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Persistent FDG Uptake at Apical Aneurysm in a Patient With Cardiac Sarcoidosis

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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Persistent FDG Uptake at Apical Aneurysm in a Patient With Cardiac Sarcoidosis

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ABSTRACT

We present a case of cardiac sarcoidosis with persistent, focal fluorodeoxyglucose uptake at the left ventricular apical aneurysm concerning for ongoing active inflammatory injury, prompting aggressive immunosuppressive therapy. This case highlights the importance of understanding the various clinical entities that may resemble disease activity on fluorodeoxyglucose positron emission tomography/computed tomography imaging. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2023;10:101763) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 71-year-old man with a history of cardiac sarcoidosis (CS) diagnosed 2 years earlier, steroid-induced diabetes mellitus, and myopathy presented to the cardiology clinic for follow-up after undergoing ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET). He reported compliance with his current immunosuppressive regimen of prednisone 10 mg/day and methotrexate 12.5 mg/week. He had a history of heart failure with improved ejection fraction while taking metoprolol, a pacemaker upgrade to cardiac resynchronization therapy with defibrillation, atrial fibrillation for which he was taking apixaban, and ventricular tachycardia for which he was taking sotalol. He denied symptoms of heart failure, palpitations, syncopal episodes, cardiac resynchronization therapy with defibrillation shocks, and a recent history of infections requiring hospitalizations. His FDG PET scan revealed persistent focal FDG uptake in the left ventricular (LV) apex (**Figure 1** [scan 7]), and a discussion regarding his immunosuppressive regimen was held.

LEARNING OBJECTIVES

- To formulate differential diagnoses of persistent FDG uptake on serial PET imaging.
- To understand the mechanistic rationale of alternative causes that may result in focal, persistent FDG uptake.

PAST MEDICAL HISTORY

The patient was initially diagnosed with pulmonary sarcoidosis on thoracic lymph node biopsy

