

Original Article

A Clinical Observation of Seroconversion on Chronic Hepatitis B Treated with a Herb Prescription

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Objective : Report on a hepatitis B patient with abnormal AST/ALT, HBeAg(+), and habitual diarrhea stemming from irritable colon.

Methods : Lab-evaluation of intervals of herb medicine treatment for a patient with hepatitis B with HBeAg and irritable colon.

Result & Conclusion : AST/ALT level was normalized and did not rise again. Seroconversion to HBeAb repeatedly appeared just during the time of the treatment, but typically repeated seroconversion between treatment period and no treatment period confirmed that the treatment was effective for the immune system against hepatitis B. The exact mechanism is not clear but the result provides an indication that oriental herbal medicine has potential capacity to treat liver diseases.

Key Words : hepatitis B, seroconversion, herbs

Introduction

The goal of antiviral therapy is HBeAg seroconversion, and preferably HB surface Ag seroconversion, as this latter end-point is associated with sustained immune control and the halting of disease progression⁶⁾.

At present, five agents are currently approved for the treatment of chronic hepatitis B infection: interferon (IFN), lamivudine, and adefovir are widely used; the more recently marketed agents are entecavir and peginterferon alfa-2a⁹⁾.

Despite the development of potent new antiviral

drugs, the percentage of HBeAg seroconversion is approximately 35%. Immunosuppression before antiviral administration has recently been investigated with contradictory results¹⁸⁾.

In traditional oriental medicine, a multi-herb decoction is used for the treatment of liver diseases such as hepatitis, fatty liver, hepatocirrhosis and jaundice³⁻⁵⁾.

Not always, but sometimes, there are effective results from treating chronic hepatitis with oriental medicine. Here we present a case of typically changed seroconversion of HBsAg and normalized AST/ALT level with just herb medicine treatment.

Report of the case

1. Name and Age

Kim o o (female, 23 at first visit)

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2. Chief Complaints

- 1) fatigue 2) indigestion
- 3) vomiting 4) diarrhea 5) edema

3. Onset

1)-5) about 3-4 years ago, intermittently severe and in progress

4. Family History

- 1) brother: hepatitis B carrier
- 2) mother: hepatitis B carrier

5. Past History

- 1) gastritis
- 2) irritable colon: diarrhea type

6. Present illness

The patient visited on 15 March 2002; she had visited several local medical centers and been diagnosed with chronic hepatitis B. She was treated with many western medicines, but the result of treatments did not meet her expectations. During the therapy, she suffered from fatigue, indigestion, diarrhea, vomiting and edema.

7. Impression

- 1) hepatitis B with HBeAg
- 2) irritable colon: diarrhea type

8. Herb med treatment

The decoction below was prescribed to the patient 8 times per day for 10 days. To treat edema and diarrhea, *Polyporus*, *Hoelen* and *Mori Cortex* were added temporarily. After consistent treatment for 6 months from the first visit, there have been only 2 further treatments.

Scientific name of Herb	Dose(g)
<i>Artemisiae capillaris</i>	16
<i>Astragali Radix</i>	12
<i>Atractylis Rhizoma</i>	16
<i>Magnoliae officinalis</i>	4
<i>Agastachis Herba</i>	4
<i>Hordei Fructus</i>	4
<i>Aurantii nobilis</i>	4
<i>Ponciri Fructus</i>	4
<i>Atractylis Rhizoma</i>	4
<i>Perillae Folium</i>	4
<i>Arecae Pericarpium</i>	12
<i>Portulacae Herba</i>	8
<i>Cassiae Cortex</i>	4
<i>Zingiberis Rhizoma</i>	6
<i>Salviae Radix</i>	6
<i>Taraxaci Herba</i>	8
<i>Polyporus</i>	0-8
<i>Hoelen</i>	0-4
<i>Mori Cortex</i>	0-8
Total amount	116

9. Progress

1) Phase 1 (2002/3/15-2002/7/26)

- Treatment : Intensive herb medicine treatment with no intermittence.

• Results of AST&ALT

Item \ Date	3/15	3/27	4/18	4/26	8/day
AST	100	84	64	61	normal
ALT	112	93	59	54	normal
Remark					other hospital lab. check

• Result of Immunology (2002/07/26)

Item	Result	Reference	Lab Remark
HBe-Ag (RIA)	Positive (2.34)	Negative <2.00	Please recheck in 3 weeks
HBe-Ab (RIA)	Positive (61.11)	Negative <49.90	Please recheck in 3 weeks

• Changes of symptoms

The symptoms of the patient are all gone.

2) Phase 2 (2002/09/03-2003/01/11)

- Treatment: No herb medicine treatment
- Result of AST&ALT : within normal range (other hospital lab. check)
- Result of immunology (2003/01/11)

Item	Result	Reference	Lab Remark
HBe-Ag (RIA)	Positive (5.29)	Negative <2.00	
HBe-Ab (RIA)	Negative (25.64)	Negative <49.90	

3) Phase 3 (-2004/03/22)

- Treatment : Intermittent herb medicine treatment
- Result of AST&ALT : within normal range (other hospital lab. check)
- Result of immunology (2004/03/22)

Item	Result	Reference	Lab Remark
HBe-Ag (RIA)	Negative (0.80)	Negative <2.00	
HBe-Ab (RIA)	Positive (54.08)	Negative <49.90	Please recheck in 3 weeks
HBs-Ag (RIA)	Positive (69.69)	Negative <1.00	
HBs-Ab (RIA)	Negative (0.38)	Negative <1.00	

