

Clearance of Hepatitis B virus from Chronic Carrier by Oriental Medicine Treatments

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Objective : To study the Oriental Medicine-based strategies or therapeutics for chronic HBV infection.

Methods : A chronic HBV carrier was treated with only oriental therapies. Then, serum biochemical parameters were serially chased, and change of HBV-DNA level was evaluated.

Result : The biochemical indicators (AST, ALT, gamma-GTP, bilirubin) fluctuated during the treatment period. After one episode of drastic elevation of serum aminotransferase, HBV-DNA disappeared from the blood along with normalization of biochemical parameters within two years of beginning treatment.

Conclusion : Oriental Medicine-based therapeutics could be an alternative strategy against chronic infection of HBV.

Key Words : Chronic hepatitis, HBV, Oriental medicine, herbs

Introduction

Hepatitis B virus (HBV) is one of the most common human infectious viruses, of which 350 million people world-wide are chronic carriers¹⁾. Approximately a million deaths per year are associated with chronic HBV infection leading to liver cirrhosis or hepatocellular carcinoma^{2,3)}. HBV is particularly endemic to Asian countries including China and Korea^{4,5)}. Although an intensive nationwide vaccination program has reduced HBV infection, a very high carrier rate of HBV (5-6%) is still closely connected with the top 5th cause of death in Korea⁶⁾.

Although many antiviral suppressants as well as interferon therapy are currently prescribed to chronic HBV carriers, they still have major limitations due to lack of response or high appearance of resistance^{7,8)}. So, more optimal strategies or new drugs promising

adequate clinical outcome have to be found. HBV has characteristics of commonly chronic infection, noncytolytic and oncogenic virus, and associated chronic liver injury is not caused by the virus itself, but by an unfavorable response of host immune cells and inflammatory cytokines⁹⁾.

Traditionally, Oriental medicine has treated patients with hepatic diseases, including chronic HBV infection, for thousands years. Oriental Medicine has emphasized the side of the body opposite to the pathogenic agent, and adopted an immunologic strategy for caring these illnesses. We herein reported a case of a chronic HBV carrier, in whom the serum HBV was completely eliminated by Oriental treatments.

We hope that this study will contribute to developing Oriental medicine-based strategies or therapeutics for chronic HBV infection.

• Received : 22 August 2008

• Revised : 30 October 2008

• Accepted : 3 November 2008

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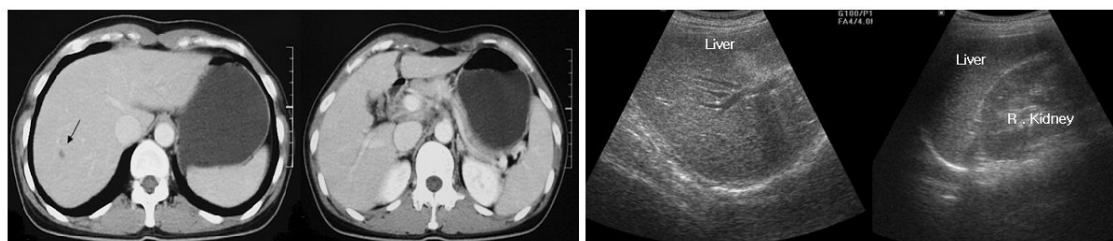


Fig. 1. Images from computed tomography and ultrasonography.

There was no specific pathologic findings except only one cyst at right lobe of liver in computed tomography and ultrasonography.

Report of the case

1. Characteristics of patient and diagnosis

A 40-year-old woman visited my department worrying about her state as a chronic carrier of HBV. She has been suffering from chronic fatigue and dysfunction of digestion. Laboratory data showed high HBV-DNA level ($1 \times 10^8 >$ copies/ml), HBeAg positive, HBeAb negative, abnormal range of serum aminotransferase (114 for AST and 134 for ALT), but lowed number of platelets and WBC. Abdominal ultrasonography and computed topography revealed no abnormal features except one cyst (1 cm) in the right liver lobe (Fig. 1). The patient had been aware of the infection of HBV since high school, with a positive family history consisting of two sisters and two brothers also infected. Although vertical transmission was strongly assumed, it couldn't be verified because of the early death of their mother from a non-HBV related disease.

2. Herbal drugs and treatments

CGX syrup regularly and other herbal prescrip-

tions such as *Soisihotang* (小柴胡湯) extract occasionally were given to the patient (Table 1). Acupuncture, moxibustion (CV4, CV8) and pharmacopuncture (CV4 with *Yidam*) were practiced weekly. She was supplied with 5% DW or normal saline with vitamin complex but no other western medicine during her periods of hospitalization.

3. Course of symptoms and lab examination

The patient had visited several western doctors about her chronic HBV carrier status before coming to the oriental hospital. However, the patient didn't get any medical treatment owing to negative expectations such as low efficacy or drug resistance. She started to take oriental therapies including herbal drugs (CGX syrup everyday), and acupuncture treatment, moxibustion and pharmacopuncture to support her natural immunity once per week. General laboratory tests, including serum HBV-DNA level and ultrasonography, were performed every three months, and computed topography yearly.

