

Possible Aggravation of Hepatitis A by Acitretin

Sir,

Transient, mild changes in liver function tests have been reported in some patients during treatment with the aromatic retinoid etretinate (1, 2). Nevertheless, prospective (3) as well as retrospective studies (1, 4) have failed to demonstrate chronic liver injury on biopsy in the majority of patients, even after long-term administration of etretinate. In a few patients with significant hepatotoxicity, acute, potentially reversible as well as chronic progressive forms of liver injury have, however, been reported after treatment with either etretinate (5 and references therein) or its active metabolite acitretin (6-8).

We here report a case with severe acute liver injury and concomitant hepatitis A infection that is possibly related to acitretin therapy. A 49-year-old man with early eczematous mycosis fungoides was started on ultraviolet-A phototherapy in

combination with acitretin on September 3, 1993. The dose of acitretin was increased from a starting dose of 10 mg by 10 mg weekly, up to 30 mg/day. Pretreatment blood chemistries were normal. After one month of treatment, there was a slight increase in liver enzymes. At the same time, the patient noted a gradual increase of fatigue, intermittent nausea, decreased appetite, diarrhea and acholic stools. He denied the use of any other drugs or significant alcohol ingestion. There was a past history of hepatitis B infection in 1970, with chronic active hepatitis over 5 years, and mild associated hepatic steatosis. Fever (39°C) and a further increase in liver enzymes prompted hospital admission on October 20, 1993, and discontinuation of acitretin therapy. On physical examination, the patient exhibited marked scleral icterus, palmar erythema, hepatosplenomegaly and abdominal pain. Hepatomegaly (16 cm) and splenomegaly

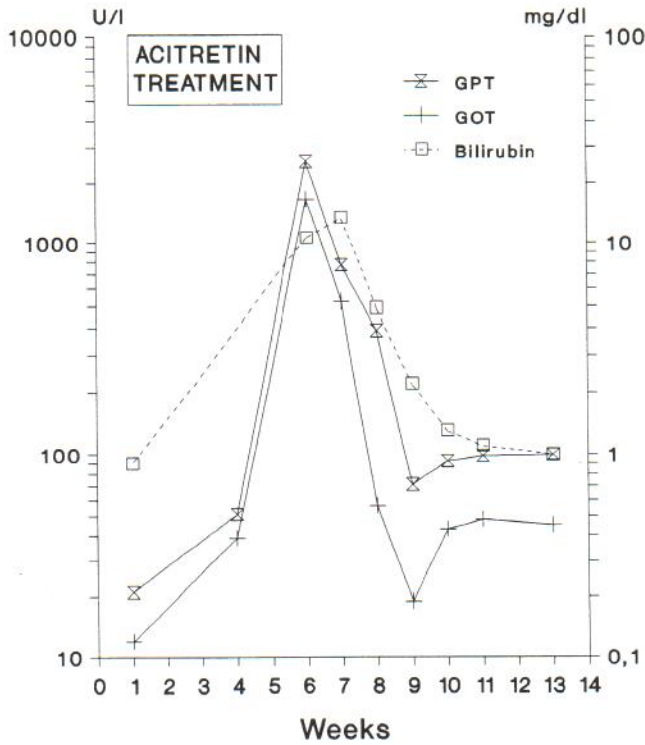


Fig 1.

(10×11.5×4) were confirmed by ultrasound. There were no signs of cholestasis. The patient refused a liver biopsy.

Laboratory values showed a marked elevation of liver enzymes. Details of the most important liver function tests over the course of the disease are shown in Fig. 1. The prothrombin time was decreased by 50%, whereas partial thromboplastin and alkaline phosphatase were normal. The complete blood cell count was within normal limits. Serologic studies showed elevated levels of IgM for hepatitis A virus and anti-Hb_c. Values for HB_sAg, anti-HB_s, anti-HIV, antimitochondrial and antinuclear antibodies were negative. The abnormal enzyme levels began to decrease within 48 h after discontinuation of acitretin, the patient's symptoms improved rapidly, and he became afebrile. His liver enzymes gradually subsided but were still slightly elevated during the subsequent months.

This case report describes for the first time an aggravated course of hepatitis A infection in association with acitretin therapy. Only one case of acute hepatitis in a patient receiving etretinate and hepatitis B vaccinations has been reported previ-

ously (9). The mechanisms of liver damage in our patient remain elusive. Whether the severe clinical picture of this patient was acitretin-induced and complicated by viral hepatitis or simply due to the viral infection cannot be proven. Rechallenge with acitretin was considered too risky because of the severity of the patient's jaundice and liver damage. An abnormal or unusual metabolic transformation of acitretin in the course of acute viral hepatitis remains a possible causative factor. Since all hepatitis parameters rapidly improved after discontinuation of treatment, and since hepatitis A infections usually take a mild or even inapparent course, we believe that the present case possibly represents acitretin-related hepatic damage.

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