Drug-induced Liver Injury Due to Lepidium meyenii (Maca) **Medicinal Liquor**

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Key words: Drug-induced Liver Injury; Maca; Prolonged Recovery

Drug-induced liver injury (DILI) is one of the most common and serious adverse drug reactions. Idiosyncratic DILI is more common than intrinsic DILI and can be classified into hepatocellular injury, cholestatic injury, mixed hepatocellular-cholestatic injury, and vascular injury.[1] Lepidium mevenii (Maca) has been intensively studied since its diverse repertoire of pharmacological properties. These experimental studies have not found any evidence of in vivo or in vitro toxicity associated with either long- or short-term consumption.^[2] Here, we reported a case of liver injury that was probably directly induced by Maca, suggesting that the safety of Maca should be evaluated by further studies.

A 30-year-old man was admitted to Kunming General Hospital of Chengdu Military Command on December 31, 2016, with abdominal distension, anepithymia, sour regurgitation, and eructation after drinking 300 ml of Maca medicinal liquor containing 50% (V/V) alcohol on one occasion 10 days ago. This was followed by jaundice lasting for one week. No known hepatotoxic medications had been taken in the previous month. He had no history of liver disease and had normal results of liver function test recorded in November 2016. No more symptoms were concomitant, such as skin itching, joint pain, epistaxis, or gingival bleeding. At presentation, physical examination showed medium jaundice, but no fever, rash, or any signs of chronic liver disease. His blood count revealed a white blood cell count of 2.8×10^9 /L (neutrophils 62.6%, lymphocytes 18.6%, and eosinophils 3.2%), and platelet count was 196 × 10⁹/L. Serum biochemical assay gave the following results: albumin 40 g/L, total bilirubin (TBIL) 83.7 µmol/L, direct bilirubin 60.1 µmol/L, alanine transaminase (ALT) 1886 U/L, aspartate aminotransferase (AST) 609 U/L, alkaline phosphatase 136 U/L, γ-glutamyl transpeptidase 125 U/L, total cholesterol 3.38 mmol/L, and triglyceride



2.93 mmol/L. Coagulation function tests showed a prothrombin time of 15.9 s and an international normalized ratio of 1.1. A urine test showed 2+ urobilirubin and negative urobilingen. The feces had a normal appearance with negative occult blood. Tests for hepatitis A, B, C, and E were negative, and autoimmune markers including antinuclear and smooth muscle antibodies were also negative. The IgM anti-cytomegalovirus, IgM anti-Epstein-Barr virus viral-capsid antigen, and IgM anti-herpes simplex virus were all negative. Abdominal ultrasound and magnetic resonance testing were normal, and there was no evidence of fatty liver disease. Viral and autoimmune hepatitis were therefore excluded. The Roussel Uclaf Causality Assessment Method score was 9, which was consistent with highly probable DILI.

In the analysis of R value, our case was 44, suggestive of hepatocellular DILI. The severity of the liver injury was level 3.[1] A diagnosis of DILI caused by Maca was made. Ursodeoxycholic acid capsules (Ursofalk), magnesium isoglycyrrhizinate injection, and ademetionine 1,4-butanedisulfonate injection (Transmetil) were administrated. Subsequently, his clinical indicators improved and the levels of ALT and AST gradually decreased since third day after medication. Furthermore, the TBIL gradually decreased after 14 days and finally became normal after three months. Even though bicyclol tablets were given for two months after discharge from hospital, his serum biochemical

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Received: 07-09-2017 Edited by: Xin Chen

How to cite this article: Xiao A, He HY, Chen Q, Ma SW. Drug-induced Liver Injury Due to Lepidium meyenii (Maca) Medicinal Liquor. Chin Med J 2017;130:3005-6.

tests remained mildly abnormal, with the result of the most recent test on March 27, 2017, showing ALT of 41 U/L and AST of 28 U/L [Figure 1].

