Caution for Anabolic Androgenic Steroid Use: A Case Report of Multiple Organ Dysfunction Syndrome

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We report a 42-year-old male amateur body builder and user of anabolic androgenic steroids, who developed ARDS, acute kidney injury, and refractory supraventricular tachycardia. He required extracorporeal membrane oxygenation, continuous veno-venous hemodialysis, and catheter ablation. We believe that long-term anabolic androgenic steroid abuse predisposed the patient to multiple organ dysfunction syndrome, from its immunomodulatory effects in an otherwise healthy patient. Anabolic androgenic steroid use should be part of the history taking process, since it may complicate diagnosis, disease progression, and prognosis. *Key words: anabolic androgenic steroid; ARDS; acute kidney injury; multiple organ dysfunction syndrome; extracorporeal membrane oxygenation.* [Respir Care 2013;58(12):e159–e163. © 2013 Daedalus Enterprises]

Introduction

Use of anabolic androgenic steroids (AAS) has become more common among professional and amateur athletes. The medical consequences of long-term AAS abuse are unclear, but there are reports of AAS abuse resulting in death.[1] We report a 42-year-old male amateur body builder and user of AAS, for muscle building, who developed multiple organ dysfunction syndrome and ARDS, and required veno-venous extracorporeal membrane oxygenation (VV-ECMO).

Case Report

The patient was a 42-year-old male (180 cm, 90 kg, body mass index 27.8 kg/m^2) amateur body builder with a previous history of smoking but no other noteworthy medical history. He admitted to injecting himself with AAS complexes, including testosterone acetate, testosterone cypionate, testosterone decanoate, testosterone propionate, testosterone phenylpropionate, testosterone enanthate, and testosterone isocaproate, for a few years. He presented to a local emergency room during the summer of 2012, with complaints of nausea, vomiting, diarrhea, and 5 days of shortness of breath and productive cough. He was hypoxic and had episodes of supraventricular tachycardia and rapid atrial flutter (ventricular rate 160–200 beats/min). He was volume resuscitated, and pharmacologic anti-arrhythmic therapy was initiated, but he was unable to maintain sinus rhythm. The initial diagnosis was "pneumonia," and he was started on a standard dose of ampicillin/sulbactam, vancomycin, and moxifloxacin.

He became profoundly hypoxic and was intubated on the following morning. Arterial blood gas analysis showed P_{aO_2}/F_{IO_2} of 76 mm Hg, and he was diagnosed with ARDS. Despite optimal ventilator support, he was unable to be adequately oxygenated, and was transferred to our hospital for further management. Upon arrival he was afebrile, in normal sinus rhythm (heart rate 80 beats/min), and his blood pressure was 111/50 mm Hg. His blood pressure dropped shortly after admission, and he required 0.5–1.3 μg/kg/min of phenylephrine to stabilize his hemodynamics. Physical exam was notable for massive edema and poor air movement. Chest x-ray revealed bilateral infiltrates (Fig. 1). He was placed on continuous mandatory

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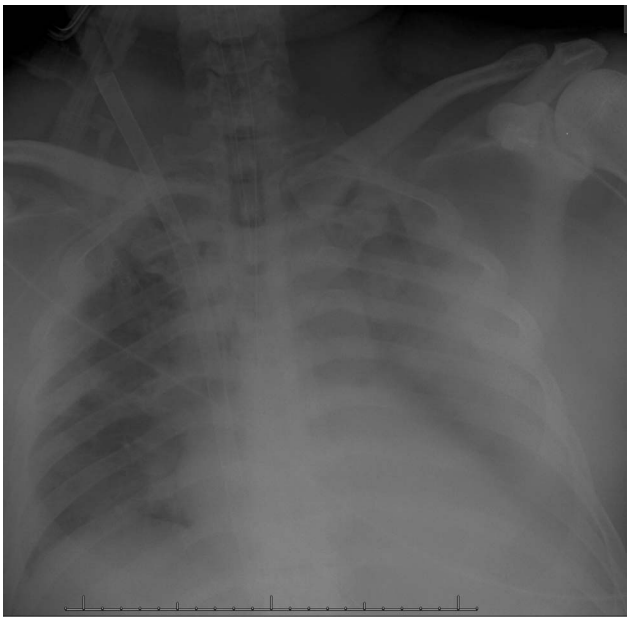

Fig. 1. Chest x-ray on admission shows bilateral infiltrates.

ventilation, an F_{IO_2} of 1.0, and PEEP of 15 cm H_2O. Arterial blood gas analysis found pH 7.26, P_{CO_2} 40 mm Hg, P_{aO_2} 67 mm Hg, base deficit 8.2 mEq/L, and arterial oxygen saturation 88%. The peak airway pressure was 36 cm H_2O. The Table shows the course of his laboratory values and ventilation modes. Urine toxicology screen test was negative. Echocardiography showed normal systolic and diastolic left and right ventricular function and no evidence of intra-cardiac shunt or valvular disease. Abdominal ultrasound was normal.