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ABBREVIATIONS AND ACRONYMS

CS = cardiac sarcoidosis

FDG = fluorodeoxyglucose

LV = left ventricular

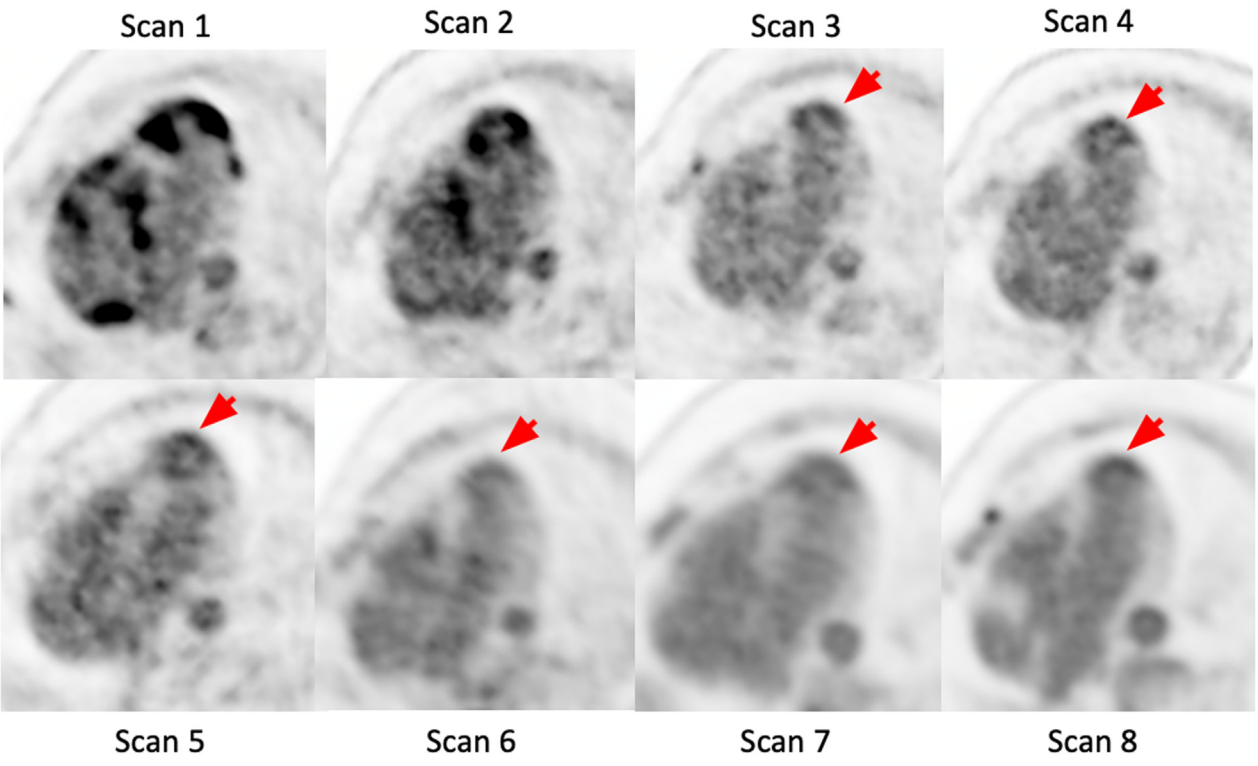
PET = positron emission tomography

TTE = transthoracic echocardiography

approximately 2 months before being diagnosed with CS. Before this, he underwent single-photon emission computed tomography myocardial perfusion imaging at an outside facility that demonstrated apical ischemia. He subsequently underwent coronary computed tomography angiography at an outside facility that showed no obstructive lesions. Cardiac magnetic resonance was not pursued because of a prior abandoned right ventricular pacemaker lead. He underwent FDG PET imaging (Figure 1 [scan 1]), which revealed avid biventricular FDG uptake and was initiated on prednisone. To assess the treatment response, he underwent follow-up PET imaging (Figure 1 [scan 2]) 3 months later, which revealed interval resolution of inflammation in the right ventricle but showed continued FDG uptake in the left ventricle. He was advised to continue taking prednisone to treat residual cardiac inflammation and to follow up approximately 4 months later. At the 4-month follow-up, PET imaging (Figure 1 [scan 3]) revealed a significant improvement from the prior study with only mild FDG uptake in the LV apex, and the decision was made to continue prednisone. Concurrently, he was diagnosed with pulmonary nocardiosis and received approximately 4 months of outpatient antibiotic treatment with a plan to return to the clinic for repeat cardiac imaging in 4 months (Figure 1 [scan 4]).

PET imaging at this time revealed persistent focal uptake in the LV apex, and he was continued on prednisone until repeat imaging 2 months later (Figure 1 [scan 5]), which again revealed uptake in the LV apex. A few weeks later, he was admitted to the intensive care unit at an outside hospital with recurrent pulmonary nocardiosis and new-onset neurologic nocardiosis. Transthoracic echocardiography (TTE) performed in the intensive care unit revealed an LV apical aneurysm with thrombus. Anticoagulation was initiated, and the patient was subsequently transferred to our facility for further care where he underwent contrast-enhanced TTE, which confirmed an LV apical aneurysm with a reduced LV ejection fraction of 35%, but no thrombus was visualized (Figure 2). During this hospitalization, he underwent another PET (Figure 1 [scan 6]), which

FIGURE 1 Serial Fluorodeoxyglucose Positron Emission Tomography Imaging of Scans 1 Through 8



Red arrows demonstrate persistent radiotracer uptake in the left ventricular apex.

revealed persistent FDG uptake at the apex. The patient was successfully stabilized and discharged on long-term imipenem and tedizolid to prevent the recurrence of nocardiosis as well as 35 mg prednisone.

DIFFERENTIAL DIAGNOSIS

Given the patient's history of pulmonary sarcoidosis and the significant FDG uptake on PET imaging, the primary diagnosis of CS was established. During follow-up, the differential diagnoses for persistent FDG uptake on serial PET scans despite immunosuppressive therapy included LV apical thrombus, physiologic blood pooling at the LV apical aneurysm, and a myocardial scar from an inflammatory or ischemic injury.

INVESTIGATIONS

The patient underwent combined metabolic/Rb perfusion PET imaging (**Figure 3**), which showed a moderate perfusion reduction in the apex and persistent focal FDG uptake at the LV apex. Repeat contrast-enhanced TTE re-demonstrated the LV apical aneurysm without thrombus.

MANAGEMENT

Shortly after discharge, the patient was evaluated in the heart failure clinic, and the decision was made to begin a slow prednisone taper while initiating methotrexate 10 mg/wk.

