



## Case Report

## Recovery from hepatitis A after Korean medicine-based treatment: a case report



Chan-Ran Park <sup>a, b, c</sup>, Gayoung Lee <sup>a, b, c</sup>, Chang-Gue Son <sup>a, c</sup>, Jung-Hyo Cho <sup>a, c</sup>, Nam-Hun Lee <sup>a, b, c, \*</sup>

<sup>a</sup> Department of Internal Medicine, Graduate School of Korean Medicine, University of Daejeon, Daejeon, Republic of Korea

<sup>b</sup> Department of Internal Medicine, Cheonan Korean Medicine Hospital of Daejeon University, Cheonan, Republic of Korea

<sup>c</sup> Liver and Immunology Research Center, Dunsan Korean Medicine Hospital of Daejeon University, Daejeon, Republic of Korea

## ARTICLE INFO

## Article history:

Received 25 June 2019

Received in revised form 1 November 2019

Accepted 2 November 2019

Available online 7 November 2019

## Keywords:

Hepatitis A

Korean medicine

Chungganplus

## ABSTRACT

**Background:** Many studies reported that Korean medicine (KM) is effective for treating liver disease, including hepatitis A. However, KM, specifically with herbal medicine (Chungganplus, CGP) has not been reported yet. We aimed to report a patient with hepatitis A who was treated with KM including CGP, acupuncture, and moxibustion for 12 days.

**Methods:** A 39-year-old man with hepatitis A who was hospitalized for 12 days after being admitted to our hospital with abdominal pain, diarrhea and vomiting. We prescribed CGP three times a day, with acupuncture performed twice daily and moxibustion at conception vessel (CV)-12 once a day. Follow-up blood tests have been done 4 times during the admission in order to access the effect of the treatment.

**Results:** In 12 days the symptoms had disappeared and the blood test results improved steadily. His AST level have declined from 1,189 IU/L to 44 IU/L, ALT from 2,423 IU/L to 127 IU/L, r-GTP from 1,347 IU/L to 339 IU/L, ALP from 384 IU/L to 205 IU/L, and total bilirubin from 3.6 mg/dL to 0.89 mg/dL.

**Conclusion:** This case suggests that KM-based treatment using CGP may be effective for hepatitis A with no adverse effect. Further research and clinical trial on CGP would be needed to make the basis more valid.

© 2019 Korea Institute of Oriental Medicine. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Hepatitis A virus (HAV) is a non-enveloped RNA virus and it causes hepatitis A infection.<sup>1</sup> HAV infection occurs worldwide with 1.4 million cases annually.<sup>2</sup> HAV is transmitted via the fecal to oral route, including direct contact with infected patients and drinking contaminated water contaminated with fecal matter.<sup>3</sup> The symptoms are similar to those of other types of viral hepatitis and include fever, anorexia, nausea, vomiting, brown urine, fatigue, abdominal discomfort and jaundice.<sup>4</sup> While approximately 70% of younger than 6 years are asymptomatic, most older individuals have typical symptoms and jaundice develops in about 70%.<sup>5</sup>

There is a safe, highly efficacious vaccine for hepatitis A, which has lowered the disease incidence. In Korea, as sanitation and living condition have improved, the antibody-positive rate in 20-

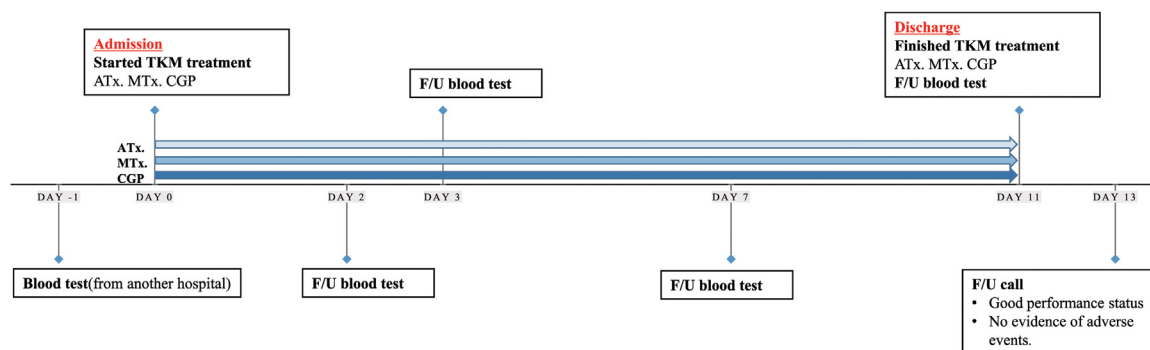
40-year-olds has decreased and they became more susceptible to hepatitis A.<sup>6</sup>

