Title: Hepatocellular carcinoma: an unexpected consequence of anabolic steroid misuse

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Background: Anabolic androgenic steroids (AAS) are well known to cause drug-induced liver injury, primarily in a cholestatic pattern. Other patterns of injury include peliosis hepatis, nodular regenerative hyperplasia as well as development of hepatocellular adenomas. Malignant transformation into hepatocellular carcinoma (HCC) is relatively rare and an unexpected event. These tumors are thought be well-differentiated and have a better prognosis compared to HCC arising in other etiologies of liver disease.

Case Presentation: A thirty two-year old male, professional bodybuilder, presented to the emergency room with severe right upper quadrant pain. He had been taking AAS as well as D-BOL (methadrostenol), a nutritional testosterone supplement marketed for bodybuilding purposes for four years. He stopped using both a month prior when routine blood tests revealed elevated liver enzymes. Patient had no known liver disease and no clear risk factors for it. Physical examination was unrevealing including absence of hepatomegaly or stigmata of chronic liver disease. Laboratory evaluation revealed ALT 46 IU/l, AST 101 IU/l, alkaline phosphatase 41 IU/l, and total bilirubin 1.2 µmol/l. Tumor markers were within normal limits (alpha-fetoprotein level of 1.3 ng/ml and a carcinoembryonic antigen level of 0.9 ng/ml). CT scan of the abdomen showed a large complex indeterminate mass in the left hepatic lobe and subtle nodular foci in the right hepatic lobe. Magnetic resonance imaging of the abdomen confirmed 5 dominant, LI-RADS 5 lesions with arterial enhancement and washout as well as numerous arterially hyper-enhancing lesions with variable washout throughout the liver. A core needle biopsy of a dominant segment 4 lesion initially favored hepatic adenoma, showing hepatocellular proliferation with patchy necrosis, with liver plates 1-2 cells in thickness. Additional immunohistochemical stains established the diagnosis of well-differentiated, beta-catenin, CK-7, and CD-34 positive, hepatocellular carcinoma. Given the biopsy findings and the extent of multifocal lesions, the patient was evaluated for liver transplantation per tumor board recommendations. Patient underwent transarterial chemoembolization as a bridge to liver transplantation and is currently undergoing phase II liver transplant evaluation.

Discussion: Having high first-pass in the liver, AAS have been associated with cases of liver damage and reported to induce significant intrahepatic structural changes [1]. It is postulated that uncontrolled hepatocyte cell growth and development driven by upregulation of androgen receptors is the likely cause of nodular regeneration and hepatic tumor formation [1]. Both beta-catenin and human telomerase reverse transcriptase mutations have been implicated in the transformation of hepatic adenomas to hepatocellular carcinomas[2]. Malignant transformation may occur in 4.5-9% of cases [3]. Given widespread use of AAS in the bodybuilding community many patients are potentially at risk for development of drug-induced liver injury and potentially HCC.

Conclusion: Our case highlights the risk of developing HCC in patients with no known risk factors for liver disease except for AAS use, highlighting the need to raise awareness of its potentially fatal adverse effect in the medical and bodybuilding communities.

Source Cited:

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3. Stoot JH, Coelen RJ, De Jong MC, Dejong CH. Malignant transformation of hepatocellular adenomas into hepatocellular carcinomas: a systematic review including more than 1600 adenoma cases. HpB (Oxford). 2010; 12(8):509-22