

## A Case of Cold Medicine-Induced Hepatitis Treated with Herbal Medicine

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**Objectives:** To inform the clinical features of drug-induced liver injury (DILI), and study traditional Korean medicine (TKM)-based strategies or therapeutics.

**Methods:** A female patient with hepatitis after long term use of medication for cold symptoms was treated with Oriental therapies, after which the clinical outcome was evaluated by serum biochemical parameters and ultrasonography.

**Results:** Clinical and biochemical levels were fluctuating during administration of cold medicine, but the patient completely recovered her health with herbal medicines.

**Conclusion:** This case report would provide information about a typical DILI by western medicine followed by treatment with traditional Korean medicine.

**Key Words :** Drug-induced liver injury, traditional Korean medicine, herbal medicine

### Introduction

Drug-induced liver injury (DILI) is one of the most critical adverse drug reactions (ADRs) because the liver is the primary organ that detoxifies and excretes drugs<sup>1)</sup>. DILI is responsible for 5% of all hospital admissions and 50% of all acute liver failures in the United States<sup>2)</sup>. More than 900 drugs have been implicated in causing liver injury, and DILI is the most common cause of aborted development or withdrawal of promising drugs from the market<sup>3)</sup>.

On the other hand, herbal medicines have been popularly used in Asia for thousands of years, and are widely considered to be relatively safe on the basis of long clinical experience<sup>4)</sup>. However, the safety of

herbal medicines often becomes a medical issue according to the rapidly growing market for them worldwide<sup>5,6)</sup>. Moreover, the possibility of herbal medicine-associated hepatotoxicity is frequently exaggerated, which leads to distortion of reputation for herbal medicine in Korea<sup>7)</sup>.

There are several studies for safety or treatment of herbal medicine-related liver injury from an Oriental medicine aspect<sup>8,9)</sup>. The major studies on the epidemiology, diagnosis, affecting factors, or treatments of DILI even for herbal medicine-associated toxicity have been conducted in the western medicine field<sup>10,11)</sup>. Traditional Korean medicine (TKM) requires more studies, improved both quantitatively and qualitatively on the safety of herbal drugs and treatment of DILI.

This study reports the case of a patient with DILI

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from cold medicine who recovered by TKM-based treatments.

## Case Report

### 1. Characteristics of patient and medical history

A 47-year-old woman visited the hepatology department complaining of severe exhaustion, chills, fever, indigestion, nausea, sleep disturbance, and general body pain. She had already been diagnosed with abnormal liver function by a western clinic just before visiting the Oriental hospital. Laboratory test showed high levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) at 323 IU/L and 632 IU/L respectively, with normal range of alkaline phosphatase (ALP) and total bilirubin. The tests for viral infection and auto-immune hepatitis were negative. Abdominal ultrasonography revealed normal features (Fig. 1).

She was within the normal range of body mass index (BMI) as 22 without abdominal obesity. The patient doesn't use alcohol usually, and has no family history of hepatic diseases. She was homemaker but has been under a high level of psychological stress due to her rebellious teen-age son. She had experienced a hepatic episode of ten-times normal level of hepatic aminotransferase during treatment for traffic accident injury in 2009.

### 2. Herbal drugs and treatments

The patient was cared for as an inpatient, then an

outpatient. The patient was treated with Chungganpus syrup (three packs per day) mainly and other herbal prescriptions such as Ohpaesan according to the accompanying symptoms. Chungganpus is a 10ml syrup containing 2g extract from 13 herbs; 5g each of *Artemisia capillaris* Herba, *Carapax Trionycis*, *Semen Raphani*; 3g each of *Rhizoma Atractylodis Macrocephalae*, *Poria*, *Alismatis Rhizoma*, *Atractylodis Rhizoma*, *Salviae Miltiorrhizae Radix*; 2 g each of *Polyporus*, *Amomi Fructus*, *Aurantii Fructus*, and 1g of *Glycyrrhizae Radix* and *Helenii Radix*. Indirect moxibustion (KI1), acupuncture (mainly at HT7, SP3, LI4), and application of Miso-pack (a poultice of traditionally fermented bean paste) on the abdomen around the navel were daily practiced for 20 min.

### 3. Course of symptoms and lab examination

The patient had recently been taking western medicines to treat cold symptoms for one month, then felt whole body pain, severe exhaustion, indigestion, and nausea symptoms. After diagnosis of non-specific hepatitis, she was hospitalized at an Oriental hospital for nine days. During treatment as an inpatient, the patient almost recovered physical feeling including fatigue, indigestion and nausea while serum levels of AST, ALT and GGT lowered near to normal range (Table 1).

After nine days treatment inpatient, the patient had almost recovered to normal condition. However, the patient caught a common cold and took a western cold-medicine, and then complained of severe abdomen

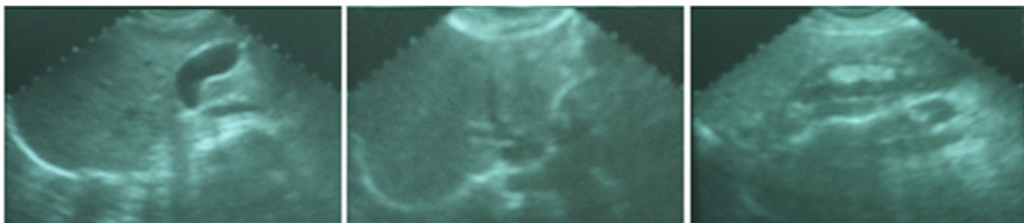


Fig. 1. Images from ultrasonography. Unremarkable sono-echogenicity was found in the both lobes of the liver and biliary system.

