

## Fulminant hepatitis during self-medication with conjugated linoleic acid

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### ABSTRACT

The present report describes a 63-year-old female who presented with fulminant hepatic failure requiring liver transplantation caused by a weight loss dietary supplement containing conjugated linoleic acid (CLA). Thorough investigation, including liver biopsy, revealed no other cause of hepatotoxicity. In the last few years, a considerable number of reports have been published on toxic hepatitis, associated with non-conventional products, attributed with weight-reducing properties. We emphasize the importance of taking a cautious approach when consuming herbal supplements for the purpose of weight loss, as all that is "natural" may not always be healthy. Only one report of CLA-induced toxic hepatitis is related in the medical literature.

**Key words.** Conjugated linoleic acid. Toxic hepatitis. Fulminant hepatitis. Liver transplantation.

### INTRODUCTION

Drugs are an important cause of liver injury. Drug-induced liver injury remains an important clinical concern, accounting for 4 to 10% of all adverse drug reactions.<sup>1</sup> More than 900 drugs, toxins, and herbs have been reported to cause liver injury, and drugs account for 20-40% of all instances of fulminant hepatic failure.<sup>2</sup> Approximately 75% of the idiosyncratic drug reactions result in liver transplantation or death.<sup>3</sup>

Dietary supplement use has become increasingly common. An estimated 83 million Americans report using alternative medical therapies, including herbal and dietary supplements.<sup>4</sup> People believe that natural remedies are free of adverse effects but some supplements are known to be associated with severe hepatotoxicity.<sup>4</sup>

The use of CLA as a weight loss supplement has increased in Europe and USA in last years. CLA refers to a group of positional and geometric isomers of linoleic acid that are characterized by the presen-

ce of conjugated dienes. In nature, the most abundant CLA isomer is *cis*-9, *trans*-11 (*c9*, *t11*), whereas in supplement forms CLA is typically sold as an equal mix of the two predominant isomers *c9*, *t11* and *t10*, *c12*. Different isomers may have different effects. The effects of CLA on lipid metabolism are not yet clear and the efficacy of CLA on maintenance or achievement of a normal body weight in humans is not proven.<sup>5</sup> Possible adverse effects of CLA may be related with lipid peroxidation induction, resulting in cell damage.<sup>6</sup>

Drug-related hepatitis secondary to CLA has been previously reported in a single case worldwide.<sup>7</sup> We report the second case of CLA induced-hepatotoxicity, this one needing hepatic transplantation.

### CASE REPORT

A 63-year-old female patient was hospitalized with complaints of anorexia, nausea, jaundice and cholelithiasis, of 3 weeks duration.

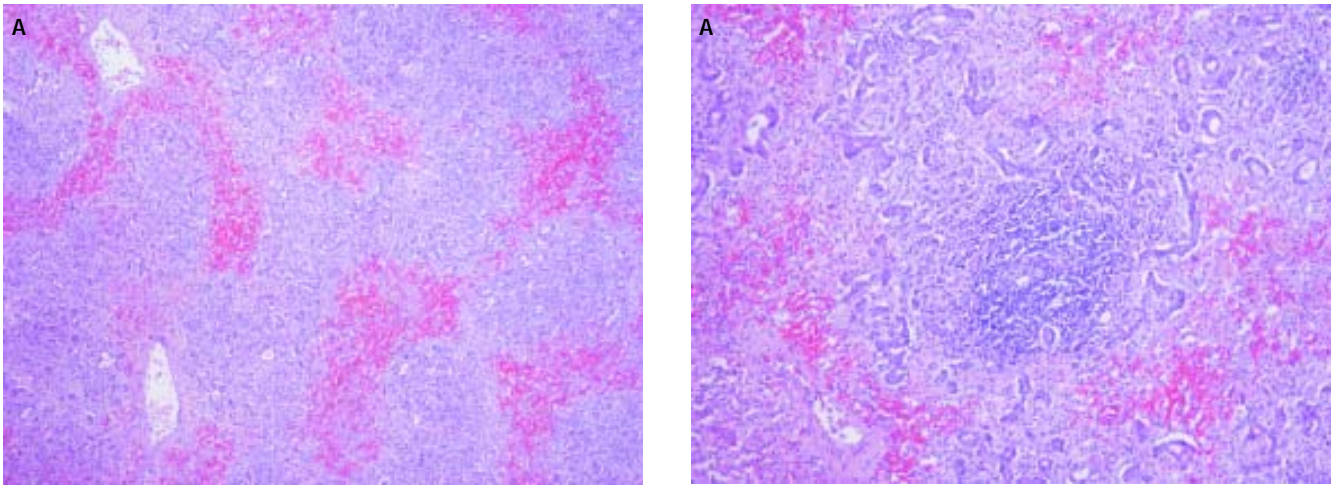
She had started CLA therapy for body fat reduction, nearly one month before, not associated with other drugs or herbal remedies. This was a purely CLA pills, containing glycerol, gelatin and water as its component parts.

