Liver Cirrhosis From Chronic Hypervitaminosis A Resulting in Liver Transplantation: A Case Report

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ABSTRACT

Herein we report a case of liver dysfunction caused by consumption of vitamin A supplements leading to liver transplantation. The patient was a 48-year-old male with a medical history of congenital ichthyosiform erythroderma in treatment with vitamin A until 12 years of age, at which point he discontinued the supplements because he had developed ascites. Liver cirrhosis was diagnosed as secondary to hypervitaminosis A on the basis of histologic examination of liver biopsy and the absence of other potential causes of chronic liver disease. Despite interruption of administration of vitamin A, the patient continued to deteriorate over the years, with development of portal hypertension signs. His medical conditions were aggravated with the development of hepatic insufficiency manifested by refractory ascites, renal insufficiency, and severe encephalopathy and he underwent orthotopic liver transplantation, followed by disappearance of all signs of portal hypertension. This case highlights the need to take a careful history of consumption of vitamin A when evaluating a patient with liver failure.

THE DIAGNOSIS of hepatic injury from chronic hypervitaminosis A is rare, likely often overlooked because of the variable clinical signs and symptoms, and it relies mainly on expert liver biopsy assessment. The spectrum of liver damage related to hypervitaminosis A ranges from noncirrhotic portal hypertension to varied degrees of fibrosis or even cirrhosis. Although most cases of toxicity are self-limiting and resolve after discontinuation of the drug, cases of fulminant hepatic failure resulting in death or liver transplantation have been reported in the literature.

CASE REPORT

We present the case of a 48-year-old male with a medical history of congenital ichthyosiform erythroderma who had been in treatment with oral corticosteroids and vitamin A until 12 years of age, when he discontinued the vitamin A supplementation due to development of ascites without other signs of hepatic dysfunction. At that time, blood work showed moderate elevation of transaminase levels and slight anicteric cholestasis. Viral serology for hepatitis A, B, and C and toxicology screenings were all negative. An abdominal Doppler ultrasond and a computed tomography scan showed ascites without other pathologic findings. Finally, hepatic cirrhosis secondary to hypervitaminosis A was diagnosed by a laparoscopic liver biopsy, after dismissing other causes of cirrhosis. Questioning revealed that the patient had, until 12 years of age, ingested large doses of vitamin A, as prescribed by his dermatologist for treatment of congenital ichthyosiform erythroderma. Despite the long period of discontinuation of vitamin A, the patient continued to deteriorate over the years, with development of portal hypertension signs that had required multiple hospital admissions due to complications (upper gastrointestinal bleeding secondary to esophageal varices treated with sclerotherapy, gastropathy of portal hypertension, refractory ascites, hypersplenism with severe thrombocytopenia that required splenic embolization, and hepatic encephalopathy) (Fig 1).

Due to a worsening of hepatic insufficiency manifested by refractory ascites, renal insufficiency, and severe hepatic encephalopathy, the patient underwent orthotopic liver transplantation with a Modified End-stage Liver Disease (MELD) score of 27 and a Child-Pugh score of C11. He recovered from all symptoms after the transplant. The hepatectomy sample demonstrated presence of septal fibrosis, ectasia,

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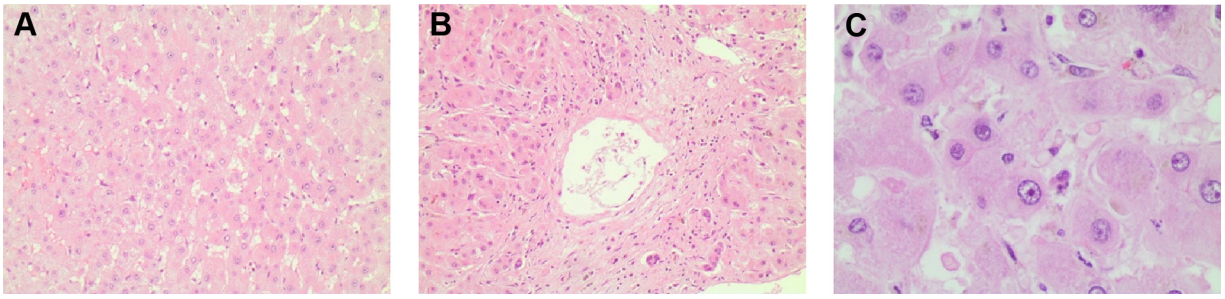