Hepatitis A has a complex pathology and various symptoms, so herbal medicines composed of multiple compounds are emerging as potential therapy.<sup>7</sup> Herbal medicines can improve liver function and patients treated with herbal medicines tend to have significantly lower risk of acute exacerbation of hepatitis, cirrhosis and hepatoma than those who did not.<sup>8</sup>

This case report examined the efficacy of KM treatment in hepatitis A. The patient was treated with herbal medicine (Chungganplus, CGP), acupuncture, and moxibustion for 12 days and his liver function test (LFT) results improved steadily. Although there are many reports on the effects of KM for hepatic injuries, few have examined hepatitis A cases treated with KM. Therefore, we present this outcome as evidence of the utility of KM for treating hepatitis A. This study followed the Case Report Guideline (CARE guidelines)<sup>9</sup> and was approved by the Institutional Review Board of Daejeon University Korean medical hospital (DJUMC-2019-BM-09).

\* Corresponding author at: Department of Internal Medicine, Graduate School of Korean Medicine, University of Daejeon, 62 Daehak-ro, Dong-gu, Daejeon, 34520, Republic of Korea

E-mail address: [nhlee@dju.kr](mailto:nhlee@dju.kr) (N.-H. Lee).



**Fig. 1.** KM treatment and blood tests during the admission period. ATx., Acupuncture treatment; CGP, Chungganplus; F/U, Follow up; KM, Korean medicine; MTx., Moxibustion treatment.

## 2. Case report

### 2.1. Patient characteristics and medical history

On May 7, 2019, a 39-year-old man visited Cheon-An Korean Medicine Hospital of Daejeon University with gastrointestinal symptoms including fatigue, abdominal pain, diarrhea, jaundice, nausea, vomiting, chills and fever more than 1 week. He had been diagnosed with hepatitis A on May 6, 2019, elsewhere one day before presenting to our hospital. He used to smoke a pack of cigarettes a day and drank 2–3 bottles of alcohol per day, at least 3 days a week. In 2009, abnormal aminotransferase levels were detected in a physical examination and he had a family history of liver cirrhosis.

### 2.2. Diagnosis, treatment, and symptom course

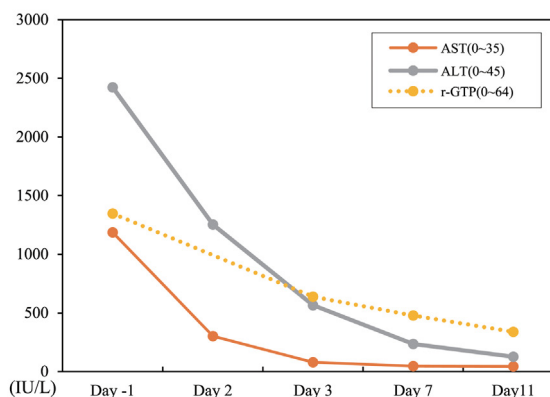
The day before the patient visited the hospital, the serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (r-GTP), alkaline phosphatase (ALP) and total bilirubin measured previously elsewhere were markedly elevated. HAV IgM was positive, so he was diagnosed as Hepatitis A. On May 8, HBs Ag, HBs Ab, and HCV Ab were all negative, so other types of hepatitis were ruled out.

