

Case Report

Acute hepatitis induced by a Chinese herbal product Qibao Meiran Wan: a case study

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Abstract: Qibao Meiran Wan is a Chinese herbal product sold as a therapy for tonifying the liver and kidney, dizziness, premature graying of hair, backache, constipation, and night sweats. It is widely available in Chinese pharmacies and drugstores and is sold without prescription. We describe a case of acute liver injury in a 26-year-old Chinese man who developed symptomatic hepatitis 1 month after starting Qibao Meiran Wan. There was no evidence of viral hepatitis, Epstein-Barr virus, cytomegalovirus, autoimmune hepatitis, or Budd-Chiari syndrome. The liver injury slowly resolved over 20 days after discontinuing the herbal product. Herbal toxicity was later confirmed by a liver biopsy. Qibao Meiran Wan contains a mixture of several plants including *Polygonum multiflorum*, which was previously associated with hepatotoxicity. To our knowledge, this is the first report of hepatotoxicity by Qibao Meiran Wan. Clinicians treating patients with acute hepatitis of unclear etiology should pay attention to the consumption of Qibao Meiran Wan.

Keywords: Drug-induced liver injury, hepatotoxicity, Qibao Meiran Wan, adverse drug reaction

Introduction

Consumption of herbal remedies is on the rise worldwide, because they are often perceived as safe and natural treatment modalities compared with Western medicines [1-3]. Herbal preparations are widely and routinely used as nonprescription medications in China [4]. Several hepatotoxicity cases caused by herbal products have been recognized and reported [5-7]. Qibao Meiran Wan (product code number Z43020465 approved by SFDA) is a Chinese herbal product made from the powdered root of *Polygonum multiflorum*, *Radix Angelica sinensis*, *Fructus Psoraleae* (Yan Shuizhi), wolfberry fruit, dodder, and *Poria cocos*. In China, it is used to tonify the liver and kidney, prevent early whitening of the beard and hair, and to treat night sweats, abnormal leucorrhea, muscle weakness, and stomachache. This product is widely sold in hospital pharmacies, drugstores, and online as a nutritional supplement. Hepato-

toxicity cases due to *Polygonum multiflorum* have been reported in many countries, but previous reports are inconclusive [6, 8-10]. We describe a case of hepatotoxicity from Qibao Meiran Wan in a young man taking this herbal product as a hair supplement.

Case report

A previously healthy 26-year-old man from Henan Province referred to our outpatient clinic following recent onset of weakness, fatigue, poor appetite, dark urine and jaundice. There was no abdominal pain or fever. To the carefully asked he said he had taken the recommended dosages of Qibao Meiran Wan for greying of hair, and his symptoms began approximately 1 month after commencing it. His liver tests revealed: elevated liver enzymes (alanine aminotransferase 1674 U/L, aspartate aminotransferase 617 U/L, total bilirubin 3.2 mg/dl, direct bilirubin 2.5 mg/dl), serologic markers

Acute hepatitis from Qibao Meiran Wan

Table 1. Initial laboratory tests

	Patient	Reference range
Hemoglobin (g/L)	165	130-175
White blood cell count (10 ⁹ /L)	6.77	3.5-9.5
Red blood cell count (10 ¹² /L)	5.16	4.3-5.8
Platelet count 9.8-13.2unt (10 ⁹ /L)	180	100-350
Prothrombin time (s)	12.5	9.8-13.2
INR	1.65	0.8-1.2
Total bilirubin (mg/dl)	3.1	0.2-1.4
Direct bilirubin (mg/dl)	1.9	0-0.40
Albumin (g/L)	46.4	36-52
Alanine aminotransferase (U/L)	1674	3-35
Aspartate transaminase (U/L)	617	15-40
Alkaline phosphatase (U/L)	110.0	45-125
Serum creatinine (μmol/L)	76	31.8-116.0
HAV IgM	negative	-
HbsAg	negative	-
HBc IgM	negative	-
Anti-HCV RNA	negative	-
Anti-HIV	negative	-
CMV-IgM	negative	-
EBV-IgM	negative	-
HSV-IgM	negative	-
ANA and ASMA titers	negative	-
Serum ceruloplasmin (g/L)	0.206	0.2-0.55

