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HEART FAILURE AND CARDIOMYOPATHIES

CASE REPORT: CLINICAL CASE

Myopericarditis Following Use of Selective Androgen Receptor Modifier "RAD-140"

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ABSTRACT

We report the case of a 16-year-old boy who had myopericarditis following the first dose of a selective androgen receptor modulator called Testolone ("RAD-140"). These drugs are widely abused by physically active young adults; however, the drugs' side effects, which can be life-threatening, are not well characterized. (JACC Case Rep 2024;29:102423) 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 16-year-old boy presented to the emergency department with chest pain that radiated to his left arm and worsened with deep breathing. His symptoms began a few hours after he took his first and only dose of a selective androgen receptor modulator (SARM) as part of the "RAD-140" fitness program.

PAST MEDICAL HISTORY

His past medical history was notable for attention deficit/hyperactivity disorder for which he was not medicated. The patient reported past use of creatine to enhance muscle gain, a "mass gaining" supplement (RAD-140), as well as marijuana and tobacco use. No other supplements were reported. His immunizations were up to date.

DIFFERENTIAL DIAGNOSIS

On arrival to the emergency department, the patient was found to have a troponin level of 4,690 ng/L,

LEARNING OBJECTIVES

- To understand that illicit use of selective androgen receptor modulators such as "RAD-140" is common in the young but is underreported so specific questions regarding use can be asked during an encounter with a health care provider.
- To know that even a short course of selective androgen receptor modulators such as RAD-140 can result in life-threatening problems such as myocarditis so this serious condition can be diagnosed early and treated.
- To understand that exercise restriction, which could be challenging in physically active young adults who typically use RAD-140, is an important component of management of acute myocarditis.
- To know that SARM-associated myocarditis is likely to be reversible on cessation of drug exposure so the family can be provided with accurate prognostic information.

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

IVIG = intravenous immunoglobulin

LVEF = left ventricular ejection fraction

SARM = selective androgen receptor modifier

which increased to 6,066 ng/L 2 hours later. An electrocardiogram revealed sinus tachycardia, slight ST-segment elevation in leads V_5 and V_6, and ST-segment depression in leads V_1 and V_2 (Figure 1). His respiratory viral panel was negative, chest radiograph was unremarkable, total white blood cell count (8,200/μL) was not indicative of infection, and erythrocyte sedimentation rate and plasma B-type natriuretic peptide concentration were both within the normal range. Echocardiogram revealed normal intracardiac anatomy and biventricular size and function with a left ventricular ejection fraction (LVEF) of 60%. The differential diagnoses at this time included myocarditis, acute coronary syndrome, and acute coronary spasm.

INVESTIGATIONS

The patient underwent imaging with cardiac magnetic resonance (CMR), which showed hyperenhancement on late gadolinium enhancement sequences. There was patchy involvement of the left ventricular free wall from basal to apical regions in epicardial distribution. In addition, the anterior interventricular septum in mid and apical regions was also involved. Enhancement of pericardium in the same regions as left ventricular free wall involvement was noted (Figures 2A to 2C and 3A and 3B). T1 mapping values were elevated in these regions. Increased signal was seen in corresponding hyperenhanced areas of myocardium on T2-weighted images (Figure 3B). These findings were suggestive of myopericarditis. There were no regional wall motion abnormalities, and biventricular function was normal with a LVEF of 57 %. The origin and proximal course of coronary arteries were also normal. Coronary angiography was also performed and revealed normal coronary arteries without any spasm or obstruction.