4) Phase 4 (-2006/04/day)

- Treatment : No herb medicine treatment & other hospital lab. recheck
- Result of AST&ALT : within normal range (other hospital lab. check)
- Result of immunology (2006/04/day) : just for (+)&(-) (other hospital lab. check)

Item	Result
HBe-Ag(RIA)	Positive (+)
HBe-Ab(RIA)	Negative (-)
HBs-Ag(RIA)	Positive (+)
HBs-Ab(RIA)	Negative (-)

Discussion

The natural history of hepatitis B e antigen (HBeAg) - positive chronic hepatitis B - is very heterogeneous. Age at acquisition is a major factor in determining the natural history of chronic infection. The vigor of the host immune response to the virus, viral factors (genotype, core promoter mutations, and duration of viral replication) as well as exogenous factors (alcohol, immune suppression) all influence the severity of disease⁶⁾.

The goal of anti-chronic hepatitis B therapy is to prevent the progression of liver disease to cirrhosis, which may develop into liver failure or HCC. The aims of treatment are reduction of HBV viral load and normalization of ALT activity. Among HBeAg positive patients, an important marker is the loss of e antigenemia followed by seroconversion to anti-HBe positivity¹⁶⁾.

NGC (National Guidelines Clearinghouse) offers guidelines for patients with HBeAg-positive chronic hepatitis B as follows:

Alanine aminotransferase (ALT) greater than 2 times normal or moderate/severe hepatitis on biopsy. These patients should be considered for treatment. Treatment should be delayed for 3 to 6 months in persons with compensated liver disease to determine if spontaneous HBeAg seroconversion occurs. Treatment may result in virologic, biochemical, and histologic response (Grade I: randomized controlled trials) and also appear to improve clinical outcome (Grade II-3: multiple time series, dramatic uncontrolled experiments). Treatment may be initiated with interferon alpha (IFN-alpha), lamivudine, or adefovir as the 3 treatments have similar efficacy.

ALT persistently normal or minimally elevated (<2 times normal). These patients should not be

initiated on treatment (Grade I). Liver biopsy may be considered in patients with fluctuating or minimally elevated ALT levels, and treatment initiated if there is moderate or severe necro-inflammation¹⁰⁾.

HBeAg positive patients can be treated with interferon alpha or lamivudine. The former requires longer treatment and the results are disappointing. Lamivudine is a promising agent in the treatment of chronic hepatitis B¹³⁾, but success is hampered by a high relapse rate and the emergence of viral resistance^{1,19)}.

Even with an HBeAg/anti-HBe seroconversion time \geq 6 months, the rate of relapse was still higher in patients with chronic hepatitis B that received lamivudine. The patients with long-term lamivudine treatment should be observed and have frequent follow-up visits. Thus, a 1-year treatment with lamivudine (LMV) for chronic hepatitis B resulted in the relapse of HBV viraemia in most of the patients who had been positive for HBeAg, although the clinical course ameliorated in some patients. In addition, HBV DNA remained positive and ALT values were elevated at the end of the follow-up in the three patients who had been treated with interferon, with or without LMV, during the follow-up²⁾.

To treat liver diseases including chronic hepatitis B, there has been various research both experimentally and clinically by doctors of oriental medicine^{4,5,15,20)}. However, the mechanism is not perfectly discovered and the herb prescriptions are so many that it is difficult to evaluate their efficacy compared with each other. In this situation, the evaluation will be made by quality, not quantity. Quality treatment means an outstanding effect for the patient who is difficult to treat.

The patient in this case was intensively treated for 6 months with herb medicine. Because of the

sequelae experienced after the treatments of western medicine, the author regarded her to be a complex patient. However, after a few weeks of treatment, the patient gradually recovered. Especially after her diarrhea stopped, her whole condition improved very fast. According to the lab findings after treatment, both HBsAg and HBsAb were positive (phase1). The laboratory was surprised and recommended a recheck after 3 weeks. The transaminase levels were normalized over 6 months and didn't rise after that. It was difficult to continue the treatment because the transaminase level was already normal and showed signs of seroconversion. Furthermore, she lived in a rural area far from the hospital of the author so she often had blood tests done at other hospitals after the improvement. At the beginning day of Phase 2, she found decreasing HBsAb. After the same herb medication was treated for two intermittent 10-day courses, HBsAb reappeared (phase3). If HBsAg had existed constantly, the author was not sure it was the effect of the decoction because there was a possibility of natural seroconversion. She now regularly has her transaminase level checked. In the last check the HBeAg reappeared again, but she was not worried and felt no need for further treatment because the transaminase level is still always normal. She believes that the seroconversion will appear someday as long as AST/ALT level is in the normal range.

Conclusion

The patient has not reached the aim of consistent seroconversion to HBsAb with herb medication treatment, but HBsAb appearing with treatment and disappearing without treatment confirmed that the decoction affected the sero-

conversion from HBsAg to HBsAb. In most cases of western medical treatment, relapse of HBsAg means increase of AST/ALT level which means failure of the treatment, but in this case, consistently normalized ASL/ALT level meant that according to the NGC, the patient was not a patient with hepatitis B but just a carrier who should not be initiated with treatment (grade I).

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