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Title:
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Date:
2022-07-01

Citation:
Milevski, S. V., Sawyer, M., La Gerche, A. & Paratz, E. (2022). Anabolic steroid misuse is an important reversible cause of cardiomyopathy: a case report. European Heart Journal Case Reports, 6 (7), https://doi.org/10.1093/ehjcr/ytac271.

Persistent Link:
https://hdl.handle.net/11343/316937

ESC European Society of Cardiology

European Heart Journal - Case Reports (2022) **6**, 1–6
https://doi.org/10.1093/ehjcr/ytac271

CASE REPORT
Heart failure

Anabolic steroid misuse is an important reversible cause of cardiomyopathy: a case report

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Received 24 February 2022; first decision 17 March 2022; accepted 29 June 2022; online publish-ahead-of-print 2 July 2022

Background Anabolic steroid misuse is very common and has been linked to the development of a severe cardiomyopathy, arrhythmias, and sudden death.

Case summary A 46-year-old miner presented to hospital with subacute dyspnoea and palpitations. Investigations revealed atrial fibrillation and a severe dilated cardiomyopathy with left ventricular ejection fraction of 12%. The patient had a history of longstanding exogenous testosterone administration. Haematological investigations demonstrated a marked polycythaemia, with haematocrit of 0.60 L/L (normal 0.40–0.54 L/L). Hormonal investigations revealed an elevated testosterone level of 46.4 nmol/L (normal 8.0–30.0 nmol/L) and suppressed luteinizing and follicle-stimulating hormones, consistent with excess testosterone use. The patient was referred to the endocrinology specialty team for support with ceasing excess testosterone use, while commencing guideline-directed heart failure therapy. At 6 months of follow-up, the patient's left ventricular ejection fraction had normalized and he was asymptomatic. Biochemical indicators of testosterone excess had also normalized.

Discussion Anabolic steroids are widely misused, particularly among young and middle-aged males. Cardiovascular complications include a potentially reversible severe cardiomyopathy, accelerated coronary disease, dyslipidaemia, arrhythmias, and sudden death. It is important to identify a history of anabolic steroid misuse when investigating cardiomyopathy and be alert for indicators such as polycythaemia. Cessation of anabolic steroid misuse may lead to complete reversal of cardiomyopathy but should be undertaken in close partnership with the patient and endocrinologists.

Keywords Anabolic steroids • Cardiomyopathy • Testosterone • Performance-enhancing drugs • Heart failure • Case report

ESC Curriculum 2.2 Echocardiography • 6.1 Symptoms and signs of heart failure • 6.2 Heart failure with reduced ejection fraction • 6.5 Cardiomyopathy

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Handling Editor: Sadaf Raza
Peer-reviewers: Aisha Gohar and Marta Cvijic
Compliance Editor: Daniel Tardo
Supplementary Material Editor: Nida Ahmed

Learning points

- Anabolic steroid abuse is extremely common globally, particularly among young men.
- Anabolic steroid excess has been associated with development of a reversible dilated cardiomyopathy and potentially severe heart failure and sudden death.
- Early suspicion of anabolic steroid cardiomyopathy is essential, along with comprehensive history taking and biochemical investigations.

Introduction

Anabolic and androgenic steroids (AASs) such as testosterone are part of a class of performance and image-enhancing drugs. Anabolic steroid misuse is extremely common globally, with approximately 4 million users estimated in the United States alone and 6.0% of Australians reporting use.[1,2] Demographically, most users are male non-athletes intending to improve appearance.[3]

The use of AASs has been linked to adverse cardiovascular outcomes including cardiomyopathy, myocardial infarction, and conduction abnormalities.[4] Despite multiple papers linking anabolic steroid misuse and cardiomyopathy on both a clinical and mechanistic level, awareness of AAS misuse has been reported to be limited among clinicians.[3]

In this case report, we describe anabolic steroids as the likely cause of a reversible severe dilated cardiomyopathy. We also detail pertinent findings on history, examination, and investigations that raise concern for an anabolic steroid-induced cardiomyopathy and outline a multidisciplinary approach to management.

