Stanozolol-induced bland cholestasis

Colestasis canalicular inducida por estanozolol

Sr. Director:

It is difficult to estimate the prevalence of toxic hepatitis, especially by anabolic-steroids, because frequently they are taken without medical prescription. The use of anabolic-steroids by sportsmen and teenagers has dramatically increased, raising the question about their adverse effects, especially hepatotoxicity. The hepatotoxic effects include cholestasis, hepatocellular carcinoma, nodular regenerative hyperplasia and variceal bleeding, secondary to portal hypertension presumably due to nodular regenerative hyperplasia. Stanozolol is a 17α-alkyl anabolic-androgenic steroid, which is used in therapeutic doses for some medical indications such as hereditary angioedema or aplastic anemia, but its use is extended among sportsmen and bodybuilders. The effect of this drug is dose-dependent, although it is influenced by individual susceptibility and the presence of other toxic habits, such as alcohol abuse.

We report the case of a 37-year-old European Caucasian man, who was admitted to our hospital after developing acute severe jaundice and itching, but without fever or chill. Furthermore, he reported passing dark urine simultaneously. He did not have problems such as abdominal pain, nausea or vomiting. There was no history of pre-existing liver disease. Furthermore, he denied unsafe sexual practices, drug abuse or other toxic habits (except smoking twenty cigarettes a day). However, he ingested a protein-enriched diet for two years to increase the muscle mass. The patient did not take other medications.

On admission, physical examination revealed jaundice. The biochemical test showed serum levels of bilirubin of 19.16 mg/dL (normally <1) (direct fraction 15.84 mg/dL), with aspartate aminotransferase (AST) 45 U/L (normally 5–37), alanine aminotransferase (ALT) 58 U/L (normally 5–41), alkaline phosphatase (AP) 152 U/L (normally 40–129) and gamma-glutamyl-transpeptidase (GGT) 19 U/L (normally 10–66). Other biochemical parameters such as creatinine, C reactive protein, sodium and potassium remained normal. Hemoglobin, leucocytes, platelet count and prothrombin time were normal as well. The presence of viral infection (hepatitis A, hepatitis B, hepatitis C, cytomegalovirus, Epstein–Barr virus and HIV) and autoantibodies (including anti-mitochondrial antibody, anti-smooth muscle antibody, liver kidney microsomal type 1 antibody and antinuclear antibodies) was excluded. An ultrasound scan of the abdomen was performed, showing a normal volume of the liver and no evidence of biliary dilatation. During admission, he admitted to have self-administered high doses of stanozolol (Winstrol®) by injections (intramuscularly, three times a week) for three weeks prior to the onset of symptoms. After that, we thought of a toxic hepatitis so we used the CIOMS scale resulting in 9 points, supporting our impression. Thus, we decided not to perform a liver biopsy. Accordingly, during admission the patient was provided with supportive medical treatment and showed a good progress.

Eight weeks after discontinuation of stanozolol, biochemical tests gradually improved, itching disappeared and he was completely asymptomatic. Finally, in three months, all tests were normal. Therefore, clinical signs and laboratory findings improved substantially in following weeks after discontinuation of stanozolol.

Discussion

Our patient developed severe cholestatic jaundice with a slight elevation of liver enzymes and itching, after self-administration of stanozolol injections. The patient mentioned that he went to the gym and ingested a protein-enriched diet to increase the muscular strength but, at the beginning, he did not recognize to take steroids, which delayed the diagnosis. The temporal relationship between the administration and the appearance of symptoms, and the return to normal values after drug withdrawal, clearly suggest the association. CIOMS scale is validated to find out the relationship between drugs and toxic hepatitis, being highly probable values over 8 points (our patient scored 9 points). CIOMS scale has the following elements: type of liver injury, time of onset of the event, time from drug intake, until reaction onset, time from drug withdrawal until reaction onset, risk factors, and course of reaction. Finally, we considered that the liver biopsy was not necessary due to three reasons: (a) the temporal relationship; (b) the CIOMS scale score; and (c) exclusion of other causes.

Bland cholestasis is almost always associated with the use of 17α-alkyl anabolic-androgenic steroids. The course of illness is marked by an insidious onset of itching followed by dark urine and jaundice, with minimal serum enzyme elevations or evidence of hepatocellular necrosis (ALT levels are usually <200 U/L, AP <230 U/L). Typically, bland cholestasis shows a slow recovery (usually, more than 4 weeks).
The mechanism most likely involves interference with hepatocyte canalicular efflux systems for bile salts, organic anions and phospholipids. Furthermore, flow cytometric analysis demonstrated an increase in the S-phase fraction of liver cells. Especially, stanozolol has been found to induce oxidative stress in rat liver despite the up-regulation of enzymatic antioxidant activities.

In conclusion, sportsmen, especially bodybuilders, taking anabolic androgenic steroids, even for a short period of time, should be considered as a group at risk for developing severe cholestatic jaundice.

Bibliografía


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