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UNUSUAL CONCURRENT HBSAG AND ANTI-HBS POSITIVITY IN CHRONIC HEPATITIS B WITH COMPENSATED CIRRHOSIS

Bui Thai Huy Nguyen[1], Hoang Phuong Tran[1], Nguyen Tra Uyen Ho[1], Thai Nguyen Ma[1], Tin Nghia Tran[2], Thi Thao Linh Nguyen[3], Duy Linh Nguyen[4]

[1] Department of Infectious Diseases, Can Tho University of Medicine and Pharmacy, Can Tho City, Vietnam
[2] Department of Biochemistry, Can Tho University of Medicine and Pharmacy, Can Tho City, Vietnam
[3] Department of Parasitology, Can Tho University of Medicine and Pharmacy, Can Tho City, Vietnam
[4] Department of Surgery, Can Tho University of Medicine and Pharmacy, Can Tho City, Vietnam

Corresponding author's e-mail: ndlinh@ctump.edu.vn

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ABSTRACT

Background: The simultaneous positivity of hepatitis B surface antigen (HBsAg) and its corresponding antibody (anti-HBs) is a rare serological paradox in chronic hepatitis B. Its pathogenesis is not fully understood but may involve hepatitis B virus (HBV) S gene mutations leading to immune escape or complex host immune dysfunction. Recognizing this pattern is clinically important, as it may indicate advanced liver disease.

Case report: A 54-year-old man with no history of alcohol abuse or liver disease presented with persistent bloating and dyspepsia. Laboratory tests revealed concurrent positivity for HBsAg (1438.5 S/Co) and anti-HBs (136.6 mIU/ml), hepatitis B e antigen (HbeAg) positivity, and a high HBV deoxyribonucleic acid (DNA) viral load (4.3 ×10^6 copies/ml). Transaminases were mildly elevated, platelet count was reduced, and liver elastography indicated cirrhosis (F4). The patient was diagnosed active chronic hepatitis B with concurrent HBsAg and anti-HBs positivity, complicated by compensated cirrhosis and started on tenofovir 300 mg daily. After 4 months of treatment, the patient showed clinical improvement, with marked reductions in liver enzyme levels and HBV DNA viral load.

Conclusion: The concurrent positivity of HBsAg and anti-HBs is a rare serological finding that may reflect a complex HBV infection with a higher risk of progressive liver disease. This case illustrates that this unusual serological pattern can be associated with a high viral load and cirrhosis, highlighting the need for close monitoring of liver function, HBV DNA levels, and antiviral treatment response.

KEYWORDS

Chronic hepatitis B, HBsAg and anti-HBs coexistence, serological paradox, immune escape variants, cirrhosis

LEARNING POINTS

- Rare serological finding involving concurrent HBsAg and anti-HBs positivity in chronic hepatitis B with cirrhosis.
- Pattern that may indicate immune escape and active viral replication requiring closer clinical attention.
- Close monitoring of liver function, hepatitis B virus deoxyribonucleic acid levels, and antiviral treatment response is essential in such cases.

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INTRODUCTION

Hepatitis B virus (HBV) infection remains a major global public health concern, driving chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC), with an estimated 820,000 deaths annually[1]. Vietnam, as a hyper-endemic region, reports hepatitis B surface antigen (HBsAg) prevalence above 8%, corresponding to nearly 10 million chronic carriers[2], highlighting the need for effective screening and management. HBsAg is the hallmark of active infection, whereas hepatitis B surface antibody (anti-HBs) indicates protective immunity, either from vaccination or resolved infection. Conventionally, HBsAg and anti-HBs are considered mutually exclusive, with successful seroconversion to anti-HBs serving as a key therapeutic goal in chronic HBV management. However, rare cases demonstrate simultaneous positivity of HBsAg and anti-HBs, a phenomenon termed a serological paradox. The clinical implications of this remain uncertain, with potential explanations including transient seroconversion, assay cross-reactivity, or circulating viral immune escape variants that evade antibody neutralization[3]. Emerging evidence suggests that such cases may be associated with advanced liver disease or high viral replication, underscoring the need for careful evaluation[4,5]. This article reports a case of a 54-year-old male with chronic HBV infection and compensated cirrhosis exhibiting concurrent HBsAg and high-titer anti-HBs positivity, aiming to provide insights into its clinical significance, underlying mechanisms, and implications for disease monitoring and management in high-risk patients.