Timeline

Timepoint	Clinical description
−10 years	Commencement of weekly exogenous anabolic steroids
−4 months	Onset of dyspnoea and palpitations
Month 0	Presentation to emergency department with dyspnoea and palpitations: found to be in rapid atrial fibrillation and have a marked polycythaemia
+2 weeks	Outpatient echocardiogram demonstrates a severe dilated cardiomyopathy Commenced on the guideline-directed heart failure therapy
+4 weeks	Review with the endocrinology team Direct cardioversion from atrial fibrillation to normal sinus rhythm
+4 months	Cardiac magnetic resonance imaging shows improvements with near-normal left ventricular (LV) function
+6 Months	Repeat transthoracic echocardiogram shows normalization of LV function

Case presentation

A 46-year-old miner and former bodybuilder reported development of subacute dyspnoea and palpitations over several months. Presentation to medical services was delayed as he initially attributed his dyspnoea to working in full personal protective equipment in tropical conditions in the mines. Following a fortnight in hotel quarantine during which his symptoms worsened, he presented to a tertiary emergency department for further assessment.

In the emergency department, he had a blood pressure of 130/70 mmHg, clear lung fields, dual heart sounds with an irregular pulse and was noted to be plethoric. There was no organomegaly or lymphadenopathy. He was clinically euvolaemic and a chest X-ray did not demonstrate signs of cardiac failure. A 12-lead electrocardiogram demonstrated rapid atrial fibrillation with a ventricular rate of 114 b.p.m. (*Figure 1*).

He was noted to have an elevated haemoglobin (208 g/L, normal 130–180 g/L) and haematocrit (0.60 L/L, normal 0.40–0.54 L/L) as well as an eosinophilia (0.6×10^9/L, normal $<0.4 \times 10^9$/L) (*Table 1*). He was commenced on metoprolol 25 mg twice daily, discharged home and an outpatient echocardiogram arranged.

Transthoracic echocardiography was performed (*Figure 2*, Supplementary material online, *Video S1*), and demonstrated severe global biventricular systolic dysfunction, with an increased left ventricular (LV) end-diastolic diameter (64.2 mm, normal <55 mm) and indexed LV mass of 126 g/m^2 (normal 61–79 g/m^2) and severely reduced left ventricular ejection fraction (LVEF) of 12%. The right ventricle was moderately dilated with evidence of severe systolic dysfunction (right ventricular ejection fraction, RVEF of 29%). Due to distorted LV geometry, the echocardiogram also demonstrated moderate functional mitral regurgitation.

With regards to risk factors for this new-onset severe global cardiomyopathy, a detailed clinical history was taken. The patient reported 10 years of regular exogenous testosterone use, in the form of injecting testosterone weekly (in various forms such as testosterone isocaproate, testosterone cypionate, testosterone propionate, and testosterone ethanthate). A three-generation family pedigree indicated a strong family history of pre-mature coronary artery disease, but no severe cardiomyopathies, cardiac device requirement, significant arrhythmias, or sudden deaths. The patient was mildly overweight (weight: 107 kg and body mass index: 28.7 kg/m^2 with pronounced muscle bulk), a non-smoker, and consumed minimal alcohol. There was a remote history of occasional illicit drug use approximately 20 years earlier. He had a history of inguinal hernia repair and took no prescribed medications.

