Clin. Lab. 2026;72:XXX-XXX

CASE REPORT

A Case of Discordant Hepatitis B Core Antibody Results Across Different Immunoassay Platforms in a Chronic HBV Patient

Miaomiao Cai, Kejie Xie

Department of Clinical Laboratory Center, Shaoxing People's Hospital, Shaoxing, P.R. China

ABSTRACT

Background: **Hepatitis B core antibody (Anti-HBc) is an antibody that appears earlier after hepatitis B virus (HBV) infection and disappears the latest after recovery of hepatitis B. Detection of anti-HBc can effectively determine the infection status of hepatitis B.**
Methods: **This report describes a rare serological pattern observed in a patient with chronic hepatitis B virus infection during routine testing. The patient had both high positive results for hepatitis B surface antigen (HBsAg) and e antigen (HBeAg), and a high level of HBV DNA. However, the initial test result of anti-HBc using a Wantai instrument was negative. By using different testing platforms and, combined with the patient's medical history, the cause of the false negative result of anti-HBc test was determined.**
Results: **After thorough examination from multiple aspects and rechecking on multiple platforms, it was found that different manufacturers' immunological detection systems (Wantai, Roche, Abbott) gave inconsistent results. On Wantai, anti-HBc was repeatedly measured as being highly negative, but the re-examination results on Roche and Abbott detection platforms were positive. This case highlights that in a specific immune activation state with high viral load, different detection methods may lead to discrepancies in the interpretation of weakly positive or borderline samples.**
Conclusions: **When the anti-HBc of patients who have been or are currently infected with the hepatitis B virus is negative, laboratory workers and clinical doctors should be aware of this potential analytical discrepancy. We should adopt multiple methods for verification to analyze and review the test results, combined with the patient's clinical case data, in order to avoid incorrect diagnosis and treatment for the patients.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250858)

Correspondence:
Kejie Xie
Medical Clinical Laboratory Shaoxing People's Hospital
No. 568, North Zhongxing Road
Shaoxing City, 312000 Zhejiang Province
China
Phone: +86 13906756226
Email: xiekej@163.com

Case Report accepted September 4, 2025

KEYWORDS

hepatitis B core antibody, interference, methodological differences, immunoassay

INTRODUCTION

Hepatitis B virus (HBV) infection is a global public health issue [1]. The "two pairs and one half" serological test for hepatitis B is the cornerstone for diagnosing the HBV infection status, determining the disease stage and immune response. Among them, hepatitis B core antibody is one of the earliest serological markers after HBV infection, and it is usually lifelong positive, serving as a key indicator for determining past or current infection [2]. This report presents a case where the false

Table 1. HBV markers result of the patient at different times.

Marker	August 6, 2023	November 7, 2024	April 26, 2025	Reference value
HBV DNA (IU/mL)	/	$3.82 * 10^8$	$1.36 * 10^7$	< 20
HBsAg (IU/mL)	> 250	> 250	69,951.49	< 0.05
Anti-HBs (mIU/mL)	0.36	0.59	< 2.00	< 10.00
HBeAg (COI)	1,619.57	1,640.99	568.50	< 1.00
Anti-HBe (COI)	60.82	72.11	2.00	< 1.00
Anti-HBc (COI)	2.22	1.87	to be confirmed	< 1.00
Anti-HBc IgM (COI)	0.14	0.15	/	< 1.00

Table 2. Repeated test results of anti-HBc on the Wantai platform.

Test items	Initial test	Double check	Dilution test	Reference value
Anti-HBc	0.49 COI	0.46 COI	< 1.00 COI	< 1.00 COI

Table 3. The results of anti-HBc in different testing platforms.

Instrument	Results	Reference value	Determination of results
Wantai	0.75 COI	< 1.00 COI	-
Roche	0.116 COI	> 1.00 COI	+
Abbott	2.47 COI	< 1.00 COI	+

negative result of anti-HBc in long-term hepatitis B virus-infected individuals was caused by the differences in detection platforms and also discusses the potential mechanism. The specific situation is as follows.

