KANSAS JOURNAL of MEDICINE

Ischemic Stroke in the Setting of Anabolic Androgenic Steroid Use

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Received Feb. 6, 2023; Accepted for publication April 3, 2023; Published online May 25, 2023
https://doi.org/10.17161/kjm.vol16.19507

INTRODUCTION

Stroke occurs in approximately 795,000 people in the United States every year, with 87% being ischemic.[1] Age is an important risk factor for stroke,[2] with 62% of stroke patients being ≥ 65 years old, with a 13% 30-day mortality in patients ≥ 85 years old.[3] Stroke risk consisted of 87% of important modifiable risk factors and included hypertension, obesity, hyperglycemia, hyperlipidemia, diabetes mellitus, and renal dysfunction.[2] Behavioral risk factors included 47% of risk and included smoking, physical inactivity, and diet. While there were overlaps in risk factors for older adults, risk factors for young adults (≤ 50 years old) also included migraine, hormonal contraceptives, and pregnancy, along with other known etiologies such as cervical arterial dissection, vasculitis, hematologic diseases, and substance abuse.[4]

Anabolic androgenic steroid (AAS) abuse is used for enhancement of athletic performance, physical appearance, and sexual function.[5] Adverse effects of AAS usage include secretion suppression of gonadotropins, neuropsychiatric effects, dyslipidemia, hypertension, arrhythmia, erythrocytosis,[5] and decreased arterial plasticity.[6] This report summarizes an instance of ischemic stroke in a young male who reported using both stanozolol and clenbuterol in preparation for a bodybuilding contest. Written, informed consent was obtained for the publication of this report.

CASE REPORT

A 27-year-old male presented to an external hospital with slurred speech, left-sided weakness, and past medical history of lower extremity compartment syndrome and decompression fasciotomy. The patient was an amateur bodybuilder preparing for a contest and had been taking testosterone and stanozolol for four to six weeks. He also had started taking clenbuterol 40 µg daily recently and that after taking the second dose, he reported developing ringing in his ears, left-sided weakness and numbness, and slurred speech within six hours resulting in a fall in the bathroom. He tried to sleep-off the symptoms, but the following morning the symptoms persisted, so he presented to the emergency department. Initial computerized tomography (CT) of the head and neck showed suspected subacute infarct in the right posterior parietal region without hemorrhage, midline shift, or mass effect. The patient was not given tissue plasminogen activator since he presented after 4.5 hours of symptom onset. A stroke alert was called, and he was transferred to a Level 1 stroke facility.

Upon arrival, the patient was seen in the emergency department; initial National Institute of Health Stroke Scale score was 6 for left facial droop, left upper extremity weakness and sensory deficit, left lower extremity weakness, dysarthria, and dysphagia. He was found to have sinus tachycardia with a heartrate between 120-130 bpm, hypokalemia with a potassium of 2.9 mmol/L, rhabdomyolysis with a creatine kinase of 3527 units/L, and a non-ST segment elevation myocardial infarction (NSTEMI) with initial troponin of 43 ng/L. Magnetic resonance imaging showed multifocal regions of infarction within the right middle cerebral artery territory and tiny microinfarcts within the left hemisphere, suggestive of a proximal embolic source (Figure 1). After consultation with the interventional radiologist, a carotid ultrasound was obtained which showed incomplete occlusive mobile thrombus or fibrin within the right carotid bulb. The patient was admitted to the Neurocritical Care Unit (NCCU).

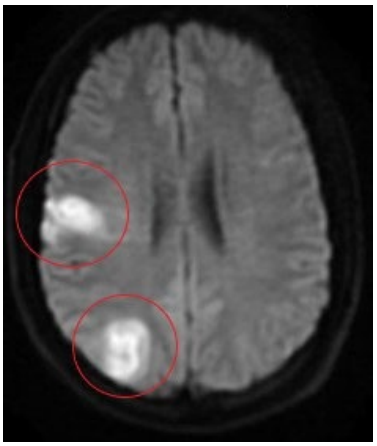

Figure 1. Magnetic resonance imaging showed multifocal regions of infarction (red circles) within the right middle cerebral artery territory, suggestive of a proximal embolic source.

The vascular surgery service was consulted and recommended to start the patient on a heparin drip per cardiac protocol since a lower extremity ultrasound was negative for deep vein thrombosis. The cardiology service was consulted for NSTEMI and transesophageal echocardiogram (TEE); however, due to the location of the thrombus in the right carotid bulb, TEE was delayed. Transthoracic echocardiogram showed possible shunt and no obvious thrombus. The patient's NSTEMI was determined to be related to demand ischemia. Troponin continued a downward trend over the next 36 hours.