Due to profound hypoxia, VV-ECMO was initiated with a 27 French Avalon dual cannula (Avalon Laboratories, Rancho Dominguez, California). He was placed on low tidal volume (4–6 mL/kg ideal body weight) ventilation, based on the ARDS Network protocol,[2] and the plateau airway pressure was kept at 20–25 cm H_2O. His oxygenation was controlled with ECMO, aiming at upper extremity arterial saturation above 85%. Cerebral saturation was kept over 50%, measured via tissue oximetry (Fore-Sight, Casmed, Branford, Connecticut) to ensure cerebral perfusion.[3] The antibiotic regimen was changed to piperacillin/tazobactam, 3.375 g intravenous every 8 hours,

Table. Laboratory and Ventilation Values

	Admission at Outside Hospital	6 Hours After Intubation	Admission to Our Hospital	After Initiation of ECMO	After 3 Days of ECMO	1 Day After ECMO Decannulation	At Discharge
White blood cells, 1,000 cells/μL	12.5	8	10.8	12.2	25.6	14.7	16.8
Hemoglobin, g/dL	16.2	13.4	13.2	11.1	9.9	9.7	8.7
Hematocrit, %	45.7	39.5	40.7	34.6	29.5	27.9	26.5
Platelets, 1,000/μL	246	206	185	231	234	131	454
F_{IO_2} of ventilator	1.0	1.0	1.0	1.0	0.50	0.60	0.21
Ventilation mode	Non-rebreathing mask	CMV	CMV	CMV	CMV	CMV	Room air
PEEP	0	5	15	10	10	12	
F_{IO_2} of ECMO				1.0	0.60		
pH	7.56	7.37	7.26	7.39	7.38	7.39	
P_{CO_2}, mm Hg	25.5	40.7	40	44	48	43	
P_{O_2}, mm Hg	50	76	67	81	104	69	
HCO_3, mEq/L	23	23	18	26	28	26	
Base excess, mEq/L	3	–1	–8.2	1.8	3.1	1.3	
S_{pO_2}, %	91	93	88	96	98	93	98
Na, mEq/L	135	139	140	144	137	137	137
K, mEq/L	4	4.4	5.5	4.8	4.7	3.8	3.8
Cl, mEq/L	97	104	108	109	105	101	102
Blood urea nitrogen, mg/dL	20	27	49	52	23	39	35
Creatinine, mg/dL	1.57	2	3.8	4.1	2.7	2.4	2.2
Glucose, mg/dL	131	151	172	170	134	87	98
Total bilirubin, mg/dL	3.4	0.3	ND	0.4	0.7	1.3	0.9
Aspartate aminotransferase, IU/L	58	46	ND	2335	94	53	16
Alanine aminotransferase, IU/L	109	67	ND	1458	387	159	24
Lactate, mmol/L	1.9	0.7	2.2	2.3	1.0	1.2	

CMV = continuous mandatory ventilation
ECMO = veno-venous extracorporeal membrane oxygenation

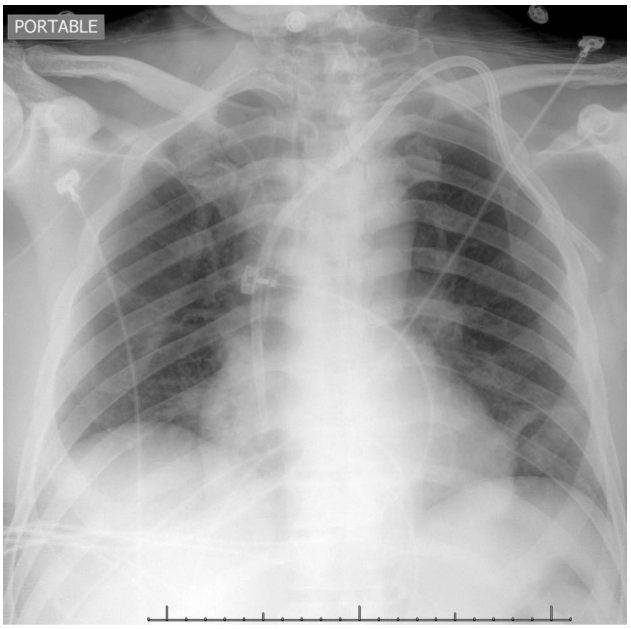

Fig. 2. Chest x-ray before discharge shows clear lung fields.

