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CASE REPORT

Cholestatic Jaundice and IgA Nephropathy Induced by OTC Muscle Building Agent Superdrol

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Over the counter (OTC) medicines are commonly used in the United States despite a lack of scientific evidence for clinical utility and toxicity associated with their use. A case of jaundice and IgA nephropathy as a consequence of use of a muscle enhancing OTC supplement that was advertised as innocuous with no hormonal activity is described. IgA nephropathy has not been described previously in association with the use of testosterone. The case highlights that, besides adulteration, the misrepresentation of chemicals present in OTC medications and supplements can create confusion and a false sense of security with their use.

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INTRODUCTION

Various renal disorders including glomerulonephritis, cryoglobulinemia, polyarteritis nodosa, renal tubular acidosis, interstitial nephritis, renal papillary necrosis, nephrotic syndrome, acute tubular necrosis, and IgA nephropathy have been described in association with a variety of liver disorders (1). Specifically, IgA nephropathy has been reported in patients with alcoholic, viral, autoimmune, and α_1-antitrypsin related liver diseases (2). The use of testosterone has been reported to produce cholestatic jaundice that spontaneously resolves within a few weeks of its onset (3). Herein is reported a case of jaundice and IgA nephropathy in an individual who was using a muscle enhancing OTC supplement that was advertised as having no hormonal ingredients.

CASE REPORT

A 23-yr-old Hispanic male bodybuilder without any known past medical history presented at the Maricopa Medical Center (MMC) with a 2-wk complaint of nausea, vomiting, decreased appetite, jaundice, RUQ abdominal pain, pale stools, dark urine, and itching. Two months before the onset of his clinical symptoms, he had started using an OTC nutritional supplement for bodybuilders named anabolic extreme (superdrol) having methasteron as its active ingredient. He consumed 72 10-mg pills of superdrol, starting at one tablet daily for 2 wk followed by two tablets daily. He did not exceed the maximal suggested dose of 126 pills (10 mg each) that was recommended over a 6-wk period. He stopped using superdrol with the onset of diffuse skin itching. He did not report any history of alcohol, recreational drugs, or tobacco use. There was no family history of liver disease. He did not have any drug allergies.

On physical examination, his vital signs were stable. He was deeply icteric with several scratch marks noted throughout the trunk and lower extremities. He was overweight with a BMI of 28. The abdomen was slightly tender in the right upper quadrant with no evidence of ascites, hepatosplenomegaly, or a Murphy's sign.

At presentation, labs revealed a total bilirubin of 36.2 g/dL, an AST of 57 U/L, ALT of 93 U/L, alkaline phosphatase of 224 U/L, total protein of 9.1 g/dL (6.3–8.2), and IgG of 669 mg/dL (751—1,560). The hepatitis viral antibodies including HAV-IgM, HB core-IgM, HBS-AG, HBV core-AB IgG, HIV-1 AB, HDV-AG as well as HCV-RNA, and HBV-DNA by polymerase chain reaction were negative. The ceruloplasmin was 76 mg/dL. Smooth muscle, antinuclear, myeloperoxidase, and LKM antibodies were negative. Alpha-fetoprotein was normal. A hepatitis A IgG-AB was positive. A 24-h urinary copper was 166 μg/dL. A urinalysis did not reveal proteinuria or hematuria. The rest of his lab reports are summarized in Table.

The patient was hospitalized for one day and discharged on oral ursodeoxycholic acid at 600 mg twice daily and hydroxyzine at 25 mg three times daily to be used as needed for pruritus. Two weeks later, he presented to the hospital because of vomiting and unrelenting skin itching. He was hypertensive with a blood pressure of 189/86 mmHg, and the use of metoprolol at a dose of 50 mg twice daily normalized his blood pressure.

A liver biopsy showed features of marked intrahepatic cholestasis, mild portal inflammation consisting predominantly of lymphocytes, foci of lobular inflammation with balloon degeneration, mild Kupffer cell iron deposition and pericellular fibrosis. There was no evidence of granulomas, peliosis, hepatic rosettes, portal fibrosis, or bile duct injury (Fig. 1). The hepatic iron index was 1.19. An abdominal ultrasound showed mild liver enlargement at 18 cm. The