The following day, TEE showed normal left ventricular size and systolic function, no significant valvular abnormalities, and no intracardiac masses or thrombi. In addition, a very small patent foramen ovale was identified by color criteria, with bubble study positive for a very small right-to-left shunt.

Laboratory evaluation showed high-density lipoprotein (HDL) at 47 mg/dL and low-density lipoprotein (LDL) at 140 mg/dL. The patient was started on oral 12.5 mg metoprolol daily by the cardiology service for sinus tachycardia, oral 80 mg atorvastatin given daily, and dual antiplatelet therapy (DAPT) with aspirin and clopidogrel (81 mg/75 mg oral daily) by the NCCU team for secondary stroke prevention.

The patient was monitored continuously over the next three days, with ataxia and dysphagia improving. After three days, hypercoagulability workup was initiated which was unremarkable. He passed a swallow evaluation. Physical and occupational therapy recommended outpatient rehabilitation. The patient was discharged and an outpatient cardiology appointment was scheduled following a 30-day event

monitor, which showed two episodes of sinus tachycardia and one 3.6 second pause. Much of the patient's deficit had resolved except for some left upper extremity weakness at the one-month follow-up. Follow-up CT of the head and neck showed resolution of the thrombus within the right carotid, and DAPT was continued for three months.

DISCUSSION

Some individuals, whether in competitive or non-competitive sports, abuse AASs to improve their performance or their physical appearance.[5] Young people (15-44 years old) abusing drugs, including AASs, were approximately 6.5 times more likely to have a stroke than non-drug users.[7] This was a case of a 27-year-old male that developed an ischemic stroke after self-administration of stanozolol and clenbuterol. Most notably, other than substance abuse, the patient had no known risk factors for an ischemic event.

AASs are a family of hormones that include testosterone and its many synthetic analogs, all of which exhibit anabolic and androgenic properties.[8] The atherogenic effects of these drugs arise from their ability to decrease HDL by 20% and concomitantly increase LDL by 20% through modification of apolipoprotein A-I and B synthesis.[7] In addition to its atherogenic effects, excess LDL-C may oxidize at the arterial endothelium and impair endothelium-dependent arterial relaxation by inhibiting nitric oxide production, predisposing the patient to vasospasm.[6,8] Concurrently, the effect of AAS abuse on the hemostatic system may alternate from an antithrombotic to a prothrombotic state. This results in abnormally high thrombin-antithrombin complexes in the plasma, higher concentrations of plasma fibrinogen, plasminogen, and plasmin inhibitor, and a reduction in fibrin clot lysis, potentially causing a procoagulant state.[9] Because of the association of AASs with changes in vascular reactivity, lipid profile, hemostasis, and platelet aggregation, ischemic stroke can occur because of atherothrombosis or embolization either in the carotids or the heart.[10] AASs also can provoke polycythemia and ischemic events by resetting erythropoietin stimulation via the reduction of hepcidin.[7]

Clenbuterol has been used by athletes in power sports with weight categories, such as bodybuilding, and is often used in conjunction with AASs. Clenbuterol is a β-2 agonist used to promote lipolysis and weight loss and has a high β-2 specificity, moderate β-1 activity (especially at high doses), and may act on β-3 adrenergic receptors.[11] Clenbuterol increases skeletal muscle, inhibits breakdown of protein, and decreases body fat. Potential adverse effects of β-2 agonists include tachycardia, arrhythmias, hypokalemia, muscle tremor, and myocardial ischemia.

The role that clenbuterol played in this patient's ischemic event is difficult to ascertain. Certianly, there is a well documented risk of ischemic events in individuals abusing AASs.[7] This patient presented with significant tachycardia, a known side effect of clenbuterol.[11] He also presented with hypokalemia and, although lacking electrocardiogram documentation, there was possibly an arrythmic episode that resulted in an embolic event. Although documented cases of ischemic events linked to clenbuterol were lacking, clenbuterol increases infarct volume in animal models,[12] so providers should be aware of concominant use in individuals abusing AASs. In fact, for cases such as this where the patient has no known risk factors, providers should explore drug history as a potential cause of disease.

Ischemic stroke is a rare but serious complication of AAS abuse. These substances have atherogenic effects that may increase the risk of an ischemic event by raising LDL and lowering HDL, and increasing vasospasm and thrombus formation risk. This case described an instance of ischemic stroke in an otherwise healthy 27-year-old male who was abusing AASs and clenbuterol. Given the relative prevalence of illegal AAS use, it is important that clinicians consider AAS as a possible cause of ischemic events in all patients, regardless of body size or physical appearance.

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Keywords: case report, anabolic androgenic steroids, ischemic stroke, clenbuterol, substance-related disorders