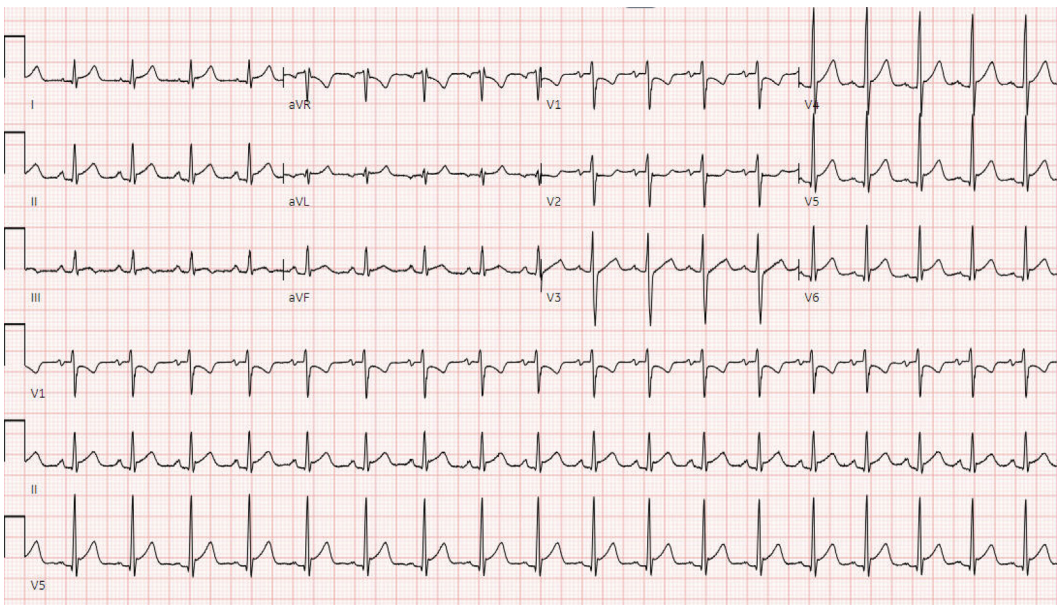
MANAGEMENT

The patient's myocarditis was classified as low risk due to normal systolic function and no demonstrable arrhythmias. He received intravenous immunoglobulin (IVIG) and was started on a steroid course during his hospital stay. He was also started on 5 mg of Lisinopril and 25 mg of Spironolactone daily to prevent adverse remodeling and restricted from any intense or competitive exercise.

DISCUSSION

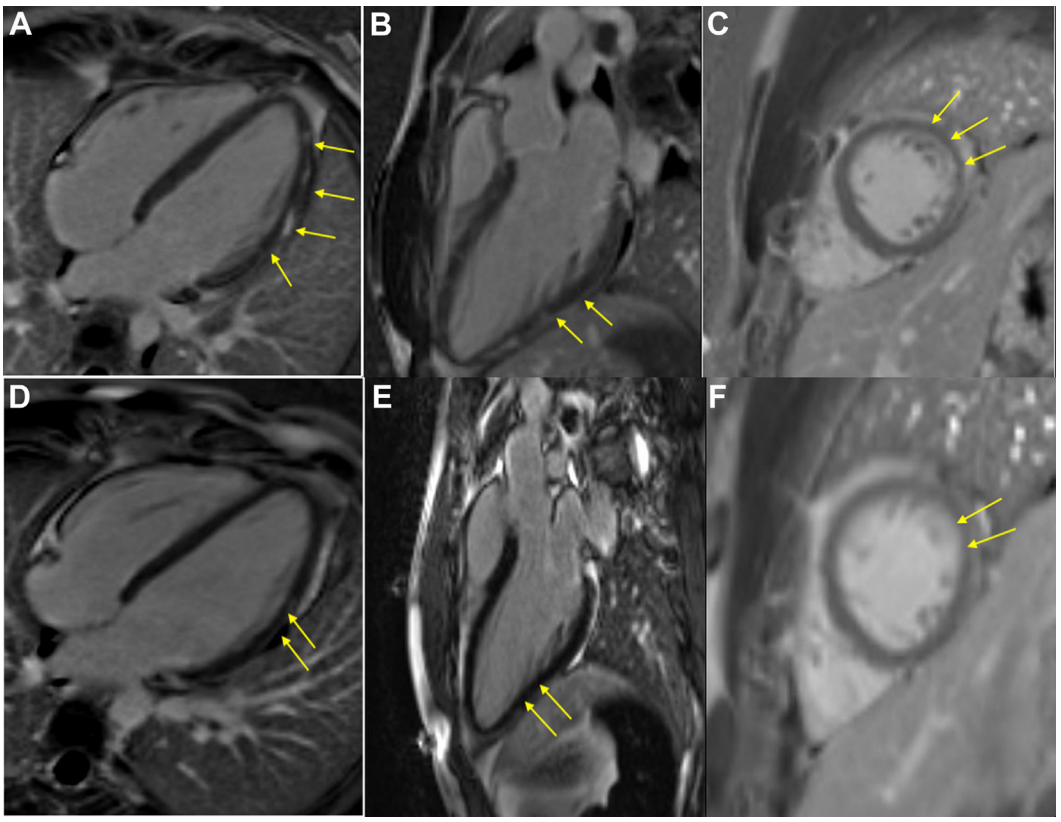
We report the case of a 16-year-old boy who developed myopericarditis following a single dose of the SARM "RAD-140," also known as Testolone. This drug acts as a musculoskeletal androgen receptor ligand, and functions like other SARMs or testosterone.[1] Besides its illicit use as a muscle growth supplement,