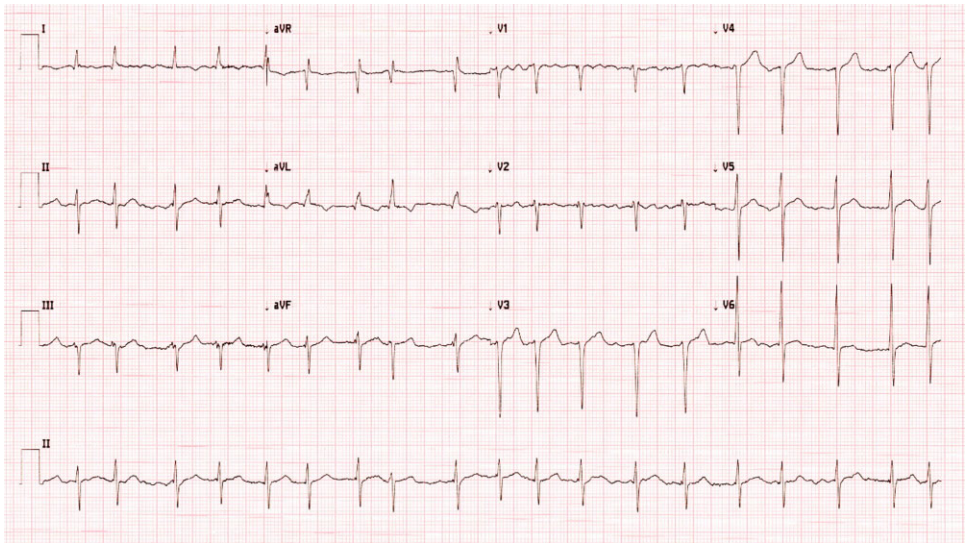

Figure 1 A 12-lead electrocardiogram on initial presentation showing atrial fibrillation.

Table 1 **Serial laboratory investigations and special investigations to rule out specific causes of polycythaemia**

Blood	Date					
	1 February 2021	10 March 2021	25 March 2021	18 April 2021	3 May 2021	24 May 2021
Hb (g/L)(130–180)	208	189		189	180	170
HCT (L/L)(0.40–0.54)	0.60	0.56		0.56	0.51	0.49
Platelets ($\times 10^9$/L)(150–400)	275	248		184	163	189
WCC ($\times 10^9$/L)(4.0–11.0)	9.9	9.6		7.1	5.4	6.8
Eosinophils ($\times 10^9$/L)(<0.4)	0.6	0.4		0.7	0.9	0.9
LH (IU/L)(0.6–12.0)			<0.1		0.2	1.3
FSH (IU/L)(1.0–12.0)			0.2		1.2	1.9
Free-testosterone (pmol/L)(270–864)			1106		115	295
Testosterone (nmol/L)(8.0–30.0)			46.4		6.7	16.5
Serum erythropoietin (U/L)(2.6–18.5)		22.2				
JAK2 mutation		Not detected				
Selenium (umol/L)(0.6–1.9)			1.2			
Zinc (umol/L)(10.7–25.0)			12.9			
Cholesterol mmol/L (<5.5)				6.4		
Triglycerides (mmol/L)(<1.7)				2.0		
HDL-cholesterol (mmol/L) (>1.00)				1.10		
LDL-cholesterol (mmol/L)(<3.5)				4.4		
LDL/HDL ratio (<3.5)				4.0		
Cholesterol/HDL ratio (<4.5)				5.8		
Troponin (ng/L) (<26)	19					

Hb, haemoglobin; HCT, haematocrit; WCC, white cell count; LH, luteinizing hormone; FSH, follicle-stimulating hormone; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Laboratory investigations indicated an elevated testosterone level of 46.4 nmol/L (normal 8.0–30.0 nmol/L) at 10 days since his last testosterone injection, elevated free-testosterone level of 1106 pmol/L (normal 270–864 pmol/L), normal sex hormone binding-globulin level of 39 nmol/L (normal 14–71 nmol/L) and profoundly suppressed luteinizing hormone (<0.1 IU/L, normal 0.6–12.0 IU/L), and follicle-stimulating hormone (0.2 IU/L, normal 1.0–12.0 IU/L). JAK-2 V617F mutation status was negative, indicating that exogenous steroids rather than an underlying myeloproliferative process were the likely cause of his polycythaemia (*Table 1*).