On admission, his sclerae were yellow due to jaundice and he kept vomiting even when he drank water and he could barely eat food. Based on his symptoms, he was diagnosed with “disharmony between liver and spleen” and received KM treatment including herbal medicine CGP, acupuncture, and moxibustion (Fig. 1). CGP includes thirteen herbs: *Artemisiae Capillaris Herba* (*Yin Chen Hao*), *Trionycis Carapax* (*Bie Jia*), *Raphani Semen* (*Lai Fu Zi*), *Atractylodis Rhizoma Alba* (*Bai Zhu*), *Hoelen* (*Fu Ling*), *Alismatis Rhizoma* (*Ze Xie*), *Atractylodis Rhizoma* (*Cang Zhu*), *Salviae Miltiorrhizae Radix* (*Dan Shen*), *Polyporus* (*Zhu Ling*), *Aurantii Immaturus Fructus* (*Zhi Shi*), *Amomi Fructus* (*Sha Ren*), *Glycyrrhizae Radix* (*Gan Cao*), *Aucklandiae Radix* (*Mu Xiang*) (Supplement 1). He was given CGP three times a day to alleviate liver damage. Acupuncture treatment at LR3, LI4, ST36, GV20, CV12 points were also performed for 15 min twice a day with 0.20 × 30 needles (DongBang Co., Seoul, Korea) to relieve the abdominal pain and improve liver function.<sup>10–12</sup> Moxibustion was performed on his abdomen at CV12 acupoint to enhance gastric motility.<sup>13</sup> With this treatment, his vomiting stopped within 2 days and the abdominal pain and diarrhea disappeared within 7 days. Finally, the general symptoms and blood chemistry improved (Fig. 2a and b).

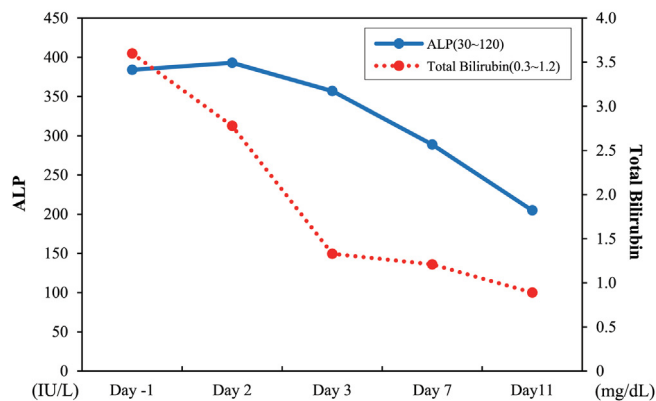
## 3. Discussion

Hepatitis A, infectious disease that occurs worldwide and is commonly transmitted in contaminated environment.<sup>14</sup> The

### (A) AST, ALT, r-GTP



### (B) ALP, Total Bilirubin



**Fig. 2.** (A) The serum ALT, AST, r-GTP; (B) The serum ALP, Total Bilirubin values examined during the admission period. ALP, Alkaline phosphatase; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; r-GTP, Gamma glutamyl transpeptidase.

seroprevalence patterns of hepatitis A in Korea have changed over the past 40 years. Asymptomatic infections in children have decreased with improved sanitation and living conditions. Consequently, the seroprevalence of HAV antibodies in young people has fallen from 63.8% of people in their 20s in 1979 to 5.4% in 1996.<sup>15</sup> In 2007, the seroprevalence of anti-HAV of Koreans in their 30s to 50s was over 70%, while it was only 2% in those in their 20s.<sup>16</sup> So the susceptible population in Korea has changed from those under 10 years of age to people 20–40 years of age.<sup>6,17</sup> With the increasing infection rate, the number of cases with atypical symptoms is increasing, and has become a socio-economic problems.<sup>18</sup>

There is no specific treatment for hepatitis A and symptomatic therapy is commonly used. Hepatitis A causes various gastrointestinal and systemic symptoms, so herbal medicines composed of multi-compounds can be useful.<sup>19</sup>

CGP soft extract which was prescribed for the patient, is comprised of 13 herbs. Some major herbs and key molecules of CGP are scopoletin of *Artemisia Capillaris* Herba, glycyrrhizin and liquiritin of *Glycyrrhizae Radix*, naringin of *Raphani Semen*, and Rosmarinic acid of *Salvia Miltiorrhiza Radix*. These components have hepatoprotective actions including antioxidative and immune modulating effects. Here, we present the fingerprinting analysis of CGP (Supplement 2).<sup>20</sup> CGP restores liver function, improves hepatic injury, chronic hepatitis and alcoholic liver disease and prevents liver cirrhosis through diverse mechanisms such as inhibition of natural killer T cell mediated liver toxicity, downregulation of TGF- $\beta$  expression and matrix metalloproteinases resulting in attenuation of liver fibrosis.<sup>21–27</sup> It can also reduce oxidative stress of liver tissues, exceeding the ability of hepatic cells to remove reactive oxygen.<sup>28</sup>