CASE PRESENTATION

A 32-year-old female patient has been infected with hepatitis B virus for over 10 years. In 2024, she started oral antiviral treatment. After stopping the medication for half a year, she came to our department of gastroenterology due to occasional fatigue and poor appetite. After examination, HBsAg and HBeAg were strongly positive, and the hepatitis B virus DNA had a high load, indicating active virus replication and strong infectivity. Strangely, the initial test of anti-HBc of this patient was negative, presenting a rare pattern of "HBsAg (+), HBeAg (+), Anti-HBc (-)". No significant abnormalities were found in the other examination indicators. This is seriously inconsistent with the clinical background of the patient's chronic infection and high viral replication. Based on the patient's history of being infected with the hepatitis B virus for over 10 years and the fact that the past tests for anti-HBc were all positive (Table 1), we hypothesized that the abnormal result this time might be caused by interfering substances in the sample or differences in the testing instrument and method. First, we ruled out the sample issue by checking the sample numbers and confirming that there were no problems such as hemolysis, lipemia, jaundice, clots, long-term storage, or improper blood collection. Then, we re-tested on the original platform and used the same serum sample to repeat the test on the Wantai instrument. The results were consistent with the previous ones and still negative. During the testing period, we ensured that the instrument and reagents were in good condition and the inter-laboratory quality control (IQC) was within the control range. After that, to rule out the "hook effect" caused by excessive antigen [3], we diluted the sample 1:10 and re-tested on the Wantai platform. The anti-HBc result was still negative, thus excluding the hook effect (Table 2). Finally, we conducted multi-platform verification. We sent the same serum sample to two other mainstream imported immunological testing platforms for testing. It was found that the Wantai platform measured a high negative result, while the Roche and Abbott platforms showed positive results (Table 3). Ul-

timately, the final report indicated that anti-HBc was positive.

DISCUSSION

The negative result of anti-HBc may be caused by various factors, such as no exposure to the hepatitis B virus, insufficient immune response after vaccination, active replication period of the virus [4], detection window period, abnormal immune system, and measurement method error. In conventional understanding, chronic HBV carriers (especially those with positive HBsAg and high viral load) have almost all positive anti-HBc. The pattern of anti-HBc negativity while HBs Ag is positive is extremely rare. However, this may occur during the stage of active viral replication, high infectivity, severe liver damage, prominent symptoms, and the early stage of hepatitis B infection or the active period of chronic carriers, as well as the initial stage of viral reactivation in an immunosuppressed state [5-8]. The core issue of this case lies in the fact that the same sample yielded completely different anti-HBc results on different testing platforms. This discrepancy is not due to errors in the sample or the operation, but stems from the methodological characteristics of the testing system itself. Since the three instruments used for detection employ the chemiluminescence method, the potential reasons for the result differences might be the variations in antigen epitopes, the differences in the affinity of the reagents, and the distinctions in the sensitivity and critical values of the reagents. Specifically, anti-HBc is an antibody spectrum rather than a single antibody, the recombinant core antigens used by different manufacturers may be coated with different combinations of antigenic epitopes.

In conclusion, this case serves as a warning that the result of "HBsAg positive but anti-HBc negative" is highly likely to be an illusion in chronic infections and must be vigilantly monitored and verified. Laboratories should not rely solely on a single testing system. When the result contradicts the clinical history or other laboratory indicators, conducting multi-platform re-examination is an important means to ensure the accuracy of the results.

Sources of Support:
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Interest:
All authors declare that they have no competing interests.

References:

1. Sarin S K, Kumar M, Eslam M, et al. Liver diseases in the Asia-Pacific region: a Lancet Gastroenterology & Hepatology Commission. Lancet Gastroenterol Hepatol 2020;5:167-228. (PMID: 31852635)

2. Deng L J, Xu Y, Huang J. Developing a double-antigen sandwich ELISA for effective detection of human hepatitis B core antibody. Comp Immunol Microbiol Infect Dis 2008;31:515-26. (PMID: 18242704)

3. Chen M, Tian Y, Zhang D, Ren W and Wang W. An improved method for rapid identification of hook effect samples in HBsAg quantitative assay. J Virol Methods 2022;309:114606. (PMID: 35963582)

4. Wang J, Yan X, Chen Y, et al. Characteristics of hepatitis B core antibody level in the natural history of chronic hepatitis B. Discov Med 2018;26:119-25. (PMID: 30586535)

5. Ram M, Anaya J M, Barzilai O, et al. The putative protective role of hepatitis B virus (HBV) infection from autoimmune disorders. Autoimmun Rev 2008;7:621-5. (PMID: 18603025)

6. Chiu C Y, Ahmed S, Thomas S K, et al. Hepatitis B Virus Reactivation in Patients Receiving Bruton Tyrosine Kinase Inhibitors. Clin Lymphoma Myeloma Leuk 2023;23:610-5. (PMID: 37150651)

7. Salpini R, D'Anna S, Alkhatib M, et al. Kinetics of hepatitis B virus replication in anti-HBc positive/HBsAg-negative people with HIV switching to tenofovir sparing therapy. Int J Infect Dis 2025; 150:107294. (PMID: 39505254)

8. Drößler L, Lehmann C, Töpelt K, et al. HBsAg-negative/anti-HBc-positive patients treated with rituximab: prophylaxis or monitoring to prevent hepatitis B reactivation? Infection 2019;47: 293-300. (PMID: 30689161)