

# Archives of Clinical Case Reports

## Case Report

# Hepatotoxic Injury Associated with Herbal Medicinal Products: A Three Cases Reports

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Received: 16 July 2020; Accepted: 25 August 2020; Published: 26 August 2020

Citation of this article: Al-traif, I., Saeed, M., Ghamdi, H., Alwan, A., Alshammari, K., Ama, A. (2020) Hepatotoxic Injury Associated with Herbal Medicinal Products: A Three Cases Reports. Arch Clin Case Rep, 3(2): 24-29.

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### Abstract

Chinese herbs are widely used in the eastern and western societies and are popular as natural remedies. They are perceived as natural product and free of side effects. We describe three cases of Chinese herb induced liver injury of patients who had taken these herbs for different complaints. The first case had taken the herb as a sexual performance enhancer that led to development of jaundice and liver cirrhosis and required liver transplantation, and the second case had taken a different herb as a weight gain remedy which resulted in cholestatic liver injury, the third one took two types of products, a Chinese medication in addition to honey paste mixed with herbal that caused acute liver injury. It may be difficult to diagnose Chinese herb induced liver injury due to lack of detailed ingredients description in each herbal packet. This raises the need to regulate such market and control their selling and usage.

**Keywords:** Drug induced liver injury (DILI), Chinese herb induced liver injury, Jaundice and liver cirrhosis

**Abbreviations:** ASMA: Anti-Smooth Muscle Antibody; AMA: Anti-Mitochondrial Antibody; IgM: Immunoglobulin M; IgG: Immunoglobulin G; ANA: Anti-Nuclear Antibody; N: Normal; BMI: Body Mass Index; ALP: Alkaline Phosphatase; ALT: Alanine Amino-Tarnsferase; AST: Aspartate Amino-Transferase; Gamma GT: Gamma Glutamyl Transferase

**Key messages:** Chinese herb induced liver injury of patients

## Introduction

Many drugs and herbs have been reported to cause hepatotoxicity and liver injury. A US study revealed that only 40% of patients informed their primary health physicians about their herbal medicine usage [1]. Herbal medicine induced liver injury and stopping early the offending herb may result in a reduction in the severity of the hepatotoxicity [2] and recovery. We hereby report three unique cases of herbal induced liver injury.

## Case 1

The first case was a 52 year old Saudi man presented with jaundice for 3 weeks. His investigations revealed the following; AST 90, ALT 174, ALP 174, T.Bili 192. ERCP showed normal biliary tree. He took a Chinese herb/supplement as a sexual enhancer. On physical examination he is jaundiced with no stigmata of chronic liver disease. Abdominal examination revealed a soft abdomen with hepatomegaly, and no ascites. Laboratory tests (Figure 1).

