CASE REPORT

Toxic Hepatitis Induced by Show-Wu-Pian, a Chinese Herbal Preparation

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Abstract

Herbal preparations are widely available and often regarded by the public as harmless remedies for a variety of medical ailments. However, some of these products or their metabolites can cause adverse effects such as liver damage. In this case report a 53-year-old female taking Shou-Wu-Pian for 8 months presented with acute hepatitis. Histopathological assessment of liver tissue obtained by biopsy was consistent with a toxic reaction. Clinical and biochemical resolution was brought about following cessation of the drug. It is important for clinicians to consider Chinese herbal preparations as a potential cause of abnormal liver function test results.

Key words: toxic hepatitis, drug induced hepatitis, herbal medicine, Shou-Wu-Pian

(Inter Med 49: 1537-1540, 2010)
(DOI: 10.2169/internalmedicine.49.3509)

Introduction

Herbal preparations are widely available as supposedly harmless remedies for a variety of medical conditions. An increasing body of literature, however, has highlighted potential risks associated with the use of these preparations (1-8). For example, traditional Chinese herbs have been implicated as a cause of acute hepatitis (9-12). The Chinese herbal product Shou-Wu-Pian is formulated from Polygonum multiflorum, a plant whose processed roots and vines have been used as a tonic for a wide range of conditions including dizziness, premature graying of hair, backache, and constipation (13). Although Show-Wu-Pian has been recommended for enrichment of the liver (14), this preparation has also been reported to cause liver injury (15-17). A prominent characteristic of Show-Wu-Pian-induced liver injury is a slow onset, in some cases as long as several months. Here, we report a case of toxic liver injury manifesting 8 months after ingestion of Show-Wu-Pian.

Case Report

In late September 2008, a 53-year-old Japanese female was admitted to our hospital because of general fatigue and liver dysfunction. She had been diagnosed with Sjögren’s syndrome when she was 25 years old. She had received short-term steroid therapy after which the only medication that she took was eye drops as hydration for dry eyes. In October 2007, her liver function was normal. In her family history, her sister had asymptomatic primary biliary cirrhosis (PBC). In the present case, there was no known exposure to viral hepatitis, recent overseas travel, or history of illicit drug use or alcohol abuse. Her physical findings on admission to our hospital were as follows: body temperature, 36.3°C; pulse, 72 beats/min and regular; blood pressure, 96/70 mmHg; respiratory rate 16/min; no anemic signs at the conjunctiva palpebra; no jaundice at the conjunctiva bulbi; the liver and spleen were not enlarged; no flapping tremor or palmar erythema was observed; the superficial lymph nodes were not palpable; and, additional neurological and general physical examination results were normal.
The patient’s liver tests revealed the following: total bilirubin, 12 g/L (normal range, 2-12); aspartate aminotransferase (AST), 417 U/L (10-40); alanine aminotransferase (ALT), 418 U/L (5-45); alkaline phosphatase (ALP), 1,425 U/L (100-325); γ-glutamyl aminotransferase (γ-GTP), 731 U/L (0-30); and albumin, 4.0 g/L (38-53). The serum IgG level was 3,059 mg/dL (850-1,800). The patient showed negative results for IgM antibodies to hepatitis A virus, antibodies to hepatitis B core and surface antigen, antibodies to Epstein-Barr virus, and antibodies to hepatitis C virus. Anti-nuclear antibody (ANA), anti-SS-A antibody, anti-mitochondrial antibody, and anti-mitochondrial-M2 antibody were positive with titers of 1 : 320, 1 : 8, 1 : 40, 1 : 62.5, respectively. Anti-DNA, antinuclear, anti-SS-B, and anti-smooth muscle antibodies were all negative. Upper abdominal ultrasound sonography and computed tomography (CT) showed no abnormalities of the liver or biliary duct system. A liver biopsy (Fig. 1a and b) revealed prominent lobular inflammatory cell infiltration, consisting mainly of lymphocytes, and spotty hepatocyte necrosis compatible with an adverse drug reaction. There were no findings of vanishing bile ducts or bile duct proliferation that would suggest primary biliary cirrhosis.

