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CASE REPORT

Toxic hepatitis due to a food supplement: ''Natural'' is no synonym for ''harmless''

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Summary
Background/aims: Herbal products are increasingly used in modern medicine for numerous indications. They are not considered as drugs and thus often not linked to side effects.
Material: A 77-year-old patient presented with silent icterus and biochemical evidence of hepatocellular damage. Because of dyslipidaemia, he was recently prescribed Controchol®, a food supplement containing red yeast and green tea extracts.
Results: Liver biopsy showed necro-inflammatory destruction of liver parenchym, collapse of reticulin matrix, cholestasis and gall duct damage, compatible with toxic hepatitis. After discontinuation of Controchol®, there was a gradual normalisation of the liver function tests. Liver injury is a known side effect of both red yeast and green tea extracts. After exclusion of other causes, we therefore concluded our patient had suffered from Controchol®-induced toxic hepatitis.
Conclusion: Products that are conceived as ''natural'' alternatives for pharmacological drugs, like food supplements, are not free of side effects per se, and should not be considered as ''harmless''.

Introduction

One of the independent risk factors for cardiovascular disease, being the number one cause of death globally, is dyslipidaemia. Depending on the individual cardiovascular risk profile, drug therapy, in addition to lifestyle changes, is

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necessary in the management of a lipid disequilibrium. While the array of pharmacological options expands, statins are still most frequently used to tackle hypercholesterolaemia in primary and secondary prevention of cardiovascular disease [1]. The elevation of hepatic transaminases is a well-known side effect of statin therapy, although the risk appears to be relatively low (0—3%), and progression to liver failure uncommon, even in patients with underlying liver disease [2]. In this modern era of unlimited information and mistrust of the pharmaceutical industry, patients and medical practitioners are looking for ''natural alternatives'' for conventional drugs. These products are often not perceived as drugs and considered to be innocuous. Also in the treatment of dyslipidaemia, a myriad of herbal products is being used, some of them containing substances that are chemically identical to statins. As illustrated in several case reports, ''natural products'' are not always harmless and can cause life threatening side effects such as acute liver failure. We report the case of a patient having developed a toxic hepatitis due to therapy with a lipid-lowering food supplement.

Case report

A 77-year-old Caucasian male was admitted to the department of Gastroenterology because of new onset painless jaundice since one day with darkening of the urine. He mentioned no other complaints nor anamnestic features suggestive of a recent cardiovascular event (like an episode of hypotension). The patient had a history of gouty arthritis, ethylism, laparoscopic cholecystectomy (for symptomatic gallstone disease) and an impaired glucose tolerance. He reported no recent use of analgesics, alcohol or illicit drugs (which was confirmed by his family). Besides his chronic medication (allopurinol 300 mg o.d.) the patient was prescribed the lipid-lowering product Controchol® (Neocare N.V., Brussels, Belgium) one tablet daily, a month before presentation because of dyslipidaemia. Controchol® is a food supplement containing red yeast and green tea extracts. Before starting this supplement, the values of the following liver function tests were within normal limits: alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH), gamma glutamyl transpeptidase (γGT), bilirubin and prothrombin time (PT). Clinically, we saw a moderately overweight (weight 85 kg, BMI 27.1 kg/m^2) male with normal vital signs (blood pressure 125/75 mmHg, heart rate 57 beats per minute, temperature 36.7 °C, 97% blood oxygen saturation breathing ambient air) and a prominent icterus at presentation (without other clinical abnormalities). The initial laboratory work-up revealed evidence of hepatocellular damage (ALT 1742 U/L, normal values < 40 U/L; AST 1634 U/L, normal values < 48 U/L; LDH 1683 U/L, normal values 313—618 U/L; ferritin 871 μg/L, normal values 18—646 μg/L), cholestasis (ALP 198 U/L, normal values 38—126 U/L; γGT 686 U/L, normal values 15—73 U/L) and hyperbilirubinaemia (total bilirubin 4.86 mg/dL, normal values < 1.4 mg/dL; direct bilirubin 3.87 mg/dL, normal values < 0.3 mg/dL). There was a mildly lower cholinesterase level (cholinesterase 4866 U/L, normal values 5320—12,920 U/L), elevated immunoglobulin A (IgA) level (IgA 4.4 g/L, normal values 0.7—4 g/L) and marked hypertriglyceridaemia (triglycerides 368 mg/dL, normal values < 150 mg/dL). Haemoglobin, leukocyte and thrombocyte levels were normal, just as coagulation tests. Ethanol, albumin, fasting glucose, total cholesterol, lipase and thyroid stimulating hormone (TSH) levels were within normal limits. The abdominal ultrasonography showed a steatotic liver and normal findings postcholecystectomy but no common bile duct dilatation, ascites nor abnormalities of other organs. Results of extended laboratory testing disclosed no serological arguments for viral hepatitis (hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis E virus, cytomegalovirus, Epstein-Barr virus, herpes simplex virus and varicella zoster virus) or autoimmune liver disease (antinuclear, anti-mitochondrial, anti-liver/kidney microsomal and anti-smooth muscle antibodies). Serum levels of α-1-antitrypsin, free copper and ceruloplasmin were also normal. Consequently, our tentative diagnose was Controchol®-induced toxic hepatitis, with predominantly hepatocellular injury (ALT > 2 times the upper limit of normal, and ALT/ALP > 5). Besides Controchol® also allopurinol was stopped due to its possible hepatotoxic properties.

Because of persistence of the biochemical abnormalities after withdrawal of Controchol® and allopurinol, a liver biopsy was performed 1 week later. Microscopically, there was prominent necro-inflammatory destruction of the liver parenchyma with hepatocyte ballooning, collapse of the reticulin matrix, intracellular and intracanalicular cholestasis and gall duct damage, indicative of toxic hepatitis (Figs. 1 and 2).

Sixty days after medication adjustments, we still noted a subtle icteric discolouration of the skin with hyperbilirubinaemia (total bilirubin 4.14 mg/dL, direct bilirubin 3.19 mg/dL), but normalisation of other liver function tests (ALT 40 U/L, AST 35 U/L, ALP 102 U/L, γGT 58 U/L). A follow-up ultrasonography showed unchanged findings. Another 4 months later, all clinical and biochemical abnormalities had resolved (e.g. total bilirubin 0.79 mg/dL).

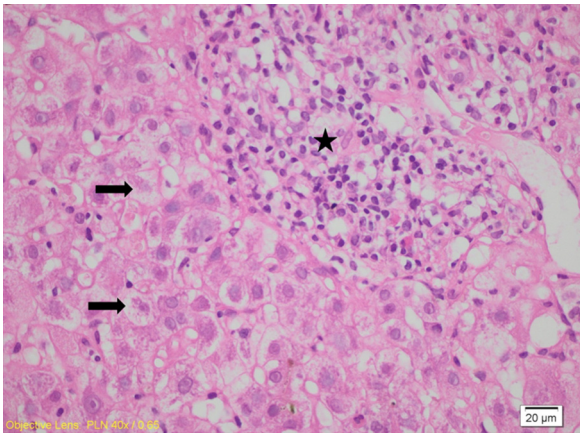

Figure 1 Hematoxylin and eosin stain: liver biopsy showed portal inflammation (asterisk) with lymphocytes, macrophages, neutrophilic and prominent eosinophilic granulocytes. A small bile duct is seen in the upper right hand corner. There is obvious ballooning of the hepatocytes (arrows) and both intracellular and intracanalicular cholestasis.

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