ANA, antinuclear antibody; Anti-HCV RNA, antibodies to hepatitis C; Anti-HIV, antibodies to human immunodeficiency virus; ASMA, antismooth muscle antibody; CMV, cytomegalovirus; EBV, Epstein-Barr virus; HAV, hepatitis A virus; HCG, human chorionic gonadotropin; HSV, herpes-simplex virus; INR, international normalized ratio for prothrombin time.

were negative for IgM antibody to hepatitis A virus, antibody to hepatitis C virus, hepatitis B surface antigen, herpes simplex virus, herpes zoster virus, cytomegalovirus, toxoplasma and Epstein-Barr virus. Budd-Chiari syndrome, Autoimmune hepatitis was also excluded by a negative test for serum and other hepatotoxic causes were excluded, such as autoimmune hepatitis by a negative serum test for autoantibodies; Wilson's disease by a test for ceruloplasmin, serum, and urine copper; alpha-1 antitrypsin deficiency; and celiac disease. The patient's full blood count, prothrombin time and international normalized ratio (INR) was normal (all determined by standard immunoenzymatic methods). Laboratory tests at her initial visit are shown in **Table 1**. Ultrasonography with Doppler showed no liver masses, biliary tract obstruction or outflow obstruction. Qibao

Meiran Wan was ceased and she was closely monitored for 20 days in our hospital. A liver biopsy revealed the hepatic lobule see spotty necrosis, hepatocyte hydropic degeneration; hepatic lobule and portal area inflammatory infiltrate consisting of lymphocytes, histiocytes and occasional neutrophils, canalicular and hepatocellular cholestasis, The immunohistochemical results suggest HbsAg (-), HbcAg (-), HCV (-), CK7 (-), CK9 (-). Special staining results show Periportal fibrous tissue mild hyperplasia, d-PAS dyeing suggest small bile duct basement membrane integrity (**Figure 1**). He did not develop any signs of hepatic encephalopathy during the admission. After days 20 of admission, her symptoms and laboratory tests began to improve. He was discharged and be follow-up 3 months (**Table 2**).

Discussion

The use of herbal remedies is becoming increasingly popular all over the world. An increasing body of literature has emerged concerning the hepatotoxic risks of herbal preparations. Herbal remedies are perceived as they are as a safe, innocuous treatment modality in comparison with pharmaceuticals [1-4]. Unfortunately these products are routinely used without a medical prescription and thought to be 'natural.' However, problems can arise when drug interactions occur between commonly used pharmaceuticals and herbal remedies. A number of severe adverse events have been reported, but circumstantial evidence indicates unclear etiology of these compounds [5-7]. For this reason they do not need approval by SFDA. The product label for Qibao Meiran Wan has a list of components that include *polygnum multiflorum*, *angelica sinensis*, *fructus psoraleae* (Yan Shuizhi), *wolfberry fruit*; *dodder*, *poria cocos*, *achyranthes bidentata*, and accessories are honey and corn gluten and them sold as a therapy for tonifying the liver and kidney, dizziness, premature graying of hair, backache, constipation, and night sweats. Herbal supplements are widely available across Chinese pharmacies and are sold without prescription.

Polygonum multiflorum is one of the main components of Qibao Meiran Wan, and because other reports have confirmed that it causes hepatotoxicity when many hepatotoxic causes