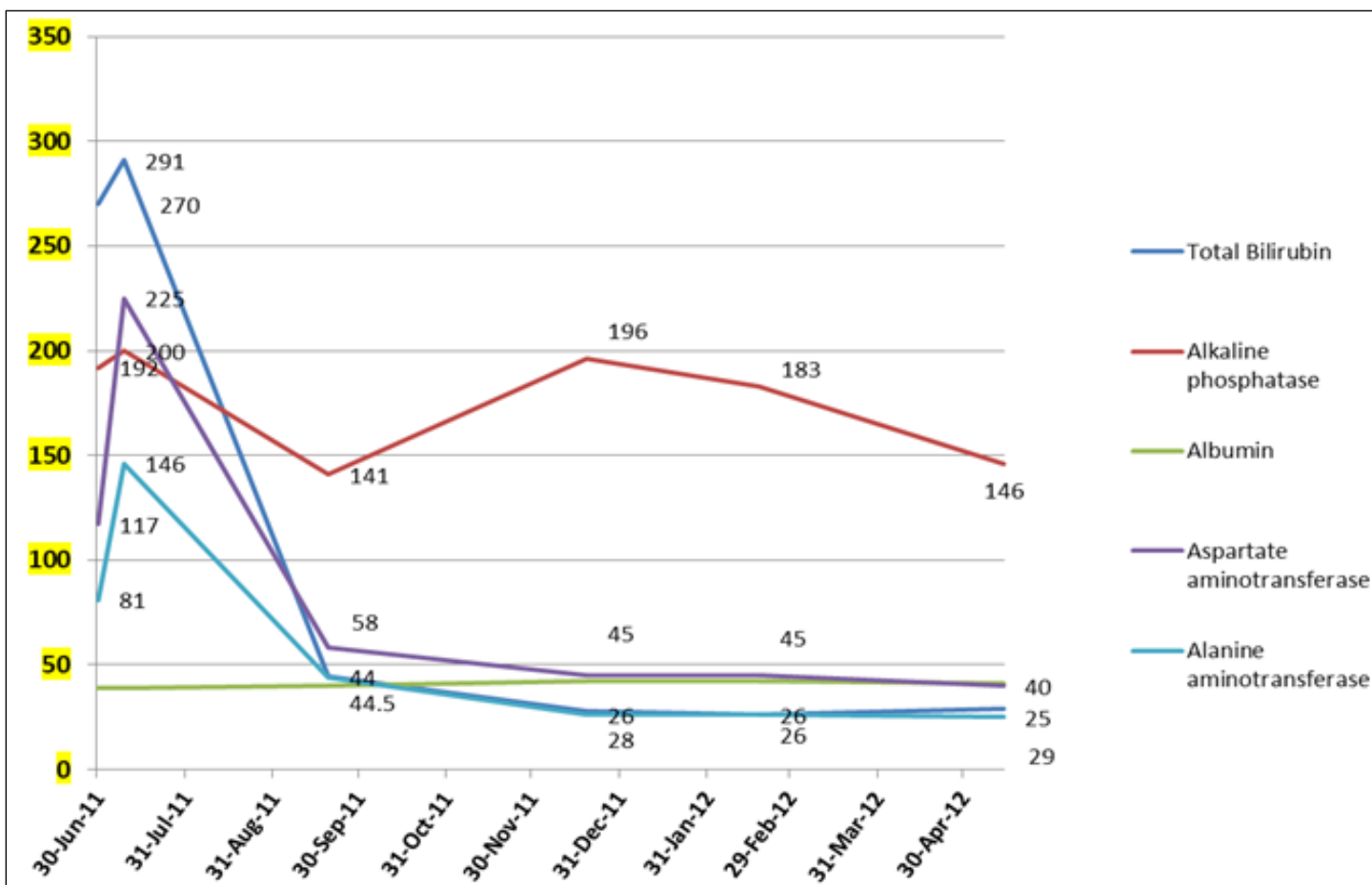


Figure 1: Results of liver function tests (dated)

The herb labeled as “Maxman”, in form of 1.1g concentrations capsules. The toxicology analysis indicated that each capsule contained high amount of Sildenafil around 130mg/capsule.

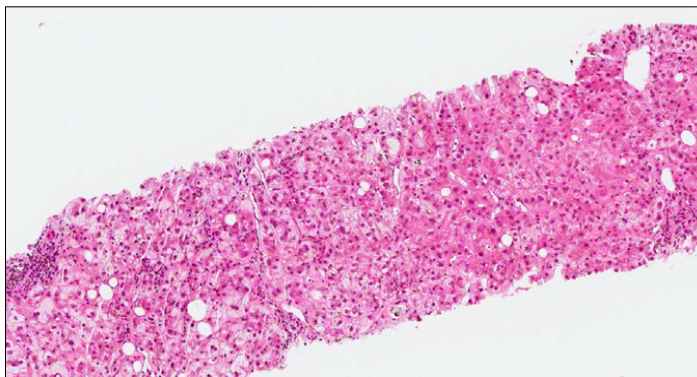
His hepatitis screening (A,B,C) and autoimmune markers were negative. Liver biopsy showed changes consistent with autoimmune vs drug/herbal induced hepatitis (Figure 2). He was started on prednisone 40mg daily and azathioprine 150mg daily. Azathioprine was discontinued after 9 months and Prednisone was tapered down over the course of 3 months. His liver function improved (Figure 1) but not normalized patient developed cirrhosis over 18 month course and decompensated then underwent successful liver transplant two and half year after his liver injury.

### Case 2

A 40-year-old female presented with pruritus and worsening liver functions. Investigations and liver biopsy were done outside, diagnosed as AMA (negative) primary biliary cholangitis. She presented with the same complaint. She took a Chinese herbal medicine to increase weight. She was started on ursodeoxycholic acid.

