, 8:e00605. [10.1002/rcr2.605](#)
8. Ribeiro Neto ML, Jellis CL, Joyce E, Callahan TD, Hachamovitch R, Culver DA: Update in cardiac sarcoidosis. *Ann Am Thorac Soc*. 2019, 16:1341-50. [10.1513/AnnalsATS.201902-119CME](#)
9. Yazaki Y, Isobe M, Hiroe M, et al.: Prognostic determinants of long-term survival in Japanese patients with cardiac sarcoidosis treated with prednisone. *Am J Cardiol*. 2001, 88:1006-10. [10.1016/s0002-9149\(01\)01978-6](#)
10. Nagai S, Yokomatsu T, Tanizawa K, et al.: Treatment with methotrexate and low-dose corticosteroids in sarcoidosis patients with cardiac lesions. *Intern Med*. 2014, 53:427-33. [10.2169/internalmedicine.53.0794](#)
11. Kondo T, Tanigaki T, Suzuki H, Tamaya S, Ohta Y, Yamabayashi H: Long-standing hiccup in a patient with sarcoidosis. *Jpn J Med*. 1989, 28:212-15. [10.2169/internalmedicine1962.28.212](#)
12. Chen XY, Ren ZC, Huang XJ: Sarcoidosis of the medulla oblongata causing intractable hiccoughs and numbness of extremities: a case report. *Medicine (Baltimore)*. 2018, 97:e13667. [10.1097/MD.00000000000013667](#)
13. Hackworth WA, Kimmelshue KN, Stravitz RT: Peritoneal sarcoidosis: a unique cause of ascites and intractable hiccups. *Gastroenterol Hepatol (N Y)*. 2009, 5:859-61.
14. Connolly JP, Craig TJ, Sanchez RM, Sageman WS, Osborn RE: Intractable hiccups as a presentation of central nervous system sarcoidosis. *West J Med*. 1991, 155:78-9.
15. Douglas AC, Maloney AF: Sarcoidosis of the central nervous system. *J Neurol Neurosurg Psychiatry*. 1973, 36:1024-33. [10.1136/jnnp.36.6.1024](#)
16. Miura S, Noda K, Ouchi A, et al.: Parkinson and intractable hiccups in a patient with relapsing sarcoidosis. *Neurol Asia*. 2010, 15:189-92.
17. John S, Parambil J, Culver D, Tavee J: Medullary neurosarcoidosis presenting with intractable hiccoughs. *J Clin Neurosci*. 2012, 19:1193-5. [10.1016/j.jocn.2011.11.031](#)