Maca has been widely used as a dietary supplement due to its high nutritional value. It has become progressively more prevalent in China and introduced as a plant into Yunnan province. The medicinal liquor is made in combination with traditional Chinese medicines. Not only herbs, such as medlar and panax, but also animal products can be infused into liquor. These are used to prevent and cure diseases, through either drinking or external application. In addition, Zhang *et al.*^[3] have reported a protective effect of polysaccharide from Maca on Hep-G2 cells and alcoholic liver oxidative injury in mice.

The mechanism of Maca-induced DILI is not clear. There are data showing a moderate increase in AST level and diastolic blood pressure increase *in vivo*, which was observed in volunteers using 0.6 g of Maca per day.^[4]

In our case, the differential diagnosis included ethanol poisoning as well as Maca-induced hepatotoxicity. We could exclude acute alcohol-induced liver disease (ALD) in this case according to the reasons as below: first, no acute ALD had been reported in humans after a single dose of alcohol. Even in animal models of acute ALD, the liver injury was caused by repeated usage. Second, the increase in serum ALT levels is rarely as high in ALD as it was in our patient. The increase in AST level is usually higher than the increase in ALT level in ALD. In ALD patients, the AST/ALT ratio typically is >1.0 and may be >2.0 in alcoholic hepatitis. Third, this patient was healthy before the liver injury and claimed that he has always had good tolerance to alcohol. Therefore, it was speculated that the idiosyncratic liver injury in this case should be probably induced by Maca, and not by the alcohol.

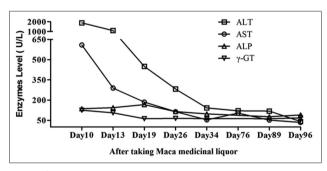


Figure 1: Trends of serum liver function results during the clinical course and follow-up. ALT: Alanine transaminase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; γ -GT: γ -Glutamyl transpeptidase.

Timely withdrawal of the suspected liver-injuring drugs is the most important treatment strategy for DILI.[1] In most cases, the drugs should be withdrawn immediately after they are identified, and approximately 95% of patients will achieve spontaneous improvement and recover completely.[1] This patient's clinical condition and the liver function tests gradually improved after admission. However, we were surprised that they did not completely normalize. A possible explanation from a prospective study in Spain showed that dyslipidemia is an independent risk factor for a prolonged recovery from DILI.[5] Thus, mild hypertriglyceridemia may be a reason for his prolonged recovery. Since the mechanism of Maca-induced DILI has not been established, more research should be carried out to determine whether Maca can cause DILI and whether some patients are more sensitive than others.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Yu YC, Mao YM, Chen CW, Chen JJ, Chen J, Cong WM, et al. CSH guidelines for the diagnosis and treatment of drug-induced liver injury. Hepatol Int 2017;11:221-41. doi: 10.1007/ s12072-017-9793-2.
- Gonzales GF, Villaorduña L, Gasco M, Rubio J, Gonzales C. Maca (*Lepidium meyeni*i walp), a review of its biological properties. Rev Peru Med Exp Salud Publica 2014;31:100-10.
- Zhang L, Zhao Q, Wang L, Zhao M, Zhao B. Protective effect of polysaccharide from maca (*Lepidium meyenii*) on hep-G2 cells and alcoholic liver oxidative injury in mice. Int J Biol Macromol 2017;99:63-70. doi: 10.1016/j.jibiomac.2017.01.125.
- Valentová K, Stejskal D, Bartek J, Dvorácková S, Kren V, Ulrichová J, et al. Maca (Lepidium meyenii) and yacon (Smallanthus sonchifolius) in combination with silymarin as food supplements: In vivo safety assessment. Food Chem Toxicol 2008;46:1006-13. doi: 10.1016/j. fct 2007.10.031
- Medina-Caliz I, Robles-Diaz M, Garcia-Muñoz B, Stephens C, Ortega-Alonso A, Garcia-Cortes M, et al. Definition and risk factors for chronicity following acute idiosyncratic drug-induced liver injury. J Hepatol 2016;65:532-42. doi: 10.1016/j.jhep.2016.05.003.