The herb was named “Ginseng Kianpi Pil” from China. Each capsule weighed 0.38g. GC-MS analysis indicated cyproheptadine, as well as lead, both at high concentrations. Used for one year at a dose of one to two capsule per day.

Liver ultrasound and ERCP were normal. Her liver biochemistry (Figure 3) and autoimmune, hepatitis (A,B,C) were negative. Her liver biopsy slides were reviewed (Figure 4), showed picture resembling primary biliary cholangitis. Ursodeoxycholic acid was



**Figure 2: Portal and lobular cholestasis hepatitis (Scheuer grade 2/4), with mild fibrosis (Scheuer stage 2/4).**

increased to 500mg twice daily. Her symptom, improved markedly in two months. Follow up revealed normalization of liver function tests and improvement of her symptom.

### Case 3

A 59 male patient presented with a complain of epigastric pain with on and off vomiting for one week and dark urine with yellow sclera.

On examination patient was jaundiced. Abdomen was soft, liver spleen were not palpable, no ascites.

Investigation showed: bilirubin of 139 umol/l, albumin 40 g/l, AST 208 U/L, ALT 524 u/l, creatinine 68 umol/l, INR 1, WBC 7.6 , Hb 162, PLT. 422. Serum was negative for HAV, HBV and HCV. Auto-immune markers were negative. Ultrasound of abdomen showed fatty liver no biliary obstruction. The liver biopsy showed mild steatohepatitis, mild portal and lobular inflammation, portal fibrosis 1/6 and mild ductitis. The increased eosinophils infiltrated with ductal injury raised the possibility of drug induced injury (Figure 5).

He took a Chinese medicine with a name XIAN LING which he used on and off for more than 6 months for joints and body aches. He also used a honey paste mixed with herbal material (Figure 6). The analysis of the honey paste showed the present of Carvacol, Oregano and wild Bergamot. Isoeugenol which is found to be carcinogenic in rats. The honey also contains carotol which inhibits human CYP3A4 and other CYP 540 enzymes. The supplement XIAN LING contains Acetaminophen, Betamethasone and Dexamethasone and is contaminated with bacteria, yeasts and molds.

The liver function improved after holding the suspected herb. In two months biochemistry normalized, the histological picture, and the fact that his liver function improved after stopping the above materials are suggestive of herbal induce acute hepatitis.

### Discussion

The diagnosis of herbal induced hepatotoxicity is one of exclusion and requires taking detailed medications and herbal intake history. It is difficult to differentiate between drug induced hepatotoxicity and other diagnoses histologically [5] There are few case reports on herbal/drugs induced autoimmune hepatitis [3,4] which