Acute hepatitis A is usually self-limited and less than 1% of patients progress to fulminant hepatic failure.<sup>29</sup> Without medical treatment, about 85% of hepatitis A patients' clinical symptoms recover within 2–3 months.<sup>30</sup> Although spontaneous remission is common in hepatitis A, the appropriate treatment can alleviate the patient's pain and discomfort. Our patient's symptoms disappeared in about 1 week. Furthermore, compared to the LFT results on admission, the follow-up LFT levels decreased steadily and rapidly. Therefore, CGP, acupuncture and moxibustion appear to be effective for shortening the treatment period compared to the spontaneous remission.

This study has some limitations. First, unfortunately follow-up blood tests after the patient had been discharged from the hospital could not be conducted. Second, it could be difficult to distinguish the genuine effect of treatment from the natural self-limited progression of the disease. However there is a study that supports the possibility of hepatitis A progressing to severe condition. Kim et al.<sup>31</sup> reported that heavy alcohol drinking is one of the risk factors that leads to fulminant hepatitis. The patient in this case report has a history of habitual heavy drinking and the prognosis of the patient's hepatitis A could be dangerous. Therefore appropriate treatment was necessary, and the KM treatment improved the patient's liver function and related symptoms.

This paper reports a patient with hepatocellular type hepatitis A successfully treated with KM, including herbal medicine CGP, acupuncture and moxibustion. We expect that this study can be a basis for further studies, and systematic study involving more patients is needed to confirm these results.

#### Author contributions

CRP: Conceptualization, Writing - original draft. GL: Conceptualization. CGS: Writing - review & editing. JHC: Writing - review & editing. NHL: Conceptualization, Supervision, Writing - review & editing.

#### Conflict of interest

The author declares no conflict of interest.

#### Funding

This study received no specific grant from any funding agency.

#### Ethical statement

This study has been approved by the Institutional Review Board of Daejeon University Korean medical hospital (DJUMC-2019-BM-09).

#### Data availability

Data will be made available upon request.

#### Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.imr.2019.11.001>.