and moxifloxacin, 400 mg intravenous four times a day. He was oliguric and massively volume overloaded, and was diagnosed with acute kidney injury, and continuous veno-veno hemodialysis was initiated for fluid removal. Multiple cultures of blood, bronchial lavage fluid, and urine, including those from the outside hospital before antibiotic therapy was initiated, were negative, as were human immunodeficiency virus 1/2 antibody, virus polymerase chain reaction for influenza A, B/parainfluenza 1–3/rhinovirus/enterovirus/metapneumovirus/adenovirus/respiratory syncytial virus, hepatitis B surface antigen, hepatitis C antibody, and antigen tests for *Legionella pneumophila* and *Streptococcus pneumoniae*; thus antibiotics were discontinued on day 7.

His respiratory status and chest x-ray gradually improved (Fig. 2), and VV-ECMO was discontinued on day 7, at which time arterial blood analysis found pH 7.39, P_{CO_2} 43 mm Hg, P_{aO_2} 69 mm Hg, and arterial oxygen saturation 93%, while on continuous mandatory ventilation with F_{IO_2} 0.60, and PEEP 12 cm H_2O. He started to make urine, and continuous veno-venous hemodialysis was discontinued on day 9, and intermittent hemodialysis was discontinued on day 11.

During his hospital stay he had multiple episodes of supraventricular tachycardia and atrial flutter. A diltiazem/amiodarone protocol was initiated and intravenous metoprolol was given, but he failed to maintain sinus rhythm. Electrical cardioversion and adenosine were able to convert to sinus rhythm, but he soon returned to supraventricular tachycardia or atrial flutter. After his oxygenation improved, he was taken to the electrophysiology lab and cava tricuspid isthmus was ablated for atrial flutter. Afterwards, further electrophysiology studies were performed, but supraventricular tachycardia was not able to be induced, so no additional ablation was done. He was placed on oral amiodarone and diltiazem, and was able to maintain sinus rhythm afterwards. Tracheostomy was performed on day 20, due to ventilator dependence. He came off the ventilator on day 27. Nausea and vomiting persisted during the hospital stay, but resolved gradually. The tracheostomy was removed prior to discharge to home, on day 38.

Discussion

The use of AAS among professional athletes and bodybuilders has been reported since the 1950s.[4] Gradually it became more popular among recreational and non-professional bodybuilders. In the 1980s AAS gained popularity among young males to increase muscle mass and physical appearance.[5] Currently, AAS use has spread to casual fitness enthusiasts and sub-elite sportsmen and sportswomen, since AAS can be obtained via the Internet, without a prescription. It is estimated that there are 3 million AAS users in the United States, and the lifetime prevalence of AAS use is 0.9% in males and 0.1% in females in the general population.[5]

The medical effects of long-term AAS abuse are unclear. The known common side effects include acne, testicular atrophy, gynecomastia, and pain at the injection site. Erectile dysfunction and libido loss may also occur.[6] Nausea and vomiting, as seen in our patient, have been reported in several case reports.[6,7] The mechanism of the chronic nausea and vomiting can be related to hypercalcemia induced by the AAS,[8] but that was not seen in our patient. Other less common but severe side effects include cardiovascular complications, hepatic dysfunction, acute kidney injury, psychiatric disorders, reduction of thyroid hormone production, infertility, and immunomodulatory effects.[6,9] Mortality risk among chronic AAS users is estimated to be 4.6 times higher than that in the normal age-adjusted population.[4]