CASE DESCRIPTION

A 54-year-old male farmer presented with persistent bloating and dyspepsia. He had no history of alcohol abuse, hepatotoxic drug intake, or substance use. Physical examination was unremarkable, without jaundice. Initial laboratory screening excluded hepatitis C virus (HCV) co-infection (anti-HCV S/Co 0.2). Serological testing revealed a paradoxical profile: highly reactive HBsAg (S/Co 1438.5) alongside a high-titre anti-HBs (136.6 mIU/ml). Virological assessment showed elevated HBV deoxyribonucleic acid (DNA) (4.3 $\times 10^6$ copies/ml), indicating active viral replication. Liver enzymes were mildly elevated (aspartate aminotransferase 70.8 U/l; alanine aminotransferase 78.3 U/l), Gamma-glutamyl transferase was elevated (114 U/l), platelets were reduced (90 $\times 10^9$/l), and alpha-fetoprotein (AFP) was markedly increased (104 ng/ml), suggesting advanced liver pathology.

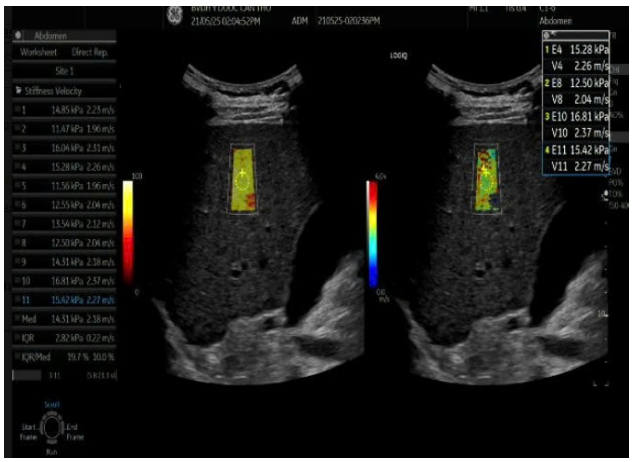


Figure 1. Transient ultrasound elastography of the liver showing multiple stiffness measurements ranging from 11.47 to 16.81 kPa (2.04–2.37 m/s), consistent with METAVIR stage F4 fibrosis and compensated cirrhosis.

Abdominal ultrasound demonstrated regional fatty liver infiltration, and multiple hypoechoic hepatic nodules. Transient elastography confirmed significant fibrosis (F4), consistent with compensated cirrhosis *(Fig. 1)*.

Based on the combination of serological paradox, high viral load, transaminitis, and imaging-confirmed cirrhosis, a diagnosis of active-phase chronic hepatitis B with compensated cirrhosis was established. Treatment with tenofovir 300 mg daily was initiated, with routine outpatient monitoring planned to assess viral suppression, liver function, and surveillance for hepatocellular carcinoma. After 1 month of treatment, the patient's symptoms improved, levels of liver enzymes decreased slightly but remained unstable, and the viral load had not yet been reassessed. The patient continued regular antiviral therapy. After 4 months of treatment, the patient experienced complete resolution of clinical symptoms. Laboratory tests showed more stable liver function and enzymes, a slight improvement in platelet

Parameter	First visit	After 1 month	After 4 months	Reference range
HBsAg (S/Co)	1438.5	–	–	<1.0
Anti-HBs (mIU/ml)	136.6	–	–	<10.0
HBeAg (S/Co)	1042.5	–	–	<1.0
Anti-HCV (S/Co)	0.2	–	–	<1.0
HBV DNA (copies/ml)	4.3 ×10⁶	–	3.9 ×10	<12 (quantification limit)

Abbreviations: HBsAG, hepatitis B surface antigen; Anti HBs, hepatitis B surface antibody; HbeAg, hepatitis B e antigen; HCV, hepatitis C virus; HBV, hepatitis B virus.