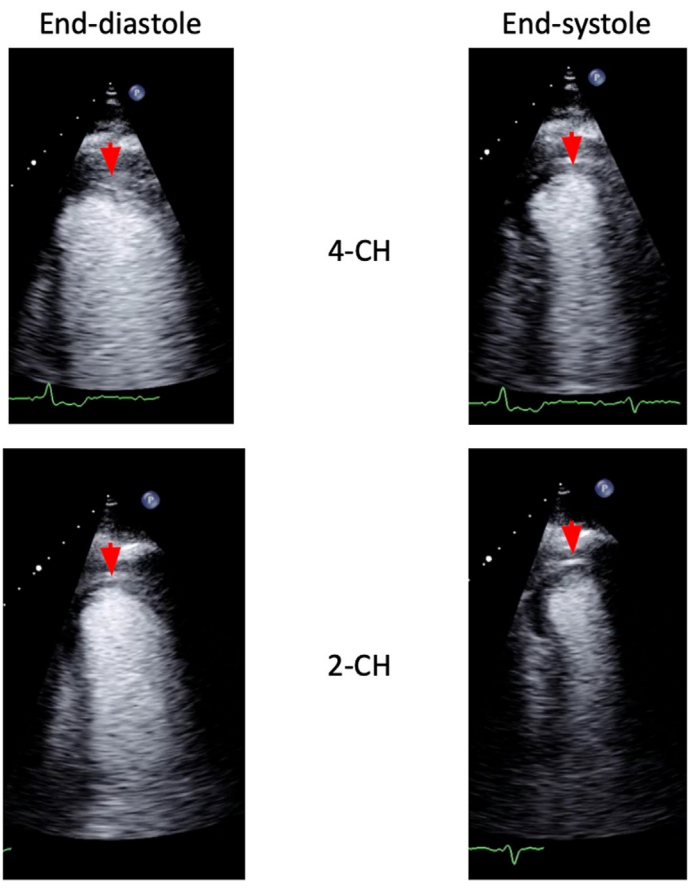
DISCUSSION

Despite histologic evidence of extracardiac sarcoidosis, the diagnosis and treatment response assessment of CS remain challenging because of its nonspecific, heterogenous array of clinical manifestations as well as the lack of specificity for myocardial inflammation. Regardless of these limitations, PET continues to play a critical role in establishing a diagnosis, monitoring disease activity, and assessing treatment response.[1] Once the diagnosis is established, immunosuppression is the standard of care, with corticosteroids being the primary choice. A favorable response is more likely with moderate- to high-intensity corticosteroid doses.[2]

As illustrated in our case, the initiation of prednisone resulted in a marked decrease in myocardial FDG uptake on serial PET. However, persistent FDG activity was still observed at the LV apex on serial imaging, and our patient continued on long-term steroid therapy, unfortunately resulting in medication-associated side effects. Therefore, it is imperative to have a better understanding of alternative causes and mechanisms of FDG activity (beyond active CS), particularly after 2 or 3 cycles of immunosuppression therapy, to consider alternative diagnoses and/or recognize an acceptable FDG suppression level when incurring medication side effects.

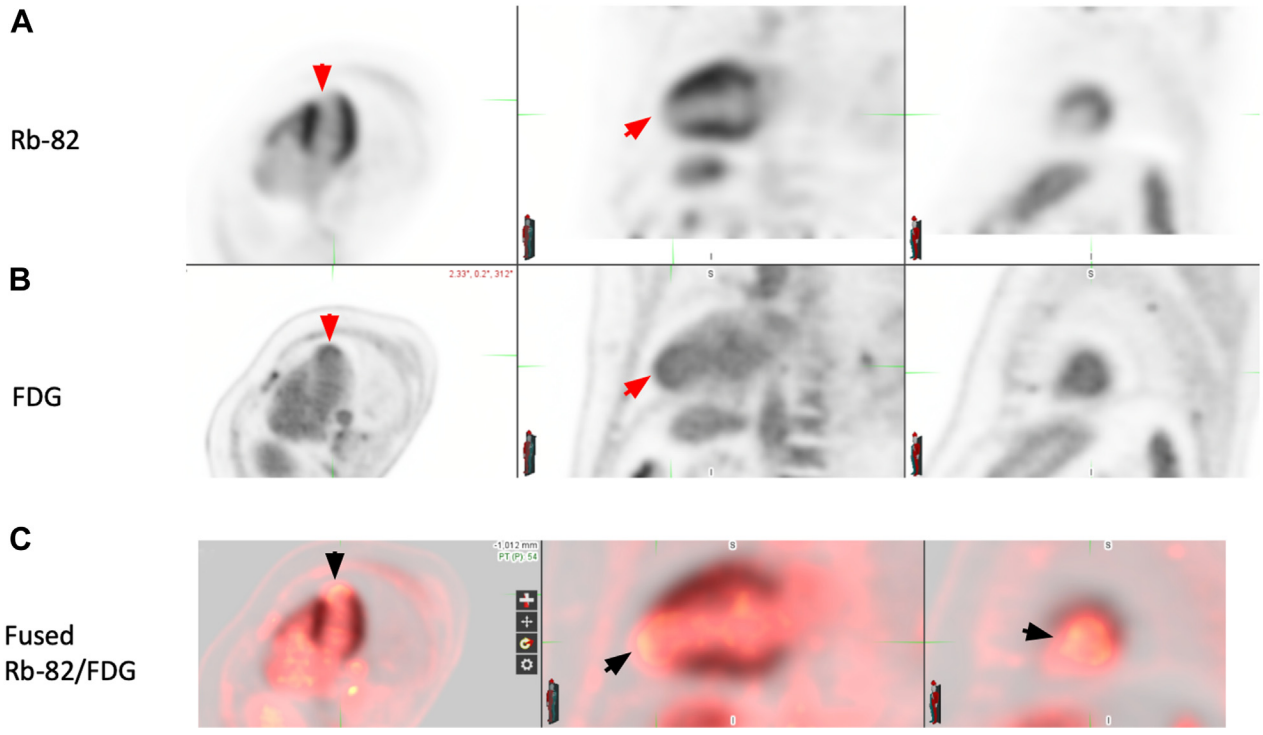
First, to improve the specificity and overall accuracy of PET imaging, it is important to achieve adequate suppression of background physiologic FDG uptake by cardiac myocytes. Despite this, nonspecific FDG uptake still may be noted in up to 10% to 38% of patients.[3] Our patient followed the same dietary preparation for each PET scan (ie, an overnight fasting period and a low-carbohydrate and high-fat diet the previous day). Pretest heparin infusion was not used.