FIGURE 1 12-Lead Electrocardiogram



The tracing shows mild ST-segment depression in leads V_1 and V_2 and mild ST-segment elevation in leads V_5 and V_6.

FIGURE 2 **Cardiac Magnetic Resonance Images**

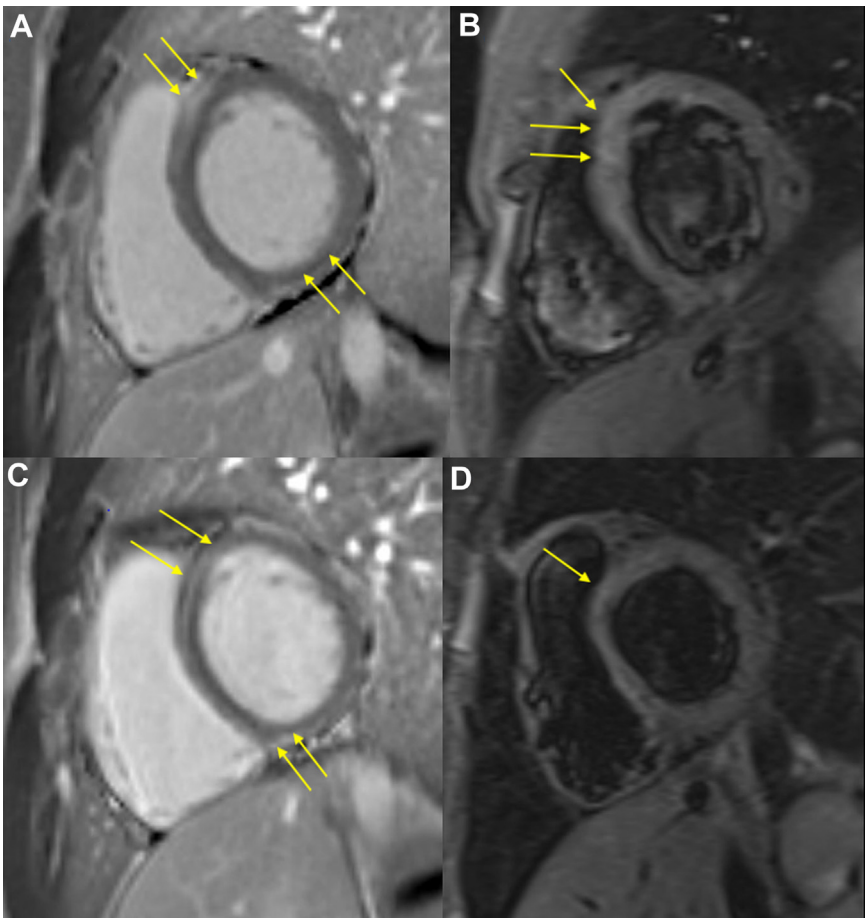


(A to C) During the patient's initial presentation, (A) the 4-chamber view. (B) the left ventricular outflow view, and (C) the short-axis view between the left ventricular midcavity and the apex show patchy inflammatory necrosis (arrows) in the acute myocarditis phase. Images were acquired late >10 minutes after contrast injection showing late gadolinium enhancement (arrows) in a characteristic epicardial or nonischemic distribution in the left ventricular free wall and apex. There is also pericardial enhancement. (D to F) Images obtained 4 months later in (D) the 4-chamber view, (E) the left ventricular outflow tract view, and (F) the short-axis view between the left ventricular midcavity and the apex show resolving inflammatory necrosis (arrows).

