THE IMPACT OF PREMATURE DISCONTINUATION OF ANTIVIRAL THERAPY IN CHRONIC HEPATITIS B : A CASE REPORT

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ABSTRAK

Infeksi virus hepatitis B (HBV) kronis menimbulkan tantangan kesehatan masyarakat yang besar, yang berpotensi menyebabkan sirosis dan karsinoma hepatoseluler (HCC). Terapi antivirus yang efektif telah meningkatkan prognosis pasien, tetapi menghentikan pengobatan dapat mengakibatkan hasil yang merugikan. Seorang pria berusia 61 tahun dengan riwayat hepatitis B menghentikan terapi antivirus, yang menyebabkan penyakit kuning yang memburuk, nyeri perut, dan gejala lainnya. Pemeriksaan mengungkapkan disfungsi hati yang signifikan. Hepatitis B merupakan masalah kesehatan global. Analog nukleosida (NA) jangka panjang sangat penting untuk mengelola HBV. Penghentian NA sebelum waktunya dapat menyebabkan kekambuhan virologis dan klinis, yang memerlukan kepatuhan ketat terhadap pengobatan dan pemantauan berkelanjutan. Kasus ini menggarisbawahi pentingnya mematuhi terapi antivirus dan menyoroti perlunya pemantauan pasien yang waspada untuk mencegah penurunan kesehatan yang parah.

Kata kunci **:** hepatitis B kronis, kekambuhan klinis, kekambuhan virologis, pemantauan pasien, terapi antivirus

ABSTRACT

Chronic hepatitis B virus (HBV) infection poses a major public health challenge, potentially leading to cirrhosis and hepatocellular carcinoma (HCC). Effective antiviral therapies have improved patient prognosis, but discontinuing treatment can result in adverse outcomes. A 61-year-old male with a history of hepatitis B discontinued antiviral therapy, leading to worsening jaundice, abdominal pain, and other symptoms. Examination revealed significant liver dysfunction. Hepatitis B is a global health concern. Long-term nucleos(t)ide analogs (NAs) are essential for managing HBV. Premature discontinuation of NAs can cause virological and clinical recurrent, necessitating strict adherence to treatment and continuous monitoring. This case underscores the importance of adhering to antiviral therapy and highlights the need for vigilant patient monitoring to prevent severe health deterioration.

Keywords ***:*** *chronic hepatitis B, antiviral therapy, virological recurrent, clinical recurrent, patient monitoring*

INTRODUCTION

Chronic hepatitis B virus (HBV) infection poses a significant public health challenge due to its potential to cause chronic liver disease. Over time, this can progress to cirrhosis and lead to a range of serious complications. Since the 1990s, various treatments have been approved for HBV, which have been instrumental in reducing the risk of developing cirrhosis, end-stage liver disease, hepatocellular carcinoma, and subsequent mortality. These advancements in treatment have markedly improved the prognosis for individuals with chronic HBV infection, helping to manage the disease more effectively and enhancing the overall quality of life for affected patients. The continuous development and refinement of therapeutic strategies remain critical in addressing the long-term impacts of HBV infection (Akbar, dkk., 2022) (Spasojević, et al., 2018) (Kaewdech & Sripongpun, 2021).

Around 257 million individuals globally are infected with hepatitis B virus (HBV), which stands as the primary cause of cirrhosis and hepatocellular carcinoma (HCC). In many cases,

the initial HBV infection results in the body clearing the virus. However, for those who do not completely eliminate the virus, their immune system typically manages to control its replication, preventing significant health issues for a time. Unfortunately, this control is not always permanent. There are instances where the immune system's ability to manage the virus weakens, leading to the reactivation of HBV replication. This reactivation can result in increased viral load and subsequent liver damage, heightening the risk of progressing to cirrhosis or developing HCC. The potential for reactivation underscores the importance of ongoing monitoring and management of individuals with chronic HBV infection to mitigate these serious health risks (Liu, et al., 2022) (Rehermann & Thimme, 2019).

Effective antiviral therapy has been a cornerstone in the management of chronic HBV, significantly reducing the risk of progression to severe liver diseases such as cirrhosis, hepatocellular carcinoma, and liver failure. Despite the availability of effective treatments, discontinuation of therapy remains a critical issue, potentially leading to adverse clinical outcomes (Nguyen, 2024) (Khoo, et al., 2021) (Marciano & Gadano, 2018). This case report aims to highlight the detrimental effects of halting hepatitis B treatment, emphasizing the importance of continuous antiviral therapy. By presenting this case, we seek to underscore the necessity of strict adherence to prescribed treatment regimens to ensure sustained viral suppression and prevent the reactivation of HBV, thereby aligning with current clinical guidelines that advocate for long-term management of chronic hepatitis B.