FIGURE 2 Contrast-Enhanced Transthoracic Echocardiogram Demonstrating Absence of Thrombus in the Left Ventricular Aneurysm



Red arrows show no filling defect(s) suggestive of mural thrombi at the left ventricular apex.

FIGURE 3 Myocardial Perfusion/FDG Correlation



(A) Myocardial perfusion (Rb-82). **Red arrows** demonstrate apical perfusion defect. **(B)** fluorodeoxyglucose (FDG). **Red arrows** demonstrate focal apical FDG uptake. **(C)** fused Rb-82/FDG. **Black arrows** demonstrate hybrid imaging showing the apical perfusion defect with corresponding FDG uptake.

A spectrum of pathophysiologic conditions may mimic active CS, such as structural changes (ie, LV aneurysm), LV thrombus, and ischemic "hibernating" myocardium, resulting in abnormal FDG uptake patterns. Coronary artery disease is not uncommon in patients with CS, and the presence of persistent FDG uptake should raise clinical suspicion for underlying myocardial ischemia. Chronic ischemia can lead to glucose upregulation and manifest as FDG uptake after a vascular distribution during PET imaging. However, our patient had no symptoms of obstructive coronary artery disease, and prior coronary computed tomography angiography performed nearly 2 years ago showed no evidence of epicardial coronary obstruction on prior testing, thus making ischemia an unlikely cause of persistent FDG uptake on serial imaging.[4] Invasive coronary angiography was not pursued because of a low clinical suspicion for ischemia.

Another potential cause of persistent FDG uptake is in the setting of structural cardiac changes, such as an LV apical aneurysm. Dysfunctional myocardial contractility results in regional stasis of blood and increases the risk of thrombus formation. Thrombus can lead to varied degrees of FDG uptake depending on its chronicity, with organized mural thrombus appearing as a photopenic defect on PET imaging.[5] Our patient was noted to have an apical LV aneurysm with thrombus formation on TTE performed at an outside hospital. Subsequent TTE at our hospital re-demonstrated the LV aneurysm but failed to show residual mural thrombi. Fused perfusion FDG PET images (**Figure 3**) confirmed that persistent focal FDG activity on serial imaging corresponded to the region of the LV apical aneurysm noted on TTE. We hypothesized that blood pooling in the LV aneurysm during image acquisition can result in increased focal FDG activity in the aneurysmal sac because of regional stasis and/or certain fibrotic tissue may remain metabolically active via mechanisms unrelated to disease activity in sarcoidosis and thus continue to depict low-level FDG activity despite treatment. Although concomitant myocardial inflammation from sarcoidosis could still be present,

this seems unlikely after 7 cycles of immunosuppression therapy. Consequently, we concluded that the apical aneurysm was the most likely explanation of the persistent focal FDG uptake in our patient.

FOLLOW-UP

The patient's immunosuppression was adjusted such that with the addition of methotrexate 10 mg/week, prednisone was serially reduced to 10 mg/day, which he tolerated well. He then underwent another PET scan (**Figure 1** [scan 8]), which revealed persistent apical FDG uptake consistent with prior imaging. In light of this, his prednisone was reduced to 5 mg/day, and he was continued on a methotrexate dose of 10 mg/week with a plan to discontinue corticosteroids and obtain repeat imaging in 6 months.

CONCLUSION

Focal, persistent FDG uptake on serial PET imaging should warrant a re-evaluation to identify alternative causes that can mimic active disease. Clinically silent CS patients may benefit from therapy de-escalation to prevent medication side effects.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS aneurysm, cardiac sarcoidosis, echocardiography, fluorodeoxyglucose, immunosuppression, positron emission tomography