Testolone has been trialed in treatment of ER+ / HER2- metastatic breast cancer.[2] There is an increasing trend towards SARM use by young athletes for muscle gain. SARMs are however not approved by the U.S. Food and Drug Administration for this indication. Moreover, their use is prohibited by the World Anti-Doping Agency. Regardless, many of these agents are sold on a black market under the label of body enhancement drugs.[3] SARMs are taken orally, making them more appealing to the average young athlete as compared to other mechanistically similar performance enhancing drugs which require intramuscular injection.

A 2021 online based randomized response technique survey found that 2.7% of male gym-goers in the Netherlands had used SARMs specifically.[4,5] True population prevalence is likely higher as illegal substance use is commonly underreported.[4,6] Social media may be the key to widespread abuse among young people, with keyword searches for SARM on platforms such as TikTok and YouTube having shown a month-on-month increasing trend.[4] In addition, popular fitness content creators continue to advertise these drugs, emphasizing a lack of side effects.[4] Therefore, the adverse effects of SARMs, particularly RAD-140, are underemphasized and poorly characterized. A 32-year-old male with poorly controlled type 1 diabetes who presented with congestive heart failure attributed to myocarditis after several doses of RAD-140 has been reported.[7] A cardiac MRI or endomyocardial biopsy was however not obtained in this patient to confirm the diagnosis. Our patient, who was previously healthy, developed myocarditis a few hours after the first dose of RAD-140. This seemingly immediate and significant reaction is concerning

FIGURE 3 Cardiac Magnetic Resonance Images



(A and B) Images on initial presentation. (A) Areas with high signal intensities in a nonischemic distribution pattern on late gadolinium enhancement images (arrows). (B) Regional high T2 signal on T2-weighted images (arrows). (C and D) Images obtained 4 months later show (C) resolving late gadolinium enhancement and (D) no T2 signal on T2-weighted images (arrows).

given that it was caused by a single dose. This reaction could be consistent with a drug-induced hypersensitivity reaction referred to as hypersensitivity myocarditis. Most patients with this reaction do not show the typical characteristics of hypersensitivity such as rash and fever. Just like in our patient, symptoms cease after discontinuation of the causative drug.[8] Aside from a hypersensitivity reaction, the pathophysiological mechanism behind heart disease caused by SARMs is largely unknown. It has been theorized that this class of drugs, including testolone, may be interfering with the enzymes involved in steroidogenesis resulting in severe cardiovascular consequences.[9] In addition to cardiac adverse effects, several patients have been reported with liver injury after RAD-140 use. These patients had abnormal liver enzymes and jaundice which resolved several months after ceasing the use of RAD-140.[10-12] The findings in this patient highlight the dangers associated with the use of illicit supplements such as RAD-140. Since there is no well-established management strategy for myopericarditis following RAD-140, our patient received IVIG and steroids and tolerated them well.

FOLLOW-UP

His serum troponin concentration normalized 2 weeks after the onset of myopericarditis. At 8-month follow-up, his echocardiogram continued to show normal biventricular size and function. He underwent follow-up CMR 4 months after the diagnosis, and the imaging showed minimal enhancement in the epicardial left ventricular free wall region. No significant hyperenhancement or edema was seen in the

interventricular septum. No pericardial enhancement was seen. T1 mapping values were mildly elevated but improved in this region (**Figures 2D to 2F and 3C and 3D**). He also underwent a stress test 4 months after the onset of myocarditis, and the results did not show any abnormality. No arrhythmia was noted on follow-up Holter monitoring. Given these findings, he was allowed to return to full activity and is doing well, without any symptoms.

CONCLUSIONS

Acute myocarditis is an important differential diagnosis to consider in the setting of elevated troponins shortly after use of an SARM. The effects are likely reversible on cessation of use.

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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 **myocarditis, RAD-140, selective androgen receptor, Testolone modulator**