The patient commenced the guideline-directed heart failure therapy, including bisoprolol 7.5 mg daily, perindopril 5 mg daily,

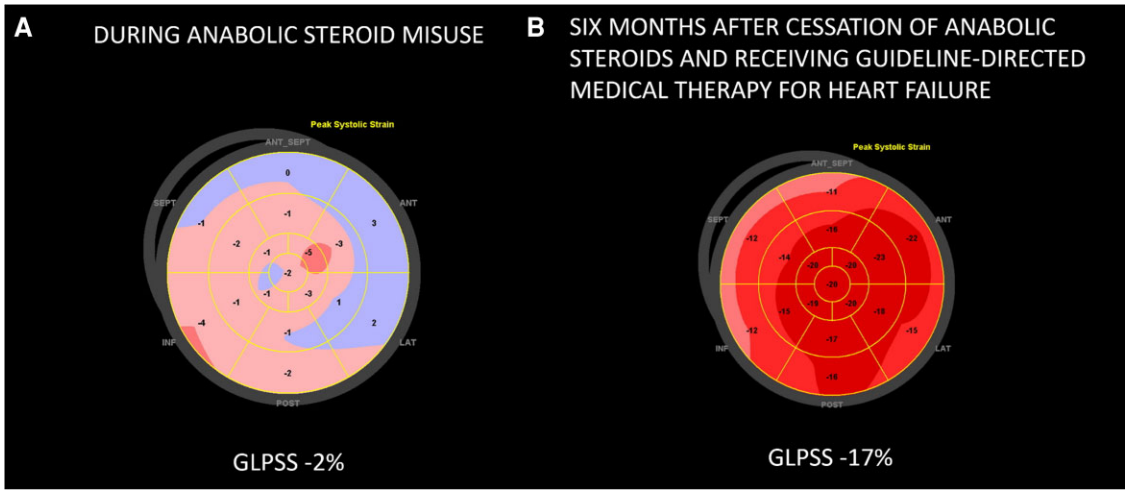

Figure 2 Echocardiographic strain images. (*A*) During anabolic steroid misuse and (*B*) 6 months after cessation and with the guideline-directed medical therapy. GLPSS, global longitudinal peak systolic strain, normal value −18% to −22%.

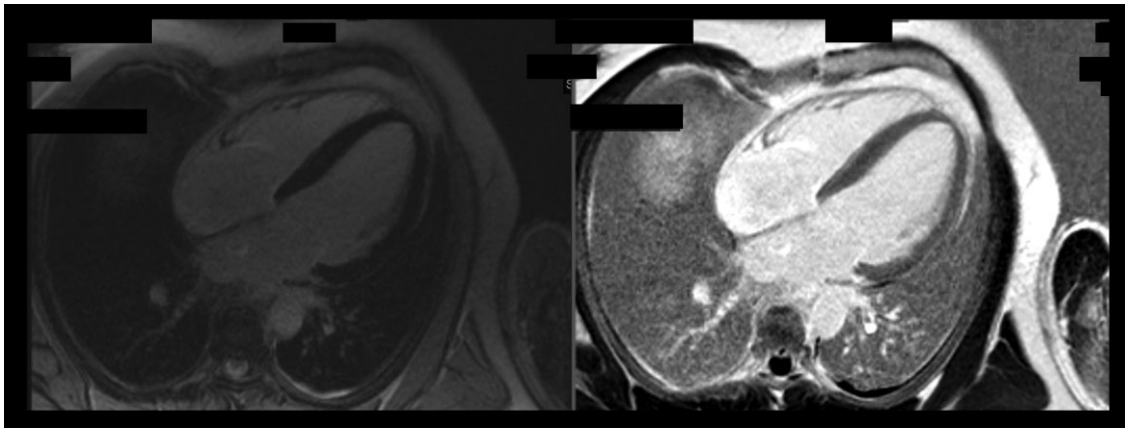

Figure 3 Sample of four-chamber images from cardiac magnetic resonance imaging, including phase-sensitive inversion recovery sequences, demonstrate a moderately dilated left ventricle with no evidence of inflammation or late gadolinium enhancement.