**Table 1.** Change of laboratory findings

Tested day(Hospitalized days)	AST(IU/L)	ALT(IU/L)	GGT(IU/L)	ALP(IU/L)	T. bilirubin(mg/dl)
Apr. 25, 2011 (Day 0)	323	632	-	83	0.3
Apr. 28, 2011 (Day 3)	58	260	46	85	0.6
May. 04, 2011 (Day 9)	50	85	45	84	0.5
May. 14, 2011 (Outpatient 7 days)	274	283	92	132	0.6
May. 21, 2011 (Outpatient 14 days)	209	265	142	136	1.0
Jun. 04, 2011 (Outpatient 28 days)	26	24	72	77	0.8
Jun. 21, 2011 (Outpatient 42 days)	20	11	21	62	-

The physiological levels of upper limit are 40, 40, 64 and 120 IU/L for AST, ALT, GGT and ALP respectively in this study.

discomfort as well as general fatigue. The blood test showed a rapid elevation of ALT and AST to 274 IU/L and 284 IU/L, respectively. The patient stopped taking the western medicine, and then the physical symptoms and laboratory values gradually were normalized. After one month later, all physical symptoms and laboratory tests reached normal status. The patient was continuously given Chungganpus syrup and other Oriental therapies.

## Discussion and Conclusion

The study of DILI is difficult due to the heterogeneity of its clinical presentation and course of injury, the delay in establishing its diagnosis, the lack of standardized criteria, and underreporting of cases of DILI or their final outcomes<sup>12</sup>. In general, the range of clinical course of DILI is very wide as from asymptomatic transient elevations in liver enzymes to liver failure. No specific biomarkers or 'gold standard' diagnostic tests for DILI exist, so many cases face difficulty in confirming DILI<sup>13</sup>.

The case of this report showed a typical pattern of acute hepatitis as she complained of general tiredness, troubles in gastric function, chills, fever, and general body pain accompanied with rapid elevation of serum hepatic enzymes about 10-fold. The accurate reason for the hepatic disorder could not identified, however hepatotoxicity by cold-drugs was easily suspected.

The causality of DILI is established based on the clinical history, chronology of exposure and injury, and exclusion of other causes of liver injury<sup>14</sup>. This patient had a similar history of hepatic injury during treatment for a traffic accident 2 year ago. The hepatotoxicity happened after taking continuously some western medicines, including acetaminophen, for one month.

Causality assessment algorithms such as RUCAM scale measuring the strength of association between suspected DILI and an implicated agent have been developed<sup>15</sup>. Acetaminophen is known as the most common cause of drug-induced liver disease and acute liver failure worldwide<sup>16</sup>. No suspected cause was presented to the patient and re-administration with acetaminophen relapsed hepatotoxicity. The RUCAM score of the patient was 13, indicating very high probability of DILI. Therefore, acetaminophen was strongly believed as a causative agent for hepatitis in this patient. The liver injury was not due to acetaminophen itself but to a toxic metabolite (N-acetyl-p-benzoquinone imine) which is produced by cytochrome P-450 enzymes in the liver<sup>17</sup>.

DILI is generally classified into three types; hepatocellular, cholestatic, or mixed type, according to the pathological features, and it is defined as a rise in either ALT or ALP level<sup>18,19</sup>. This case showed a typical hepatocellular type of hepatotoxicity because of both ten times of upper limit of physiological

ALT level and normal range of ALP. Acetaminophen-induced hepatic damage is known as hepatocellular type<sup>20</sup>. Symptoms related to cholestasis, such as fatty liver, high level of bilirubin, itching and jaundice, were not present.

The patient felt severe fatigue under western medicine, so she wanted to consult an Oriental doctor. The key treatment for DILI is to quit the administration of the causing agent and to take full rest. In order to avoid physical and psychological stress, she was hospitalized, and given an herbal drug (Chungganpus syrup), acupuncture, moxibustion and Miso-pack on the abdomen. Chungganpus syrup is a multi-herbal extraction, and has been evidenced to possess hepatoprotective and antioxidant actions<sup>21,22</sup>. The treatment principle for the patient was to support the recovering ability of hepatic damage, and minimum herbal drugs were prescribed. After recovering healthy status and discharge from hospital, she had a relapse due to cold medicine from a western clinic. The reason was thought to be that the liver was extremely sensitive to the re-challenge of the same drug. About one month later, the patient completely recovered from DILI and was strictly advised to avoid acetaminophen in the future.

In general, any drug, including herbal medicines, can cause hepatic injury. The full knowledge of DILI and paying attention are important in reducing the risk of DILI and its proper treatment. This case report might provide helpful information for caring for patients with DILI, whether from western or herbal drugs.

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