Fig 1. Results of liver biopsy obtained before liver transplantation. **(A)** Ectasia and sinusoidal dilation. **(B)** Perivenular fibrosis. **(C)** Stellate cell hyperplasia and hypertrophy.

sinusoidal dilation, stellate cell hyperplasia and hypertrophy, and perivenular fibrosis, all consistent with vitamin A toxicity (Fig 1). The postoperative course was uneventful and a liver biopsy at 3 months showed no evidence of recurrence of disease.

DISCUSSION

The liver is the main storage site for vitamin A, but signs of toxicity from chronic hypervitaminosis A are most frequently in extrahepatic tissues. Toxicity in adults is most commonly manifested by dry, fissured skin, brittle nails, hair loss, gingivitis, anorexia, and fatigue. However, there is evidence that long-term ingestion of large doses of vitamin A may be lead to complications, possibly even hepatic fibrosis, obstruction of portal blood flow, impaired hepatic function, and development of ascites and portal hypertension [1]. The primary indication for prescription of vitamin A is dermatologic, as a treatment for a wide variety of conditions such as acne, pityriasus rubra pilaris, nonspecific skin eruption, ichthyosis, and dry skin [2]. The diagnosis of hypervitaminosis A is usually based on a history of vitamin A intake, absence of any other detectable causes of chronic liver disease, and the demonstration at liver biopsy of stellate cell hyperplasia and hypertrophy [3]. Stellate cells, also known as Ito cells, are located in the space of Disse, under the endothelial cell layer, and contain vitamin A–rich lipid droplets. In addition, these cell express α-smooth muscle actin. In the chronically diseased liver, the stellate cell differentiates into a myofibroblastlike cell with high fibrogenic capacity due to production of a large amount of extracellular matrix.

In vitamin A intoxication, hypertrophy and proliferation of stellate and myofibroblastlike cells may lead to noncirrhotic portal hypertension, fibrosis, and cirrhosis [4]. There was a significant positive correlation between the severity of perisinusoidal fibrosis and the daily consumption of vitamin A suggesting the existence of a dose-effect relationship [5]. Vitamin A is transported in plasma as unesterified free alcohol, retinol, which is bound to a specific carrier protein, retinol-binding protein. This protein may not only regulate the supply of retinol to tissues but can also protect tissues against the surface-active properties of the vitamin [6]. Currently, there is no noninvasive marker available for the assessment of vitamin A excess. Serum retinol is likely a better biomarker of vitamin A deficiency rather than excess. Although serum retinol elevations may reflect increased hepatic stores, the threshold value to indicate elevated hepatic stores remains unknown [7]. Most cases signs of portal hypertension disappear after the withdrawal of vitamin A. If hepatic decompensation occurs despite cessation of the medication, liver transplantation can be considered as an option [8].

CONCLUSION

Chronic vitamin A consumption may represent a rare but well-described cause of chronic liver disease and is likely often overlooked because the diagnosis mainly relies on expert liver biopsy assessment. Prescription of vitamin A for treatment of benign conditions should be for only for limited periods and under close medical supervision, because hipervitaminosis A–related liver toxicity may be severe and can lead to liver injury, ranging from stellate cell hyperplasia and hypertrophy-induced portal hypertension to varied degrees of fibrosis and noncirrhotic portal hypertension as well as cirrhosis. Thus, we have highlighted the importance of obtaining a detailed history of dietary supplement intake when evaluating a patient presenting with liver dysfunction with unknown causes of chronic liver disease.

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