Herr et al reported a 30-year-old bodybuilder who developed ARDS secondary to sepsis from an abscess at the injection site.[10] Herr suggested that the long-term use of AAS caused immunosuppression and resulted in sepsis in an otherwise healthy patient. In our patient, despite extensive workup, the etiology of the ARDS remained unknown. One differential diagnosis was aspiration pneumonia caused by persistent nausea and vomiting. Elevated white blood cell count and procalcitonin suggested bacterial infection, but all the cultures were negative. Voigt et al reported that a respiratory syncytial virus infection resulted in ARDS in an adult patient with human immunodeficiency virus.[11] A viral infection may have been the cause of our patient's nausea, vomiting, and diarrhea prior to the hospital visit, and he may have had a micro-aspiration during those symp-

toms. It is possible that the combination of an undetected viral infection and aspiration caused sepsis that was worsened by the immunosuppressive effect of long-term AAS abuse, which led to ARDS. Injection of supraphysiologic concentrations of AAS suppresses natural killer cell activity and lymphocyte development into effector and memory cells, which decreases antibody sensitivity and secretion, resulting in immunosuppression.[9]

The treatment of ARDS consists of fluid management, lung-protective ventilation with low tidal volume and moderate PEEP, multi-organ support, and treatment of the underlying cause. ECMO is indicated for ARDS with severe hypoxemia ($P_{aO_2}/F_{IO_2} \leq 80$ mm Hg, despite high PEEP), uncompensated respiratory acidosis (pH $<$ 7.15, P_{aCO_2} $>$ 60 mm Hg), and/or unable to tolerate conventional mechanical ventilation.[12] The Avalon cannula is designed for VV-ECMO, drawing de-oxygenated blood from the superior/inferior vena cava and returning oxygenated blood toward the tricuspid valve. Contraindications to the Avalon cannula include intracardiac shunt and other general contraindications to ECMO, such as intracranial bleeding.

A few reports have shown a possible relationship between AAS use and altered cardiac electrical activity. Steroids may increase the rate of cardiac repolarization and shorten the QT interval.[1] Myocardial structural and molecular remodeling induced by AAS have also been reported, and can lead to severe atrial arrhythmia,[13] as observed in our patient. Other cardiovascular complications in AAS users are acute myocardial infarction related to premature atherosclerosis caused by increased low-density lipoprotein cholesterol and decreased high-density lipoprotein cholesterol.[4] There is an increased risk of arterial and pulmonary embolism, due to elevated hemoglobin level.[1] Additionally, impaired left-ventricular systolic and diastolic function may develop secondary to direct toxic effects on myocytes, endothelial cells, and/or increased collagen cross-links between myocytes. The mechanism of AAS-induced arrhythmia remains unknown.

Serum creatinine level is proportional to body muscle mass, and those who have well-developed musculature may have higher baseline serum creatinine, dependent on clearance. Acute kidney injury can be caused by dehydration and rhabdomyolysis caused by strenuous exercise; use of non-steroidal anti-inflammatory drugs to ease musculoskeletal pain caused by exercise; or use of diuretics to reduce weight, maintain muscular body habitus, or to clear banned substances.

Daher reported 2 cases of AAS-related interstitial nephritis causing acute kidney injury.[6] Habscheid and Yoshida separately reported a type of AAS (stanozolol) causing cholestasis that resulted in acute kidney injury in an otherwise healthy young male.[14,15] They thought that AAS abuse triggered cholestasis and jaundice, which subsequently decreased systemic vascular resistance and caused hypotension and hypoperfusion of the kidney, leading to acute kidney injury. In our patient the acute kidney injury may have been due to the combination of persistent hypoxia and septic condition.

Our patient's liver enzymes were only slightly elevated when he presented at the emergency room at the local hospital, but were elevated when he was transferred to our hospital. We believe this transient liver dysfunction was related to the combination of hypoxia and septic conditions, rather than direct toxicity from AAS. Although his echocardiography was normal, multiple episodes of supraventricular tachycardia, massive fluid resuscitation for low blood pressure, and acute kidney injury and low urine output may have resulted in fluid overload and hepatic congestion. His amino-terminal pro-brain natriuretic peptide was mildly elevated upon admission to the local hospital (917.8 pg/mL), and pleural effusion on ultrasound supports that hypothesis. However, it would be unusual if the cause of hypoxia were cardiogenic pulmonary edema, since he was rather dehydrated and hypovolemic when he arrived at the outside hospital, and echocardiography showed good left-ventricular function. The liver enzymes quickly improved after correction of the volume status and initiation of VV-ECMO and continuous veno-venous hemodialysis.

The relationship between AAS use and multi-organ dysfunction is not completely clear in our patient, but we believe that his long history of AAS abuse played a crucial role in causing the systemic inflammatory response and multiple-organ dysfunction in this otherwise healthy patient.

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