#### References

- Linder KA, Malani PN. Hepatitis A. *JAMA* 2017;318(23):2393.
- Wooten D, Karris M. The As and Bs of HIV and hepatitis co-infection. *Trop Med Infect Dis* 2019;4(2):55.
- Nainan OV, Xia G, Vaughan G, Margolis HS. Diagnosis of hepatitis A virus infection: a molecular approach. *Clin Microbiol Rev* 2006;19(1):63–79.
- Koenig KL, Shastry S, Burns MJ. Hepatitis A virus: essential knowledge and a novel identify-isolate-inform tool for frontline healthcare providers. *West J Emerg Med* 2017;18(6):1000–7.
- Matheny Samuel C, Kingery Joe E. Hepatitis A. *Am Fam Physician* 2012;86(Dec 1(11)):1027–34.
- Lee H, Cho HK, Kim JH, Kim KH. Seroepidemiology of hepatitis A in Korea: changes over the past 30 years. *J Korean Med Sci* 2011;26(6):791–6.
- Yarnell Eric, Kathy Abascal BS. Herbal medicine for viral hepatitis. *Altern Complement Ther* 2010;16(3):151–7.
- Hong M, Li S, Tan HY, Wang N, Tsao SW, Feng Y. Current status of herbal medicines in chronic liver disease therapy: the biological effects, molecular targets and future prospects. *Int J Mol Sci* 2015;16(12):28705–45.
- Carpenter J, Barber M, Aronson JK, et al. The CARE guidelines: Consensus-based clinical case reporting guideline development. *Glob Adv Heal Med* 2013;2:38–43.
- Fernandez Rojas R, Liao M, Romero J, Huang X, Ou KL. Cortical network response to acupuncture and the effect of the hegu point: an fNIRS study. *Sensors (Basel)* 2019;19(2).
- Cha MH, Bai SJ, Lee KH, et al. Acute electroacupuncture inhibits nitric oxide synthase expression in the spinal cord of neuropathic rats. *Neuro Res* 2010;32(suppl 1):96–100.
- Liu HJ, Hsu SF, Hsieh CC, et al. The effectiveness of Tsu-San-Li (St-36) and tai-chung (Li-3) acupoints for treatment of acute liver damage in rats. *Am J Chin Med* 2003;29(02):221–6.
- Su YS, Xin JJ, Yang ZK, et al. Effects of different local moxibustion-like stimuli at Zusanli (ST36) and Zhongwan (CV12) on gastric motility and its underlying receptor mechanism. *Evid Based Complement Alternat Med* 2015.
- Zhang XS, Lo Iacono G. Estimating human-to-human transmissibility of hepatitis A virus in an outbreak at an elementary school in China, 2011. *PLoS One* 2018;13(9):1–14.
- Roh HO, Sohn YM, Park MS, et al. A seroepidemiologic study of hepatitis A virus in the healthy children and adolescent in Kyonggi-do Province. *Korean J Pediatr Infect Dis* 1997;4(2):232.
- Song YB, Lee JH, Choi MS, et al. The age-specific seroprevalence of hepatitis A virus antibody in Korea. *Korean J Hepatol* 2007;13(1):27–33.
- Heo JY, Song JY, Noh JY, et al. Low level of immunity against hepatitis A among Korean adolescents: vaccination rate and related factors. *Am J Infect Control* 2013;41(10):e97–100.
- Park HS, Choi BY, Kwon YD. Rapid increase in the national treatment costs for hepatitis A infections in Korea. *Tohoku J Exp Med* 2012;226(1):85–93.
- Stickele F, Schuppan D. Herbal medicine in the treatment of liver diseases. *Dig Liver Dis* 2007;39(4):293–304.
- Kim HG, Han JM, Lee HW, et al. CGX, a multiple herbal drug, improves cholestatic liver fibrosis in a bile duct ligation induced rat model. *J Ethnopharmacol* 2013;145(2):653–62.
- Kim JY, Joung JY, Kang JY, Son CG, Cho JH. Acute viral hepatitis A with cholestatic hepatitis treated with traditional Korean medicine: a case report. *J Korean Med* 2015;36(4):114–21.
- Shin JW, Wang JH, Park HJ, Choi MK, Kim HG, Son CG. Herbal formula CGX ameliorates LPS/d-galactosamine-induced hepatitis. *Food Chem Toxicol* 2011;49(6):1329–34.
- Kim HG, Han JM, Lee HW, et al. CGX, a multiple herbal drug, improves cholestatic liver fibrosis in a bile duct ligation-induced rat model. *J Ethnopharmacol* 2013;145(2):653–62.
- Shin JW, Son JY, Oh SM, et al. An herbal formula, CGX, exerts hepatotherapeutic effects on dimethylnitrosamine-induced chronic liver injury model in rats. *World J Gastroenterol* 2006;12(38):6142–8.

25. Choi WJ, Shin JW, Son JY, et al. Toxicological study of the hepatotherapeutic herbal formula, chunggan extract, in beagle dogs. *World J Gastroenterol* 2006;12(46):7497–502.
26. Cho J, Lee Y, Seo S, Yoo H, Choi W, Lee Y. A clinical report about 57 patients with chronic liver disease. *J Korean Oriental Med* 2000;21(4):112–21 [In Korean, English abstract].
27. Shin JW, Wang JH, Kim HG, Park HJ, Bok HS, Son CG. CGX, a traditional Korean medicine ameliorates concanavalin A-induced acute liver injury. *Food Chem Toxicol* 2010;48(12):3308–15.
28. Hu XP, Shin JW, Wang JH, et al. Antioxidative and hepatoprotective effect of CGX, an herbal medicine, against toxic acute injury in mice. *J Ethnopharmacol* 2008;120(1):51–5.
29. Lemon SM. Type a viral hepatitis. *N Engl J Med* 1985;313(17):1059–67.
30. Koff RS. Clinical manifestations and diagnosis of hepatitis A virus infection. *Vaccine* 1992;10(Suppl 1):S15–7.
31. Kim JI, Kim YS, Jung YK, et al. Factors influencing the severity of acute viral hepatitis A. *Korean J Hepatol* 2010;16(3):295–300.