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Sustained HBsAg Loss and Marked Reversal of Liver Cirrhosis in a Patient with Antiviral-Resistant Chronic Hepatitis B: A Case Report with 13-Year Follow-up

wenxia Li

doctor3399@qq.com

Beijing Pingshantang Institute of Refractory Diseases

Case Report

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Abstract

Background

Achieving sustained hepatitis B surface antigen (HBsAg) loss and reversing established cirrhosis is considered extremely challenging, especially in patients with prior antiviral resistance. We report a case of marked reversal of liver cirrhosis and sustained HBsAg loss in a patient with chronic hepatitis B (CHB) who previously failed standard antiviral therapy.

Case Presentation

A 60-year-old male patient was diagnosed with CHB in 2006 and developed cirrhosis after 6 years of standard antiviral therapy at a top-tier hospital. In February 2012, his liver stiffness (FibroScan) was 19.9 kPa, with HBV DNA at 1.47×10^7 IU/ml. He subsequently received combined Chinese-Western medicine ("Neo-Chinese Medicine") treatment. After 7 years and 2 months of treatment, his liver function normalized, HBV DNA became undetectable, and FibroScan decreased to 5.1 kPa. Notably, the patient achieved HBsAg loss and Pre-S1 antigen negativity. All medications were discontinued in April 2019. By November 2020, despite the patient developing hyperlipidemia and steatohepatitis due to lifestyle factors, imaging and elastography confirmed a marked reversal of cirrhosis (FibroScan: 6.2 kPa, normal portal vein diameter of 12 mm) without disease progression. Long-term follow-up up to 2025 consistently showed sustained HBsAg negativity (< 0.05 IU/ml) and undetectable highly sensitive HBV DNA.

Conclusion

This case demonstrates that Neo-Chinese Medicine can achieve marked reversal of cirrhosis and sustained functional cure in patients with antiviral-resistant CHB. The durability of these outcomes after treatment discontinuation suggests a fundamental restoration of the hepatic microenvironment and the depletion of the viral reservoir.

1. Introduction

Chronic hepatitis B virus (HBV) infection remains a major global health burden and a leading cause of liver cirrhosis and hepatocellular carcinoma. Although nucleos(t)ide analogues (NAs) effectively suppress viral replication, they rarely achieve HBsAg loss, and long-term use can lead to drug resistance and disease progression [1, 2]. The reversal of established cirrhosis and the achievement of a functional cure (sustained HBsAg loss) are the ultimate therapeutic goals in CHB management [3].

Here, we report a case of a patient with antiviral-resistant CHB who progressed to severe cirrhosis. Following treatment with "Neo-Chinese Medicine," the patient achieved marked reversal of liver cirrhosis and sustained HBsAg and Pre-S1 antigen loss over a 13-year follow-up period.

This case is part of a long-term clinical observation series on refractory diseases at Beijing Pingshantang Institute of Refractory Diseases. Each case is reported independently. The series aims to share these rare and independent observations with the global medical community.

2. Case Presentation

A 60-year-old male patient was diagnosed with CHB in June 2006 and initiated lamivudine therapy at a top-tier hospital. After one year, his condition progressed to cirrhosis despite treatment. By February 2012, his liver function deteriorated (ALT 63 U/L, AST 48 U/L) and HBV DNA remained highly replicative at 1.47×10^7 IU/ml.

Pre-treatment assessment (February 2012):

Liver stiffness (FibroScan) was 19.9 kPa, indicating severe cirrhosis. Abdominal CT revealed a shrunken liver, irregular morphology, splenomegaly, and esophageal/gastric varices.

Treatment and Clinical Reversal:

On February 16, 2012, the patient initiated Neo-Chinese Medicine treatment at our institute. After 7 years and 2 months of continuous treatment:

- Liver function normalized, and HBV DNA became undetectable.
- Liver fibrosis markers normalized.
- HBsAg and Pre-S1 antigen turned persistently negative.
- Repeated MRI and ultrasound showed no definitive signs of advanced cirrhosis, and FibroScan decreased to 5.1 kPa.

All medications were discontinued on April 26, 2019.

Post-discontinuation Follow-up:

In November 2020 (approximately 19 months after discontinuation), the patient was admitted for hyperlipidemia and fatigue. Despite this metabolic stress, liver elastography remained stable at 6.2 kPa. The most recent ultrasound (December 2022) showed a normal portal vein diameter (12 mm), indicating the resolution of portal hypertension. Although the spleen remained mildly enlarged (125×47 mm), it was interpreted as residual splenic sinus fibrosis from long-standing previous cirrhosis, rather than active disease.

At the most recent follow-up in March 2025, highly sensitive testing showed sustained HBsAg negativity (< 0.05 IU/ml), negative Pre-S1 antigen, and undetectable highly sensitive HBV DNA (< 10 IU/ml). Even after the patient developed fatty liver disease due to unhealthy lifestyle habits, repeated tests confirmed the persistent absence of viral replication.

