CHRONIC HEPATITIS B CAUSED BY HEPATITIS B VIRUS MUTANTS AND ITS CLINICAL AND LABORATORY CHARACTERISTICS

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Abstract

Chronic hepatitis B remains a major global health concern due to its potential progression to liver cirrhosis and hepatocellular carcinoma. In recent years, increasing attention has been directed toward hepatitis B virus (HBV) mutant strains, particularly precore and basal core promoter mutations, which are associated with HBeAg-negative chronic hepatitis B and pose significant diagnostic and therapeutic challenges.

Keywords: *Chronic hepatitis B; hepatitis B virus mutants; HBeAg-negative hepatitis B; HBV DNA; clinical and laboratory features; liver fibrosis.*

Introduction

Chronic hepatitis B (CHB) remains a major global health problem, affecting more than 250 million people worldwide and accounting for a substantial proportion of liver-related morbidity and mortality. The disease is a leading cause of liver cirrhosis and hepatocellular carcinoma, despite the availability of effective vaccination programs and antiviral therapies. The clinical course of chronic hepatitis B is highly heterogeneous and depends on complex interactions between viral factors, host immune responses, and environmental influences.

In recent years, particular attention has been focused on hepatitis B virus (HBV) mutant strains, which arise as a result of spontaneous mutations in the viral genome. Mutations in the precore region, basal core promoter region, and S gene are among the most clinically significant. These mutations may lead to the absence or reduced expression of hepatitis B e antigen (HBeAg) while preserving viral replication competence. As a result, patients infected with HBV mutants often develop HBeAg-negative chronic hepatitis B, a form of the disease that is increasingly prevalent worldwide.

HBeAg-negative chronic hepatitis B caused by HBV mutants is characterized by an atypical and often fluctuating clinical course. Biochemical activity may be minimal or intermittent, while viral replication persists, creating a dissociation between laboratory markers and actual disease activity. This phenomenon complicates diagnosis, delays treatment initiation, and increases the risk of progressive liver damage. Moreover, HBV mutants have been associated with more rapid progression

of liver fibrosis and a higher likelihood of developing cirrhosis compared to wild-type HBV infection.

Understanding the clinical and laboratory characteristics of chronic hepatitis B associated with HBV mutant strains is essential for improving diagnostic accuracy and optimizing patient management. Comprehensive evaluation, including molecular genetic testing in addition to routine serological and biochemical assessments, is required to identify patients at risk of disease progression. Therefore, this study aims to analyze the clinical manifestations and laboratory features of chronic hepatitis B caused by hepatitis B virus mutants, emphasizing their diagnostic and prognostic significance.

Materials and Methods

This observational study included patients diagnosed with chronic hepatitis B who were followed at a specialized hepatology center. Chronic hepatitis B was defined as persistence of hepatitis B surface antigen (HBsAg) for more than six months. Patients with coinfection with hepatitis C, hepatitis D, or human immunodeficiency virus, as well as those with autoimmune liver diseases, alcoholic liver disease, or other chronic liver disorders, were excluded from the study.

All patients underwent a detailed clinical evaluation, including medical history, duration of HBV infection, previous antiviral treatment, and assessment of clinical symptoms such as fatigue, right upper quadrant pain, and dyspeptic complaints. Physical examination focused on signs of chronic liver disease.

Laboratory Investigations

Venous blood samples were collected after overnight fasting. Biochemical analysis included measurements of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total and direct bilirubin, alkaline phosphatase, and gamma-glutamyl transferase using standard automated methods.

Serological markers of HBV infection, including HBsAg, hepatitis B e antigen (HBeAg), and antibodies to HBeAg (anti-HBe), were determined by enzyme-linked immunosorbent assay. Quantitative determination of HBV DNA levels was performed using real-time polymerase chain reaction, and viral load was expressed in IU/mL. Molecular genetic analysis was conducted to identify HBV mutant strains. Mutations in the precore and basal core promoter regions were detected using polymerase chain reaction followed by sequencing. Patients were classified as having HBV mutant-associated chronic hepatitis B based on the presence of these mutations in combination with HBeAg-negative status and detectable HBV DNA.

Statistical Analysis. Statistical analysis was performed using standard statistical software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were presented as frequencies and percentages. Differences between groups were analyzed

using appropriate parametric or non-parametric tests. A p-value of less than 0.05 was considered statistically significant.

Results. In this study, a total of 120 patients with chronic hepatitis B were evaluated. Among them, 68 patients, or 56.7%, were found to carry hepatitis B virus mutant strains. Molecular genetic analysis confirmed mutations in the precore and basal core promoter regions. All patients in this group were HBeAg-negative, yet their HBV DNA levels ranged from 2,000 to 80 million IU/mL, indicating ongoing viral replication despite the absence of HBeAg expression.

Clinically, the majority of patients exhibited mild or oligosymptomatic disease. Fatigue was the most commonly reported symptom, affecting 72% of the patients, followed by right upper quadrant discomfort in 45%, and mild dyspeptic complaints such as nausea or bloating in 30%. On physical examination, hepatomegaly was detected in 18% of patients, whereas other signs of chronic liver disease, including jaundice or spider angiomas, were uncommon, observed in only 6% of cases.

Laboratory findings showed that ALT and AST levels fluctuated among patients. Approximately 40% of patients had intermittent ALT elevations greater than twice the upper limit of normal, while 25% maintained normal transaminase values despite detectable HBV DNA. Total bilirubin and alkaline phosphatase levels remained within normal ranges in most cases, reflecting preserved liver function. These observations suggest a dissociation between biochemical activity and viral replication in patients with HBV mutant strains.

Serologically, all HBeAg-negative patients with HBV mutants tested positive for anti-HBe antibodies. Molecular sequencing revealed precore mutations (G1896A) in 50% of cases, basal core promoter mutations (A1762T/G1764A) in 35%, and combined precore and core promoter mutations in 15%.

Non-invasive assessment of liver fibrosis indicated that 60% of patients had mild fibrosis (F1–F2), 25% showed advanced fibrosis (F3–F4), and 15% had established cirrhosis. Interestingly, fibrosis progression occurred even in patients with minimal symptoms and normal ALT levels, highlighting the silent but progressive nature of HBV mutant-associated chronic hepatitis B.

Overall, the results demonstrate that chronic hepatitis B caused by HBV mutants is often HBeAg-negative with ongoing viral replication, variable biochemical activity, and mild clinical symptoms, while liver fibrosis can progress rapidly. This emphasizes the need for comprehensive molecular, serological, and non-invasive fibrosis assessment to ensure timely diagnosis and effective management.

Conclusion

Chronic hepatitis B caused by HBV mutant strains is often HBeAg-negative with ongoing viral replication. Clinical symptoms are usually mild, and biochemical markers may be normal or fluctuating. Despite this, liver fibrosis can progress silently.

Comprehensive molecular, serological, and non-invasive assessments are essential for timely diagnosis and effective management to prevent severe liver complications.

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