The patient had no exposure to other possible hepatotoxic agents during that period, and her past medical history was no remarkable.

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*Figure 1. Biopsy shows massive hepatic necrosis suggesting toxic liver damage.*

On examination she was conscious and icteric, without hepatomegaly or stigmata of chronic liver disease.

At the time of admission routine liver enzyme tests revealed:

- Alanine aminotransferase-2,300 U/L (normal 35 U/L).
- Aspartate aminotransferase-1,100 U/L (normal 41 U/L).
- Alkaline phosphatase-255 U/L (normal 104 U/L).
- $\gamma$ -glutamyl transferase-142 U/L (normal < 50 U/L).
- Total serum bilirubin-26 mg/dL (normal < 1.2 mg/dL).
- Conjugated bilirubin-21mg/dL (normal < 0.3 mg/dL).

The prothrombin time was 19.3 seg (INR 1.65).

The cell blood count, albumin and factor V were normal, and there was no eosinophilia.

Tests for acute viral hepatitis (A, B and C), autoimmune hepatitis, hemochromatosis,  $\alpha$  1-antitrypsin deficiency, Wilson's disease, and  $\alpha$ -fetoprotein were all negative.

Abdominal ultrasonography and CT scan revealed a normal liver structure, intrahepatic bile ducts, and gallbladder.

Given the time course of starting CLA and the development of abnormal liver tests, the presumptive diagnosis of toxic hepatitis was made.

The patient experienced an unstable clinical course during the first week of hospital admission. She developed hepatic encephalopathy and worsening of cholestasis. The prothrombin time was progressive-

ly increasing. Factor V remained in normal range. No liver biopsy was performed because clotting disturbance did not allow a percutaneous approach and transjugular biopsy was not available. The patient fulfilled the King's College Hospital Criteria for Liver Transplantation in fulminant hepatic failure and liver transplantation was performed. Microscopic features of the disease liver showed hepatic parenchyma with extensive haemorrhagic and necrotic areas; mixed septal mononuclear cell infiltration; massive hepatic necrosis suggesting toxic liver damage (Figure 1).

A full recovery occurred in this patient and she was discharged three weeks after liver transplantation maintaining periodic follow-up at Hepatology Department.

## DISCUSSION

We present a case of toxic hepatitis associated with CLA ingestion. To the best of our knowledge, this is the second case report of hepatotoxicity caused by this supplement. A MEDLINE search of adverse reactions to CLA retrieved one other case reported in Portugal, but with recovery after discontinuation of the CLA take.

The diagnosis of acute CLA-related hepatitis was based on the patient's history, clinical picture, abnormal results of liver function tests, exclusion of other causes of acute hepatocellular necrosis, the time association between the ingestion of the CLA and the onset of symptoms. There was no previous history of liver disease or of alcohol abuse, and the serological markers of viral and autoimmune hepatitis were negative. Abdominal ultrasound and CT

scan showed no evidence of other hepatic lesions. The absence of systemic disease findings or a previous history of heart failure or hypotension excluded other causes of liver damage. Other toxic agents were ruled out, and histological findings were concordant with toxic hepatitis. Causality of toxic liver injury was assessed using the CIOMS/RUCAM scale, yielding a score of 6 (probable).<sup>8</sup>

This case highlights the importance of a thorough clinical history that considers alternative medicines, herbal remedies and unconventional diets.

Physicians need to be more familiar with weight loss supplements and recognize those that are potentially harmful. It is important that such severe reactions are reported to the relevant licensing authorities. Consequently, it also raises questions regarding the regulation, licensing and safety of herbal and alternative health products.

#### ABBREVIATIONS

- CLA: Conjugated linoleic acid.
- CT scan: Computed tomography scan.
- CIOMS: Council for international organizations of medical sciences.
- RUCAM: Roussel Uclaf Causality Assessment Method.

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