CLINICAL VIGNETTE

Hyperlipidemia as a Clue to Anabolic Steroid Use

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Introduction

Hyperlipidemia encompasses a variety of disorders in lipid homeostasis, which frequently present with decreased levels of high-density lipoprotein cholesterol (HDL-C), increased levels of low-density lipoprotein cholesterol (LDL-C), and often concomitantly elevated triglyceride levels. This imbalance drives atherosclerotic plaque formation which contributes to an estimated doubling of cardiovascular risk compared to the normal population.[1] This leads to increased mortality from stroke and myocardial infarction, which are currently the leading causes of death among adults in the United States.

Hyperlipidemia can result from numerous etiologies, with hereditary and metabolic causes being the most common. These processes have been thoroughly reviewed in the biomedical literature.[2] Less frequently described is mixed hyperlipidemia induced by anabolic steroid use. Initially developed in the 1930s, anabolic-androgenic steroids (AAS) are synthetic testosterone derivatives that have been frequently used among athletes to increase performance and lean body mass development. Self-reported AAS use among body builders have ranged from 29 to 67%.[3] These are most often used in highly supraphysiologic doses in order to achieve desired effects. Despite its ban in all major sporting organizations and listing as a Schedule 3 Drug in the United States, AAS use remains highly prevalent and is easily obtainable via the internet. This has led to many adverse outcomes including hepatotoxicity, gonadal suppression, cardiovascular events, psychological disorders and even death.[4] We describe a case of severe mixed hyperlipidemia associated with AAS use.

Case Report

A 25 year-old male with no known prior medical history or FH of hyperlipidemia presented to clinic. Labs revealed LDL-C 497 mg/dL (nl <99), Tg 307 mg/dL (nl 40-160) mg/dl, HDL 18 mg/dL (nl >40), total cholesterol (TC) of 576 mg/dL (nl < 200), ALT 173 U/L (nl 7-45), AST 69 U/L (nl 13-35). Labs reviewed from 5 months prior revealed LDL 150 mg/dl, Tg 96 mg/dL, HDL 50 mg/dl, and TC 220 mg/dl. HgA1C of 5.2%, ALT 173 (nl 29-33), AST 69 U/L (nl 5-40). TSH 0.61 mIU/L (nl 0.55-4.78).

The patient acknowledged that he was taking an anabolic supplement which contains testosterone precursors including 17B-OH-2A and 17B-dimethyl-5A-androstan-3-one-azine. He had further liver evaluation with normal liver ultrasound and hepatitis serologies.

After counseling, the patient agreed to discontinue the AAS. Three months later his lipid profile improved: LDL-C 158 mg/dl, Tg 97 mg/dl, HDL 44, TC 221 mg/dl, and LFTs normalized. At initial consultation he also had labs consistent with hypogonadotropic hypogonadism, and these labs also returned to normal after discontinuation of AAS.

Date	HDL-C	LDL-C	TG	Total Chol	ALT
6/2019	50	150	96	220	
11/2019	18	497	307	576	173
12/2019	40	243	132	299	
2/2020	44	158	97	221	57

Discussion

This case illustrates the potent effect of AAS in increasing LDL-C and TG, and decreasing HDL-C. Following discontinuation of AAS, the patient's lipid profile returned to baseline levels. This pattern is consistent with prior reports showing 8-14 weeks of AAS use cause a 90% increase in LDL and 50% decrease in HDL, with normalization back to baseline in ~10 weeks.[5] The biochemical mechanisms by which anabolic steroids affect HDL-C and LDL-C concentrations are not completely understood. It has been postulated that induction of hepatic triglyceride lipase (HTGL) activity and modification of apolipoprotein A-1 and B synthesis play important roles in the alteration of HDL and LDL levels.[6] HTGL facilitates catabolism of HDL and produces significant decreases in HDL-C and Apo-A-I concentrations. This effect is usually reversible, with normalization of lipid profiles with discontinuation of anabolic steroids.

The patient's lipid and liver abnormalities were discovered at initial clinic visit and fortunately no significant adverse events occurred in this case. A 2010 meta-analysis investigating the cardiovascular effects of AAS, included 49 studies on 1467

athletes found evidence suggesting increased mortality due to cardiovascular causes.[7] A retrospective case-control study showed a standardized mortality ratio of 20 vs 6 for AAS-users compared to controls.[8] A post-mortem study of 34 Caucasian AAS users aged 20-45 showed likely primary cardiac causes in 12 of the deaths.[9] In addition to its effects on lipids, AAS have been postulated to have a direct effect on cardiac tissue through promotion of growth followed by premature apoptosis mediated by calcium influx channels and dysregulation in mitochondrial permeability.[10] This may result in hypertrophic cardiomyopathy, ventricular remodeling and sudden cardiac death.

Conclusion

This case illustrates the potent effect of AAS on cardiovascular health. On a molecular level, AAS produces an atherogenic lipid profile which is closely related to oxidative stress, endothelial dysfunction, and elevation in LDL and Lipoprotein (a) levels.[11] Furthermore, AAS promote a pro-thrombotic state through its effects on the coagulation cascade.[12] Clinically, AAS has been linked to elevated blood pressure, left ventricular hypertrophy, acute myocardial infarction, and sudden death due to arrhythmia.[13] The etiology of these clinical outcomes are still being elucidated but may be in part due to coronary artery disease as well as direct action on cardiac tissue associated with cardiomyopathy. The effects of AAS are usually reversible, with normalization in lipid profiles with discontinuation of anabolic steroids. As AAS use is often recurrent in 8-12 month cycles, it is important to continually counsel patients on these significant lipid effects.

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