Acute hepatitis from Qibao Meiran Wan

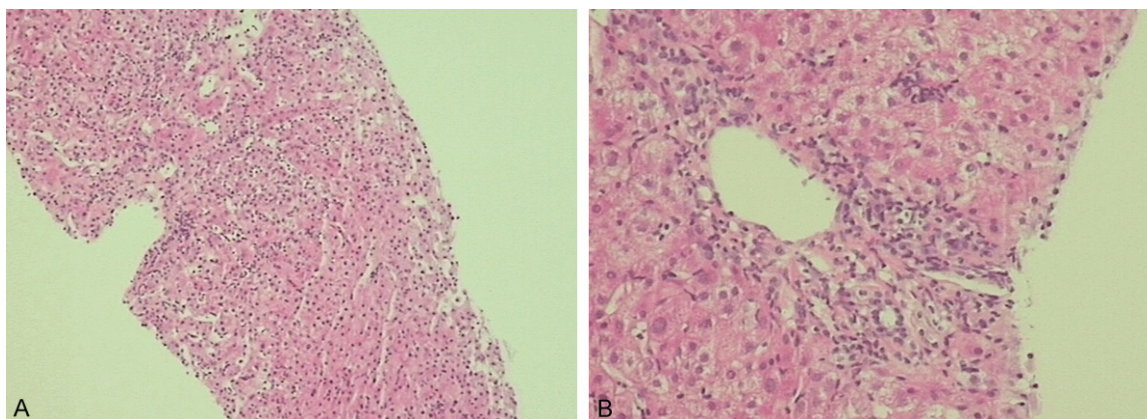


Figure 1. A. Liver biopsy showing portal and lobular inflammation consistent with toxic hepatitis (Hematoxylin and Eosin staining; original magnification $\times 40$); B. Higher magnification showing focal necrosis ($\times 100$).

Table 2. Evolution of liver function tests

	At presentation	Day 3	Day 6	Day 9	Day 12	Day 20	Day 50	Day 80
ALT	1674	1120	615	206	97	40	36	33
AST	617	261	127	44	35	43	37	32
TBILI	3.1	3.2	2.9	1.3	1.3	1.1	1.0	2.0
DBILI	1.9	2.1	2.0	0.8	0.7	0.4	0.4	0.6
ALP	-	110	88	77	72	68	-	-
Albumin	47.1	46.4	41.2	40.0	44.7	45.6	46.8	48.1
GGT	-	199	173	148	130	72	66	41

ALT indicates alanine aminotransferase (U/L); AST, aspartate aminotransferase (U/L); TBILI, total bilirubin (mg/dl); DBILI, direct bilirubin (mg/dl); ALP, alkaline phosphatase (U/L); Albumin (g/L); GGT glutamine transpeptidase (U/L).

were excluded, so we believe this is the case in this patient [6, 8, 9, 11, 12]. *Polygonum multiflorum* was first recorded in the herbal materia medica Kai pao pen tsaio issued by the imperial court of the Song Dynasty (973-974 AD), a database of CHIMERA reporting herbal poisoning, established by Chinese Medicinal Material Research centre at the Chinese University of Hong Kong, reported cases of hepatitis associated with Shou-Wu-Pian including rash, pruritus, erythema, fever, abdominal pain, and palpitations [9]. Anthraquinones are known constituents of *Polygonum multiflorum* which was speculated to be the herb's hepatotoxicity, but previous reports were nonconclusive and the mechanism of liver injury remains unknown [11, 12].

We used a clinical diagnostic scale to diagnose drug-induced liver injury. First, the time from drug intake and withdrawal to the apparent onset of the reaction was "suggestive" of drug hepatotoxicity or compatible with drug hepatotoxicity. Moreover, the young patient had liver

injury just 30 days after initial drug intake. Second, the course of the reaction after cessation of the drug was "very suggestive" or "suggestive" of drug hepatotoxicity. When the patient discontinued the drug, there was a decrease in the liver enzymes by $\geq 50\%$ of the excess over the upper limit of normal within 8 days. Third, alternative causes of the reaction were excluded by relevant investigations. Serological markers were negative and other hepatotoxic causes were excluded. Furthermore, ultrasonography with Doppler showed no abnormal results. While a final positive test would be a response to continuation of the medication, this was not possible in this case.

Although *Polygonum multiflorum* was previously associated with hepatotoxicity, to our knowledge this was the first reported case of hepatotoxicity from Qibao Meiran Wan as an herbal preparation sold though the Internet. A search revealed that this product is widely sold in drugstores and many websites without prescription.

Conclusion

Qibao Meiran Wan, an herbal product used as a supplement for hair growth, may cause acute hepatitis with prolongation of prothrombin time and a slow normalization of serum liver enzymes and other laboratory parameters. It is commonly assumed that herbal remedies are safe and “natural”, but physicians should be aware of potential adverse effects. Surveillance programs and quality control of herbal manufacturing should be established, and clinicians must always inquire with patients about herbal supplement intake in cases of unexplained liver injury.

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Disclosure of conflict of interest

None.

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