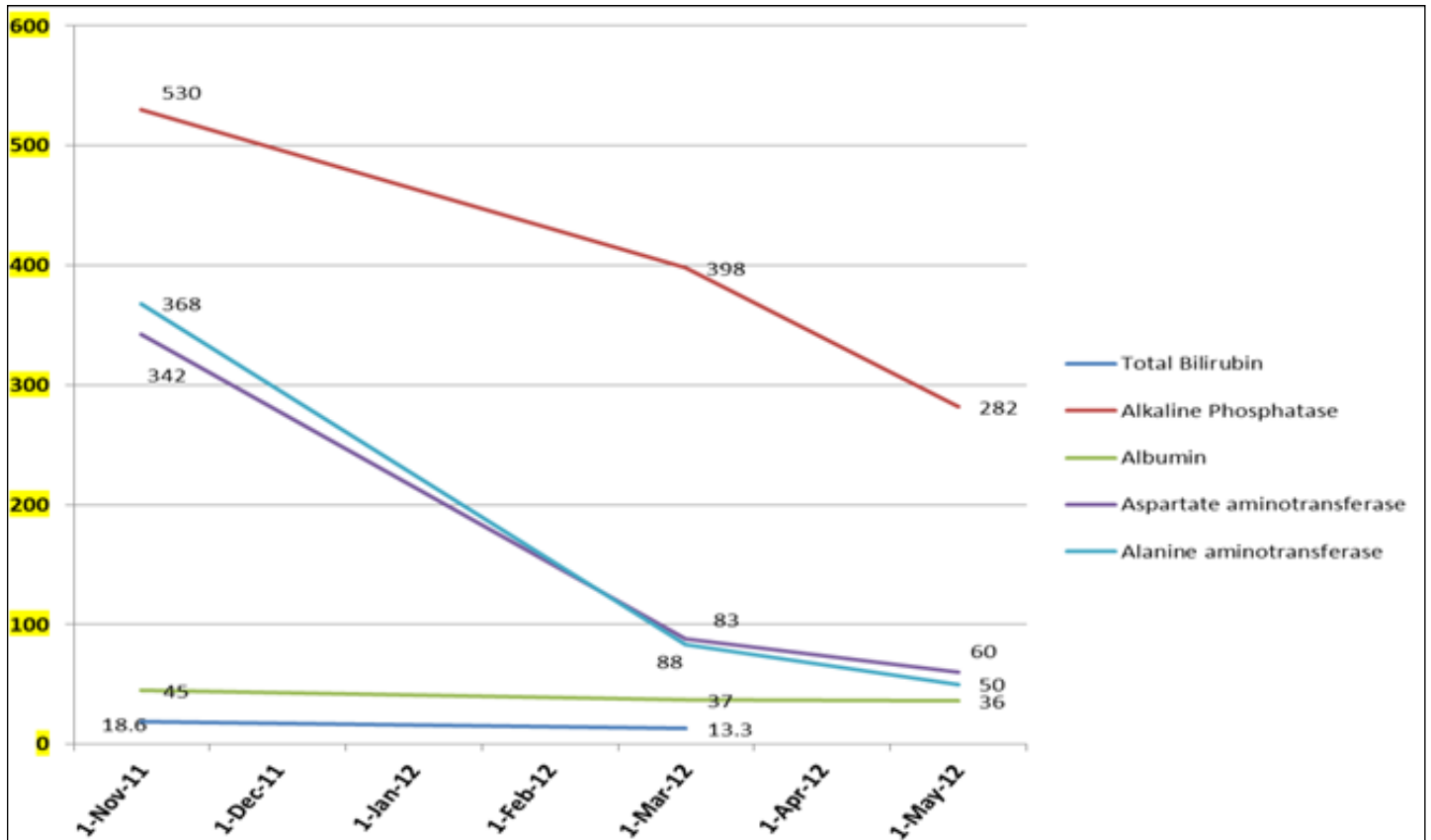


Figure 3: Results of liver function tests (dated)

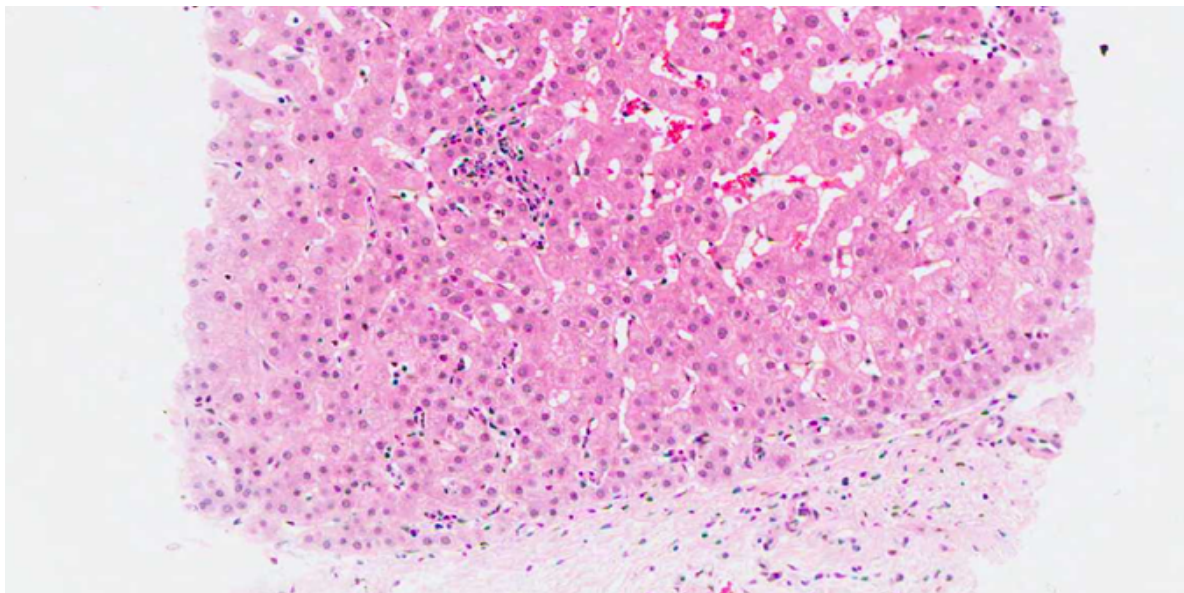


Figure 4: Abundance of plasma cells and no fibrosis.