Table Laboratory Summary

Description	Bilirubin	AST	ALT	ALP	Creatinine	BUN	Hb	WBC
At the admission	36.2	57	93	224	1.7	21	13.7	6
Second hospital admission (2 wk later)	42	52	78	280	3.4	49	11.2	7.7
	40.3	46	57	216	3.2	41	9.3	6.4
	38.8	71	62	239	3.1	38	8.6	9.3
	37	45	70	218	2.9	36	9.2	8.5
	32.2	43	64	206	2.7	37	8.4	7.2
Third hospital admission (1 month later)	22.3	39	61	187	2.3	28	9.8	
	21.8	51	61	223	2.1	27	9.4	
Follow-up after discharge (6-wk since the 1st admission)	6.8	56	104	126	1.2	16	9.9	5.6

Normal values: Total bilirubin- 0.2–1.3 mg/dL; AST (serum aspartate aminotransferase) 17–59 U/L; ALT (serum alanine aminotransferase) 21–71 U/L; ALP (Alkaline phosphatase) 38–126 U/L, Creatinine-0.8–1.5 mg/dL; BUN-9-20 mg/dL, and ceruloplasmin-22–58 mg/dL, Hb (hemoglobin 14–17 g/dL) and WBC (white blood cells).

gallbladder and bile duct were normal. The kidneys were slightly echogenic. The CT scan of the abdomen with IV and oral contrast did not show any liver lesion, ascites, or biliary obstruction. A kidney biopsy showed interstitial edema containing a mild lymphohistiocytic infiltrate with numerous esoinophils. An immunofluoresecence stain showed diffuse granular mesangial staining for IgA (2+) (Fig. 2). After 1 wk of hospitalization, the patient was discharged and readmitted 4 days later because of rectal bleeding and a hemoglobin level of 7.9 gm/dL with an MCV of 89 fL. The upper and lower gastrointestinal endoscopies did not reveal any varices. After receiving 2 units of packed red blood cells, his hemoglobin increased to 9.4 g/dL and he was discharged home. Two wk later, he followed up in the outpatient clinic, feeling better without any itching and near-normalization of his lab reports including both kidney and liver function.

DISCUSSION

Anabolic extreme is a nutritional OTC supplement manufactured for bodybuilders by Befit Health & Fitness (BHF). It is a conglomerate of eight products including superdrol and is available OTC as well as on the Internet. All products are advertised to have varied affects on enhancing muscle strength. Anabolic extreme-superdrol, which was self-administered by the reported patient, has an active ingredient methasteron. This product is advertised on the Internet as "definitely not a pro-hormone . . . it is a very active form of a designer supplement that is also highly anabolic . . . It will give you dramatic and immediate gain in size and strength, significantly improve endurance and has zero estrogen conversion" (4). There is no mention of side effects associated with superdrol either on the bottle label or on the Internet. The chemical structure of superdrol, however, resembles 17α-alkylated anabolic-androgenic steroids (AAS) such as methyltestosterone (Fig. 3). Based on telephone contact and Internet search, no reports of anabolic extreme induced toxicity could be found reported to the FDA.

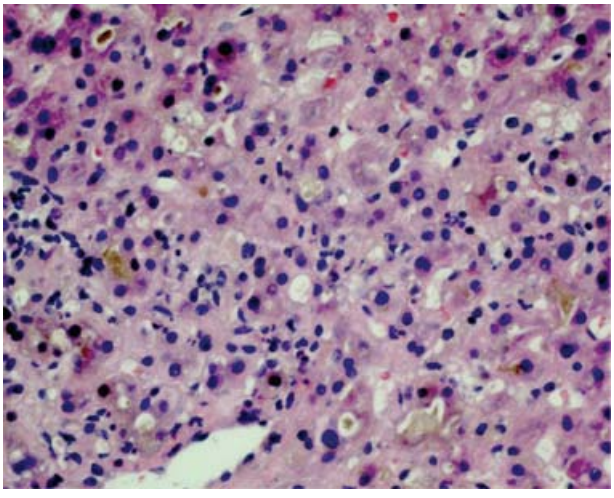

Figure 1. Liver biopsy-–marked cholestasis with mild inflammatory infiltrate. ×400.

Despite numerous reports of toxicity and a lack of scientific evidence for therapeutic efficacy of natural remedies, Americans spend more than $27 billion annually on complementary and alternative medicine (CAM) (5). Individuals who seek CAM are either frustrated with traditional medicine or believe that CAM is innocuous and experiment with such agents in order to find out if they are right for them (6). In order to achieve a particular body image, professionals and amateurs both have been widely reported to use AAS through the black market, health clubs, or Internet (7).