spironolactone 25 mg daily. In addition, the patient was also commenced on rivaroxaban 20 mg daily for atrial fibrillation. He underwent a direct cardioversion with reversion to normal sinus rhythm. The endocrinology unit oversaw the cessation of his testosterone use, followed by physiological supplementation in the setting of symptomatic hypogonadotrophic hypogonadism. A computed tomographic scan of the coronary arteries was performed (Supplementary material online, *Figure S1*) and demonstrated a coronary artery calcium score of zero Agatston units and normal coronary arteries.

Cardiac magnetic resonance imaging was performed (*Figure 3*) after approximately 3 months of the guideline-directed medical therapy and demonstrated low-normal biventricular function with an LVEF of 52.4% (RVEF of 57.5%), and mildly increased myocardial mass (108 g/m^2), wall thickness (12 mm septum) without evidence of inflammation or scar.

After 6 months of the guideline-directed medical therapy for heart failure as well as testosterone supplementation to physiological levels, the patient recovered clinically with normalized cardiac function and continued to remain in sinus rhythm. Repeat echocardiogram (Supplementary material online, *Video S2*) demonstrated normal LV size and systolic function, with an estimated LVEF of 61% and normal global longitudinal strain of −17%. The patient's haemoglobin level and haematocrit also normalized to 170 g/L and 0.49 L/L, respectively.

Discussion

Our case report illustrates an important cause of a severe reversible dilated cardiomyopathy. This is particularly pertinent in light of widespread use of exogenous AAS globally, with a recent Canadian study finding that AAS misuse was responsible for 1.5% of cardiomyopathies diagnosed in patients under 65 years of age.[5]

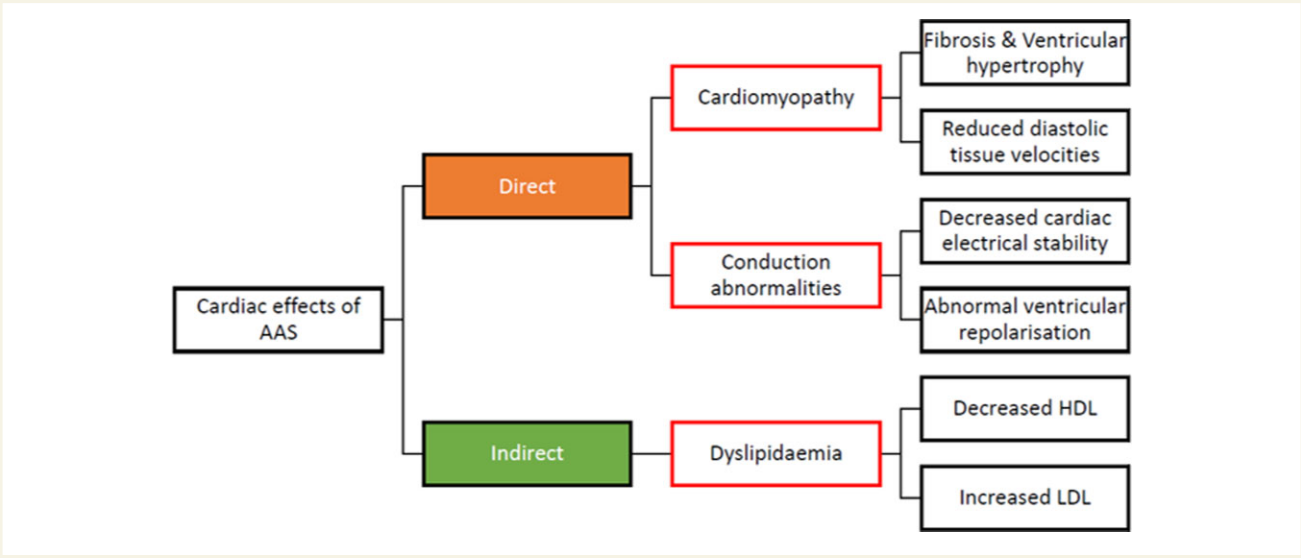

Figure 4 Interplay of anabolic steroids with cardiovascular risk factors.