is similar to the first case we described. Serological markers were borderline and the liver biopsy is consistent with autoimmune vs drug induced hepatitis. The second case has diagnosis of AMA negative primary biliary cholangitis with negative AMA which is unlikely diagnosis but rather herb induced liver injury in addition to the intake of herbal material may exacerbate her present disease as her condition improved after holding the suspected herb. The third case took multiple material including medical drugs like acetaminophen and steroid, some of the ingredients may inhibit hepatic enzymes which can increase the effect of the other components. Most of the time herbs can be contaminated with lead and toxins which can add to its toxicity. In his case it is difficult

to identify single causative material, and interaction between the different components is possibility in all three cases there was no etiology other than these herbs are causing liver injury.

### Conclusion

Herbal remedies may be associated with hepatotoxicity, making it important to discuss the use of herbal and dietary supplements in attempt to prevent their toxicity. The use of herbal remedies should be considered as possible etiology in any case of acute or chronic liver injury of unknown etiology. Features suggestive of drug/herb toxicity include lack of prior illness, clinical illness or biochemical abnormalities developing after beginning the drug/herb, and im-

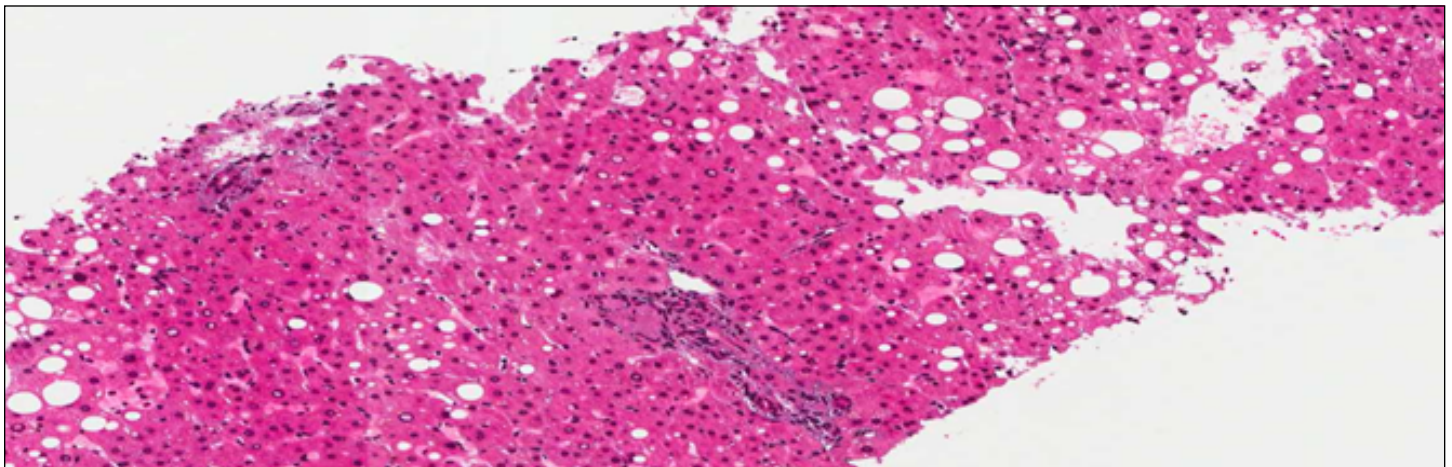


Figure 5: liver biopsy showing portal and lobular inflammation



Figure 6: The chinese medication XIAN LING and the honey paste mixture

provement after the product is withdrawn. The mainstay of therapy for herbal hepatotoxicity is withdrawal of the offending toxin in addition to supportive measures. Health education for the public about the potential toxicity of herbal and dietary supplements are important.

### Acknowledgment

We would like to thank Mr. Raul Palad for his efforts in arranging the manuscript and his secretarial support.

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