AAS are derivatives of testosterone that can impair hepatic excretory functions by interfering with both the bile salt-dependent and bile salt-independent bile flow. Although AAS with predominant anabolic or androgenic affects have been described, there is an overlap between various activities of AAS (7). The hepatotoxicity of AAS typically manifests as cholestatic jaundice, although a predominant hepatocellular toxicity (3) and peliosis hepatic have been also published (8). Liver biopsy features of AAS-associated jaundice typically show a normal hepatic parenchyma and marked intrahepatic cholestasis as seen in the described patient. Occasionally, mild hepatic parenchymal injury with sinusoidal acidophilic bodies and small foci of necrosis are also noted. The prognosis for complete recovery from AAS-induced jaundice is

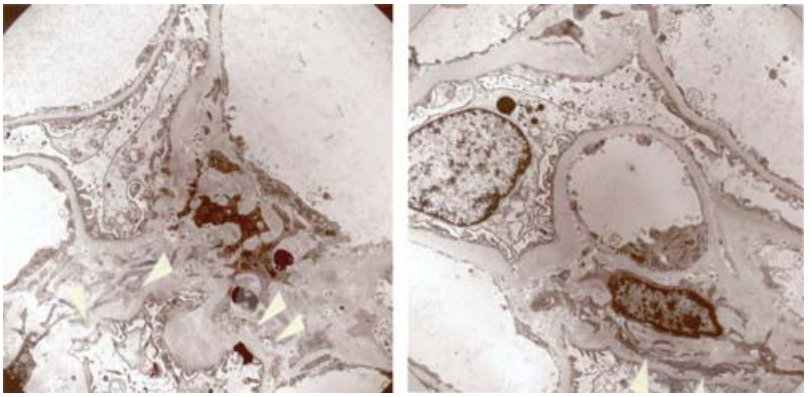

Figure 2. Electron microscopy of kidney showing mesangial IgA deposits—see arrows.

excellent for anicteric patients and hepatic function promptly returns to normal on cessation of the drug. The resolution of jaundice occurs in icteric patients as well although it can take up to several months (9–11).

Because of ongoing worsening of renal function that did not correct with intravenous hydration, the reported patient underwent a kidney biopsy that showed IgA nephropathy and interstitial nephritis. On a Medline search, no reports of testosterone-induced intersitital nephritis or IgA nephropathy were found. IgA nephropathy is a kidney disorder characterized by a predominant IgA deposition in the glomerular mesangium. Interestingly, IgA nephropathy has been associated with many liver diseases including alcoholic liver disease, viral hepatitis A, B, and C, alpha-1-antitrypsin deficiency, autoimmune hepatitis, Alagille syndrome, as well as liver cirrhosis (2, 12, 13). Other causes of IgA mesangial deposits include familial, HIV infection, and gluten entheropathy (14).

The reported patient was not rechallenged with superdrol because it could not be ethically justified. Although, the occurrence of IgA nephropathy with the use of superdrol may be purely coincidental, the temporal association of the onset of jaundice and IgA nephropathy with the consumption of superdrol implies that the association is more than casual. Because there have been no reports of renal toxicity associated with the use of testosterone, we speculate that IgA nephropathy most likely occurred secondary to hepatic dysfunction and resultant hypergammglobulinemia induced by superdrol. The reported patient presents a unique case of severe intrahepatic cholestasis with a peak bilirubin level of 42 mg/dL and renal failure related to IgA nephropathy and acute interstitial nephritis that occurred as a consequence of an OTC bodybuilding supplement. The case highlights that because of a lack of governmental control in the manufacture, distribution, and advertisement of OTC medications, misrepresentation of ingredients present in such remedies is possible and policies for regulation of OTC/CAM must be reviewed.

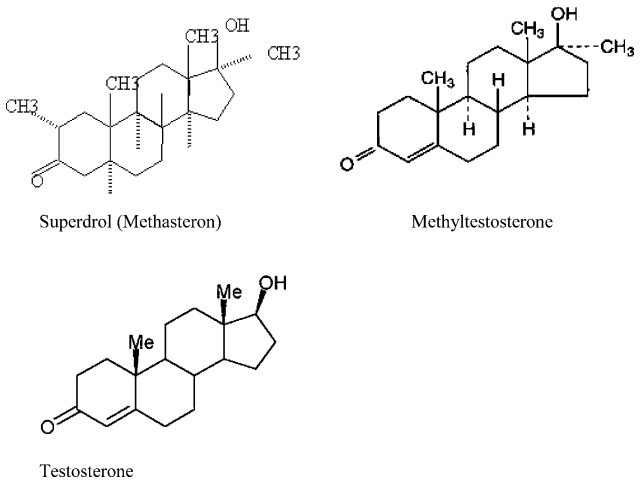

Figure 3. Structure of superdrol compared to testosterone.

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