Acute hepatitis induced by an Aloe vera preparation: A case report

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INTRODUCTION

Aloe vera is a chemically ill-defined extract of the Aloe barbadensis miller plant. There is no doubt that this compound is bioactive[1]. Phytomedicine ascribes anti-inflammatory, analgetic, liver-protective, anti-proliferative, anti-carcinogenic, anti-aging, and laxative effects to this plant[2-5]. These effects are thought to be the result of radical scavenging, inhibition of COX-2, and immuno-modulatory mechanisms. The drug is widely used as a self-prescribed anti-aging drug in Western European countries as well as in the USA. Even though it is in widespread use as an over-the-counter drug, its toxicology has not been systematically examined. Here, we describe the first case of liver damage associated with Aloe vera ingestion.

CASE REPORT

Medical history and physical examination

A 57-year-old female patient presented to our department with an 1 wk history of progressive jaundice, pruritus, acholic bowel movements, and right-upper quadrant abdominal discomfort. Past medical history did not reveal any preexisting liver disease. There was no history of illicit drug use and no sexual promiscuity. In the hope to delay aging, the patient had begun using Aloe vera tablets containing 500 mg of an extract of Aloe barbadensis miller about 4 wk before admission. She also used zinc and vitamin C supplements as directed by the manufacturers. The Aloe vera tablets had been purchased in Spain as they were less expensive there than in Germany.

Clinical examination revealed a mildly overweight (70 kg bodyweight, 167 cm height) jaundiced patient with right-upper quadrant discomfort on deep palpation. Liver and spleen sizes were normal. There was no lymphadenopathy. The remainder of the physical examination was unremarkable.

Laboratory and technical examinations

On abdominal ultrasound examination, a reduced echogenicity of a normal sized liver was noted. Dilatation of intra- or extrhepatic bile ducts was absent. Patency of the hepatic artery, portal vein, and hepatic veins was ascertained using Doppler ultrasound. Splenic size was normal, the examination of kidneys, pancreas and retroperitoneal space was normal as well.

Laboratory abnormalities included a bilirubin concentration of 8.9 mg/dL (normal: <1.1 mg/dL), ALAT 1480 U/L (normal: <22 U/L), ASAT 711 U/L (normal: <15 U/L), LDH 506 U/L (normal: <240 U/L), alkaline phosphatase 265 U/L (normal: <160 U/L), GGTP 244 U/L (normal: <18 U/L). Creatinine, serum electrolytes, amylase, total protein, electrophoresis, serum concentrations of IgG, IgA, and IgM, white blood cell count, hemoglobin concentration, platelet count, and differential blood cell count were all within the normal range. Coeruloplasmin concentration was normal as was the alpha-1-antitrypsin concentration.

Serologic examinations for hepatitis A, C, and E infection were negative. Anti-HBc-IgG and anti-HBs-IgM were positive, while HBsAg and anti-HBc-IgM were negative. There was no serologic evidence for recent infections with cytomegalovirus, Epstein-Barr-virus, or herpes virus. Autoimmune markers showed negative titers for antimitochondrial and borderline titers for antinuclear antibodies (1:40; normal titer defined as <1:40).

Liver biopsy was performed and revealed severe acute hepatitis with portal and acinar infiltrates predominantly consisting of lymphocytes, plasma cells, and eosinophilic granulocytes along with bridging necrosis and bilirubinostasis (Figure 1).
Aloe vera, the dried extract from the leaves of *Aloe barbadensis miller* plants, contains several alkaloids that may induce or block hepatic enzyme systems such as cytochrome P450 as well as the enzymes of ethanol metabolism. This interference with detoxification processes leading to dose-related liver damage or direct cytotoxic effects of Aloe[7] or biotransformed constituents[8] are probably not important mechanisms in our case as the resolution of liver damage occurred much too slowly. It is more likely that an idiosyncratic immunological mechanism (hypersensitivity) is responsible for the hepatitis. A role for hypersensitivity is further supported by the presence of eosinophilic granulocytes in the periportal fields seen in the liver biopsy. As there was no evidence for the presence of an autoimmune hepatitis, especially no hypergammaglobulinemia[9] or autoantibodies[10], several compounds present in Aloe vera may interact with the host’s immune system[10]. This activation of the immune system was also discussed as a possible mechanism for a reported anti-tumor activity of Aloe vera[11]. The interactions with the immune system may inhibit the release or cause the rapid detoxification of reactive oxygen species[12]. This antioxidant effect of Aloe vera is also implicated in the potential anti-hepatocarcinogenic and hepatoprotective properties of the drug[13-17]. Conversely, some constituents of Aloe vera have been reported to be biotransformed to mutagenic compounds with equivocal evidence for *in vivo* carcinogenicity. The growth-inhibiting effect of Aloe vera is mediated through pro-apoptotic pathways. One could speculate that this effect may also be present in normal liver cells and leads to liver damage or to the triggering of an immune response directed toward intracellular antigens. A similar mechanism may be present in kidney damage associated with other Aloe species.

Herbal medicines are widely used in almost all segments of the population. A variety of herbal medicines can cause liver damage. Again, our case emphasizes that phytotherapeutic drugs should be subjected to the same toxicologic studies and pharmacovigilance that synthetic drugs are subjected to.

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