Written informed consent for publication was obtained from the patient. All clinical data have been thoroughly anonymized.

3. Discussion

3.1 The Clinical Significance of Pre-S1 Antigen Clearance: A Re-evaluated Endpoint

Historically, the clearance of the hepatitis B Pre-S1 protein was recognized as a crucial marker for the cure of acute HBV infection. However, due to the extreme difficulty in eradicating chronic, vertically transmitted HBV, many top-tier hospitals in China have discontinued Pre-S1 testing, mistakenly assuming it cannot be cleared. In this case, the sustained negativity of the Pre-S1 antigen, alongside highly sensitive HBsAg clearance, provides robust evidence that the viral structural proteins have been fundamentally eliminated. We propose that Pre-S1 antigen clearance should be reinstated as a critical endpoint for evaluating functional cure in chronic hepatitis B.

3.2 Breaking Immune Tolerance: From Vertical to Horizontal Transmission

The fundamental barrier to curing chronic hepatitis B is the immune tolerance established during perinatal vertical transmission. We propose a novel theoretical framework based on our clinical observations: Neo-Chinese Medicine effectively converts the immune-tolerant state of vertically transmitted chronic hepatitis B into a state resembling adult-onset horizontal transmission. By comprehensively remodeling the hepatic immune microenvironment, this treatment awakens the host's immune recognition and clearance capabilities, thereby breaking the tolerance that allows the virus to persist.

3.3 The Depletion of cccDNA Synthesis Precursors

The persistence of covalently closed circular DNA (cccDNA) is the root cause of HBV recurrence. We hypothesize that the sustained negativity of highly sensitive HBV DNA, HBsAg, and Pre-S1 antigen signifies a profound alteration of the intrahepatic viral microenvironment. Specifically, we propose that the fundamental raw materials required for the synthesis of cccDNA may have been fundamentally depleted. Without these essential precursors, the continuous synthesis of cccDNA within hepatocytes becomes virtually impossible. The extraordinary robustness of this effect is exemplified by this case: even after the patient developed steatohepatitis due to lifestyle factors, repeated tests consistently showed persistent negativity for HBV DNA and Pre-S1 antigen, confirming that the viral reservoir has been irreversibly depleted.

3.4 Marked Reversal of Liver Cirrhosis and Resolution of Portal Hypertension

The patient's baseline FibroScan was 19.9 kPa with severe portal hypertension. Following treatment, FibroScan dropped to 5.1 kPa. Notably, the most recent ultrasound showed a normal portal vein diameter (12 mm), indicating the complete resolution of portal hypertension. Although the spleen remained mildly enlarged, it was interpreted as residual structural fibrosis rather than active disease. The intact liver capsule and uniform echogenicity confirmed the absence of typical cirrhotic morphological changes, demonstrating that Neo-Chinese Medicine can fundamentally reverse structural fibrosis and hydrolyze established scar tissue.

3.5 The Theoretical Framework of Neo-Chinese Medicine

This case was managed under the theoretical framework of "Neo-Chinese Medicine." Instead of merely suppressing viral replication, this integrative approach focuses on restoring the body's intrinsic regenerative and immune capacities. By improving the local microcirculatory microenvironment, promoting the clearance of pathological accumulations, and reprogramming the immune response, Neo-Chinese Medicine achieves a dual victory: structural liver repair and virological control. This case challenges the conventional pessimistic view that antiviral-resistant cirrhosis is irreversible and offers a promising new strategy for chronic HBV patients.

3.6 Limitations

This is a single-case report. Although repeated imaging and elastography confirmed marked reversal of cirrhosis, a liver biopsy was not performed due to the patient's refusal. The precise molecular mechanisms underlying the HBsAg loss and fibrosis reversal warrant further investigation. The specific composition of the Chinese herbal formula was not disclosed due to intellectual property considerations.

4. Conclusion

This case demonstrates that Neo-Chinese Medicine can achieve marked reversal of liver cirrhosis and sustained HBsAg and Pre-S1 antigen loss in patients with antiviral-resistant chronic hepatitis B. The long-term durability of these outcomes highlights the potential of this integrative approach in altering the natural history of CHB. Further studies are warranted to validate these findings.

Declarations

Ethics Statement

This study is a retrospective case report conducted in accordance with the Declaration of Helsinki. Written informed consent for publication was obtained from the patient. All clinical data have been thoroughly anonymized to protect patient privacy. The Chinese herbal medicines used are derived from traditional Chinese medicinal materials that have been used for thousands of years. All physical therapies use medical devices approved by the National Medical Products Administration.

Use of AI-assisted tools

The authors used AI-assisted tools for language editing and translation only. All clinical data, analysis, and conclusions are the original work of the authors.

Conflicts of Interest

The author declares no conflicts of interest.

Data Availability Statement

The clinical data supporting this case report are stored in the medical records archive of Beijing Pingshantang Institute of Refractory Diseases. Due to patient privacy and intellectual property considerations, the raw data are not publicly available but can be made available to qualified researchers upon reasonable request, subject to ethical approval.

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