Anabolic steroid misuse is common, pre-dominantly among young and middle-aged males. Although AAS misuse has been strongly linked with athletic behaviour,[4] the majority of users overall are non-athletic and report using AAS for image-enhancing purposes. It has been estimated that approximately 30% of AAS users will develop dependence.[1] In the athletic population, it has been reported that mortality among AAS users is up to 20-fold that of non-users, with one-third of deaths due to cardiovascular causes.[6]

Testosterone is essential for cardiovascular health, with endogenous testosterone levels inversely related to cardiovascular outcomes when within physiologically normal ranges.[7] However, when excess testosterone is taken, as in the case of our patient, this supraphysiological testosterone exerts adverse impact on the cardiovascular system (*Figure 4*). Importantly, synthetic anabolic steroid preparations such as those taken by our patient have been reported to be up to 15 times more potent than prescribed testosterone replacement therapies.[7] Pre-clinical studies demonstrate direct evidence of toxicity, with reduced beta-adrenoreceptor sensitivity, increased oxidative stress, and induction of myocyte apoptosis.[8] In the clinical setting, anabolic steroid misuse has been associated with dyslipidaemia, accelerated coronary atherosclerosis, a dilated cardiomyopathy, arrhythmias, and sudden death.[9] The dilated cardiomyopathy specifically is thought to result from adverse myocardial remodelling due to dysregulation of androgen receptors on cardiac myocytes.[10]

AAS cardiomyopathy appears to be highly reversible, provided the excess anabolic steroids are ceased.[7] For patients who do not cease AAS misuse, progressive cardiomyopathy, heart failure, and sudden death have all been described.[9] While transthoracic echocardiogram is the first-line investigation for diagnosis and monitoring recovery, early cardiac magnetic resonance imaging may also be useful to quantify any late gadolinium enhancement present and assist with prognostication for recovery and counselling of the patient.

It is important for clinicians to be alert to the possibility of AAS cardiomyopathy. The first step in recognizing this condition is to include questioning regarding AAS misuse when investigating potential causes of a cardiomyopathy.[11] High-risk groups where this is particularly relevant would appear to be young and middle-aged males, especially those involved in bodybuilding or security-related professions.[3] All patients diagnosed with a cardiomyopathy should have a full blood examination performed with haemoglobin and haematocrit, and this is a readily-accessible investigation that may flag the presence of AAS misuse if elevated.

Once AAS cardiomyopathy is diagnosed, sensitive interactions with the patient and a multidisciplinary supportive plan to wean AAS misuse while commencing the guideline-directed heart failure therapy is essential. Many patients may be reluctant to cease AAS misuse due to concerns regarding strength and performance reduction, reduced libido, and fatigue.[4,7]

Conclusion

This case report describes a middle-aged man with anabolic steroid-induced severe dilated cardiomyopathy. Cessation of anabolic steroids and commencement of the guideline-directed therapy led to normalization of cardiac function. Given the widespread use of anabolic steroids, their significant cardiovascular dangers, and the potential reversible nature of AAS-induced cardiomyopathy, greater public health awareness around the side-effects of their use would be welcomed.

Lead author biography

Stefan V. Milevski is a medical registrar who is currently completing his basic physician training. He has an interest in cardiology and general medicine.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that the written consent for submission and publication of this case report, including images and associated text, has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

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