Table 1. Serological and virological findings. Serological tests were performed by enzyme-linked immunosorbent assay; HBV deoxyribonucleic acid measured by reverse transcription-polymerase chain reaction.

Parameter	First visit	After 1 month	After 4 months	Reference range
AST (U/l)	70.8	90.7	62	5–34
ALT (U/l)	78.3	103	86	<55
GGT (U/l)	114	121.3	77.9	9–64
Platelets (×10^9/l)	90	98	101	150–400
AFP (ng/ml)	104	115	12.1	≤8
Prothrombin time (s)	17.5	16.8	16.2	13.0
INR	1.34	1.28	1.23	0.8–1.2
Albumin (g/l)	40.9	–	48.8	35–50
Total bilirubin (μmol/l)	8.2	–	7.5	≤17.1
Elastography	Liver stiffness measured 14.31 kPa with an IQR/median of 19.7%, corresponding to METAVIR stage F4 fibrosis (cirrhosis)	–	Liver stiffness measured 13.2 kPa with an IQR/median of 18%, corresponding to METAVIR stage F4 fibrosis (cirrhosis)	–

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; AFP, alpha-fetoprotein; INR, international normalised ratio; IQR, interquartile range.

Table 2. Liver function, hematology, and elastography.

count, and a marked reduction in HBV DNA viral load. AFP returned to within the normal range, and abdominal ultrasound revealed no lesions suggestive of hepatocellular carcinoma. The timeline of serological, and virological findings is summarized in *Table 1* and liver function, haematology, and elastography are summarized in *Table 2*.

DISCUSSION

This case highlights the rare serological paradox of simultaneous HBsAg and anti-HBs positivity in a patient with active chronic hepatitis B and compensated cirrhosis. While HBsAg and anti-HBs are typically mutually exclusive, recent reports indicate that coexistence, although uncommon (1–7% prevalence)[6,7], may occur more frequently in patients with high viral loads or specific S gene mutations[5]. Our patient had high HBV DNA (4.3 ×10^6 copies/ml), elevated transaminases, thrombocytopenia, and markedly raised AFP, underscoring a high-risk phenotype for advanced liver disease and hepatocellular carcinoma.

The underlying mechanism likely involves viral immune escape, where S gene mutations alter HBsAg antigenicity, rendering anti-HBs antibodies non-neutralizing. Partial host immune dysfunction may further permit active viral replication despite robust antibody production[8]. The coexistence of HBsAg/anti-HBs in this context should not be interpreted as benign or indicative of imminent seroclearance; rather, it may serve as a biomarker of complex, uncontrolled infection requiring intensive monitoring.

Concurrent HBsAg and anti-HBs positivity in chronic hepatitis B indicates complex immune changes and potential liver disease progression. Recent studies have shown that patients with this serological profile often have higher HBV DNA loads, prolonged elevation of liver enzymes, and increased rates of cirrhosis or HCC compared with those who are positive for HBsAg alone[9,10].

Limitations of this report include single-patient observation, and short follow-up, preventing definitive conclusions regarding prognosis or treatment response. Nonetheless, the paradoxical simultaneous positivity of HBsAg and anti-HBs represents a complex serological phenomenon in chronic hepatitis B. This case report illustrates that this phenotype can be strongly correlated with high-risk clinical parameters, including high viral replication and advanced liver disease (compensated cirrhosis). The underlying pathology is highly suspected to involve the development of viral immune escape mutants or severe immunological dysfunction, which prevents effective antibody-mediated viral clearance. Identification of this unusual serological pattern mandates heightened clinical suspicion and intensive follow-up to effectively manage the associated significant risks of liver disease progression and malignant transformation.

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