The patient felt a good physical feeling such as decrease of fatigue severity along with treatments,

Table 1. Prescription and compositional volume of drugs

CGX syrup (grams per prescription)	Artemisia capillaris Herba (5), Trionycis Carapax (5), Raphani Semen (5), Atractylodis Macrocephalae Rhizoma (3), Poria cocos (3), Alismatis Rhizoma (3), Atractylodis Rhizoma (3), Salvia Miltiorrhizae Radix (3), Polyporus (2), Amomi Fructus (2), Ponciri Fructus (2), Glycyrrhizae Radix (1), Helenii Radix (1)
Soisihotang (grams per prescription)	Bupleuri Radix (12), Scutellariae Radix (8), Ginseng Radix (4), Pinelliae Rhizoma (4), Glycyrrhizae Radix (2), Zingiberis Rhizoma (4), Zizyphi inermis Fructus (2)

while high levels of AST and ALT became normalized over 6 months. Thereafter, the patient suddenly felt severe fatigue, poor digestion, slight tenderness and mild jaundice, and presented rapid increase of serum aminotransferase (by 450-500 for AST and ALT respectively), AFP (over 1,000 ng/ml) and decrease of albumin level (by 2.8 g/dL) after 14 months of treatment. The patient was hospitalized to take bed rest and intensive management in the oriental hospital for 2 weeks. Intensive examination considering hepatitis type A virus (HAV) or hepatitis type D virus (HDV) infection, malignant tumor or toxic liver injury were all negative.

After 2 weeks treatment in hospital, the serum aminotransferase level rapidly decreased and normalized within 2 months. In particular, HBV-DNA level began to reduce by 7.2×10^3 (copies/ml), and it reached at undetectable level ($<2 \times 10^3$ copies/ml) in the following three consecutive tests having 3-month intervals. However, the HBsAg test continually was positive as combination with negative in HBsAb test. As per expectations, all blood or biochemical parameters including AST, ALT, GGT, AFP, albumin, ESR and platelet counts were maintained within

normal ranges (Table 2).

Discussion and Conclusion

HBV is a noncytopathic virus, so induces cellular destruction not by virus itself but from immunopathologic mechanisms^{10,11}. Accordingly, the clinical outcome of HBV-infection depends on interactions between the host's protective immunity and HBV. Many factors such as genotype, virus titer, time or route of infection are importantly associated with this immune response^{12,13}.

This patient is strongly supposed to have been infected from her mother via vertical transmission. In general, infection with HBV at birth when the human body is immature in immune status becomes a chronic carrier up to 90% of the time, giving higher risk of progression into liver cirrhosis and hepatoma^{14,15}. This patient also had kept high titer of HBV-DNA in serum $>1.0 \times 10^8$ before visiting the Oriental hospital. The serum aminotransferase was usually maintained as slightly higher or rarely as high as double normal range.

The level of AST and ALT radically increased to

Table 2. Change of laboratory findings and HBV-DNA number

Tested days	AST (IU/L)	ALT (IU/L)	GGT (IU/L)	ALP (IU/L)	T. bil. (mg/dl)	AFP (ng/ml)	Albumin (g/dl)	ESR (mm/hr)	platelets (104/ μ l)	HBV-DNA [†] (copies/ml)
06년 01월*	83	95	38		1.0		3.6			
06년 03월	114	134	57	102	1.1	121.3		22	9.3	$>1.0 \times 10^8$
06년 06월	52	77	40	175		58.9		24	11.8	4.5×10^6
06년 10월	25	23	19	89		6.04		15	12.8	2.0×10^6
07년 02월	35	41	18	93		2.76		21	13.3	2.1×10^6
07년 03월	448	485	113	113	2.4	1033	2.8	35	10.6	5.2×10^7
07년 04월	162	223	107	94	1.6	1008	3.0	35	9.4	4.3×10^6
07년 05월	33	33	54	73	1.3	330	3.8	43	14.8	7.2×10^3
07년 07월	22	18	24	65	1			25	11.5	$<2.0 \times 10^3$
07년 10월	19	15	19	56	0.8			22	13.8	$<2.0 \times 10^3$
08년 01월	19	18	15	52	0.5	6.88		9	15.5	$<2.0 \times 10^3$

* It was tested before visiting Dunsan Oriental hospital.

† HBV-DNA number was quantified in NEODIN Medical Institute (Seoul, Korea).

over 10 times normal with corresponding physical symptoms at the time point of 14 months treatment. The clinical pattern seemed like acute hepatitis, which led the patient admit herself to my hospital. Thereafter, titer of HBV-DNA started to decrease rapidly along with normalization of serum AST and ALT. As in the present case, strong and adequate response to HBV chronic infection likely shows severe inflammation of the liver. This phenomenon frequently brings clearance of HBV by immunological response. However, disappearance of HBsAg and production of HBsAb generally takes over ten years after the HBV-DNA undetectable event⁷⁾. Thus, this patient needs to track the final defense response of appearance of HBsAb.

Oriental medicine has been developed based on an immunologic strategy, which enhances the body's defense capacity against pathogenic microorganisms including HBV¹⁶⁾. This patient had received Oriental therapies supporting natural immunity in the form of herbal drugs, acupuncture, moxibustion and pharmacopuncture. It is proposed these Oriental treatments therapeutically reacted to chronic HBV infection in this case.

To date, no curative anti-viral drug has been developed against any viruses infecting the human body. Currently, many Oriental medical resources-based studies are being performed on new drugs with anti-viral activity against HBV or anti-cirrhotic effects¹⁷⁻¹⁹⁾. Especially, anti-inflammatory or hepatoprotective effects of herbal drugs in clinical reports indicate the potential of Oriental medicine as immune-based treatment^{20,21)}. Those facts may provide us a clue to successfully fight HBV or HBV-related chronic liver diseases in the future. However, we need to explore the complex interaction between HBV and host reaction further, as well as oriental therapies and liver environment.

I herein briefly described one chronic HBV carrier, probably infected from infancy, in whom HBV was cleared via Oriental medicine treatment. It is hoped that this report helps promote development of Oriental medicine-derived therapies for chronic HBV carriers.

Acknowledgement

This study was supported by a grant from the Oriental Medicine R&D Project (B070031), Ministry of Health and Welfare, Republic of Korea.

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