The patient’s liver function test improved gradually (Table 1), and normalized 2 months after admission following bed rest only. A detailed interview of the patient revealed the use of Shou-Wu-Pian for 8 months, which was discontinued upon admission. Her husband also took Shou-Wu-Pian but showed normal liver function test results.

Discussion

Herbal medicines are widely perceived by the public as being healthful and innocuous. However, hepatotoxicity associated with herbal medicines is being increasingly reported in parallel with the rising popularity of herbal medicines in industrialized societies (18-21). It is possible that some herbal products could prove to be beneficial for people with liver disease, however, at the present time, the benefits of these preparations in human remain largely unproven, and greater awareness of their potential to cause adverse effects is needed. Patients often do not disclose their use of herbal preparations, and this can result in delayed diagnoses and perpetuation or exacerbation of organ injury.

Shou-Wu-Pian is the tablet form of the root tuber of Polygonum multiflormum, the common name of which is the fleece flower root. In the present case, the patient made her own preparation by boiling water with diced root tuber of Polygonum multiflormum, and she consumed the liquid extract on a daily basis. The first known recorded mention of the Shou-Wu-Pian herb is found in the herbal material medica “Kaibao Bencao” issued by the imperial court of the Song Dynasty (973-974 AD) (17). Since then, it use has been associated with youthfulness and longevity. The English translation of Shou-Wu-Pian is “Mr. Black Hair”, and the herb is sold under that name for the treatment of a variety of symptoms associated with aging, including baldness and graying hair.

In England, the Medical and Healthcare Products Regulatory Agency (MHRA) reported 7 cases of adverse reactions associated with the use of Shou-Wu-Pian up to 30 April, 2006. All cases showed abnormal liver function test results. They ranged in age from 36 to 70 years, and 5 of the patients were female. In all cases, Shou-Wu-Pian had been used for hair restoration, and time interval until the appearance of symptoms ranged from 2 weeks to several months. Recovery from liver dysfunction occurred in all cases following discontinuation of Shou-Wu-Pian (17, 22).

Based on the scoring system proposed by a workshop on drug-induced liver injury held during Digestive Disease Week-Japan 2004 (in Fukuoka, Japan), it was deemed highly possible that the liver dysfunction in our case was drug-induced (23). The autoimmune hepatitis (AIH) score according to American Association for the Study of Liver Diseases (AASLD) practice guidelines (24) was very low, and the histological findings were different from those observed in AIH. Hence, we determined that this was a case of drug-induced hepatitis, and not AIH.

The mechanism of Shou-Wu-Pian-induced hepatotoxicity is not fully understood. The liver is the primary site of me-
Table 1. Clinical Course of Liver Function Test Results after Discontinuation of Shou-Wu-Pian

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AST: asparate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, γ-GTP: γ-glutamyl aminotransferase

The metabolism of most xenobiotics and it is particularly vulnerable to injury during biotransformation of these compounds. The product packaging information reports the anthraquinone, substance of Shou-Wu-Pian, derivates emodin, physcin, chrysopanol, rhein and chrysophanol anthrone and the stilbene derivates 2,3,5,4′-tetrahydroxystilbene-2-O-β-D-glucopyranoside and its 2′- and 3′-O-monogalloyl esters to be present in the polygonal tablets. Panis et al proposed that the acute hepatitis induced by Shou-Wu-Pian is likely related to the presence of 2,3,5,4′-tetrahydroxystilbene-2-O-β-D-glucopyranoside and/or emodin (16). One of the major dilemmas in determining the potential causative hepatotoxins in herbal preparations is the complexity of ingredients. Individual ingredients may not be pure substances and not all components may be listed or, indeed, known. Chinese herbal products are not subjected to the controls and rigorous testing for safety and efficacy that drugs have undergone. Frequently, they become adulterated with impurities and contaminants such as heavy metals (25).

Our report represents the first documented case in Japan of biopsy-proven hepatitis induced by Shou-Wu-Pian derived from Polygonum multiflorum. Clinicians should be aware of the toxic potential of herbal products like Shou-Wu-Pian when encountering cases of unexplained liver injury.

References

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