CASE REPORT

A 61-year-old male presented to the emergency department of RAA Soewondo Pati Hospital with complaints of jaundice, which he had been experiencing intermittently since 2010. His medical history is significant for hepatitis B, diagnosed in 2014 at the same hospital. In 2018, the patient was admitted to RS Kariadi Semarang with a confirmed diagnosis of chronic hepatitis B. He was prescribed antiviral medications, specifically Entecavir and Telbivudine, as part of his treatment regimen. Despite initial improvements in his clinical condition and laboratory parameters, the patient elected to discontinue the antiviral therapy after a few months, against medical advice.

One week prior to his current hospital admission, the patient reported a marked exacerbation of his jaundice, accompanied by symptoms including a sensation of fullness and bloating in the abdomen, abdominal pain, generalized weakness, nausea, and two episodes of vomiting containing food and water. Additionally, he noted swelling in both lower extremities and dark yellow urine. Three days before presenting to the hospital, his symptoms deteriorated further, characterized by increased abdominal distension and intensified pain. Initially, he sought treatment at RSUD Kayen Pati, where he was managed for three days before being referred to RS Kariadi Semarang. However, he refused further treatment at RS Kariadi and left against medical advice.

On physical examination in the emergency department of RAA Soewondo Pati Hospital, the patient appeared moderately ill but was alert and oriented, with a Glasgow Coma Scale (GCS) score of E4M6V5, indicating a compos mentis state. His vital signs revealed a blood pressure of 150/90 mmHg, a pulse rate of 96 beats per minute, a respiratory rate of 20 breaths per minute, a temperature of 36.5°C, and an oxygen saturation of 98% on room air. The physical examination was notable for icteric sclerae, significant abdominal distension with positive shifting dullness, and a positive fluid wave, indicative of ascites. Hepatomegaly and splenomegaly were not appreciable on palpation, but bilateral lower extremity edema was present.

Laboratory investigations were concerning for significant abnormalities, including thrombocytopenia with a platelet count of 58,000/µL, markedly elevated liver enzymes with

aspartate aminotransferase (SGOT) at 415.7 U/L and alanine aminotransferase (SGPT) at 299.5 U/L, and an increased creatine kinase-MB (CK-MB) level of 41.3 U/L. Hepatitis B surface antigen (HBsAg) was reactive, indicating ongoing HBV infection. A prior viral load test performed at RS Kariadi Semarang on December 3, 2018, had shown an HBV DNA level of 2,576 IU/mL.

DISCUSSION

Hepatitis B is a liver infection caused by the hepatitis B virus (HBV). HBV infection represents a significant global health concern, particularly in Indonesia. Among the healthy population, the prevalence of hepatitis B is estimated to range from 4.0% to 20.3%. The most common genotypes of the virus identified are genotype B (60%), genotype C (26%), genotype D (7%), and genotype A (0.8%). According to research, hepatitis B is classified into two types: acute hepatitis B and chronic hepatitis B. Acute hepatitis B progresses through three phases: the pre-icteric phase, the icteric phase, and the convalescent (recovery) phase. In cases of chronic hepatitis B, hepatomegaly is often observed, sometimes accompanied by splenomegaly or other signs of liver disease such as spider nevi and palmar erythema (Agarwal, 2022) (Knolle, et al., 2021) (Freshman, 2021)

The primary goal of hepatitis B treatment is to save lives by reducing mortality associated with liver cancer, decreasing the need for liver transplantation, and slowing or reversing the progression of liver disease and its infectiousness. Currently, seven medications are approved for treatment: two standard formulations of interferon and pegylated interferon, and five nucleos(t)ide analogs including lamivudine, telbivudine, entecavir, adefovir, and tenofovir. In cases of chronic hepatitis B, complications such as portal hypertension, cirrhosis, and hepatocellular carcinoma can occur. Hepatitis B is responsible for 80% of primary hepatocellular carcinoma cases and is the second leading cause of cancer after smoking. Additionally, 15-25% of patients with chronic hepatitis B infection die from chronic liver disease (Wang, et al., 2021) (Moghadam, et al., 2021) (Li, et al., 2021)

Long-term nucleos(t)ide analogs inhibit the reverse transcriptase activity of viral polymerase, effectively suppressing hepatitis B virus replication, reversing liver fibrosis, and reducing the risk of hepatocellular carcinoma. However, nucleos(t)ide analogs do not directly affect intrahepatic covalently closed circular DNA or virus transcription in the liver. Consequently, a functional cure, defined as hepatitis B surface antigen clearance with or without anti-hepatitis B surface antibody seroconversion, is seldom achieved, necessitating long-term or even lifelong nucleos(t)ide analog therapy for most patients (Zhao, et al, 2018) (Thomas, et al., 2022) (Dimond, 2008).

The optimal timing for discontinuing nucleos(t)ide analog therapy before achieving hepatitis B surface antigen clearance remains uncertain due to high rates of post-treatment recurrence. Systematic review analyses indicate a virological recurrent rate of approximately 50% to 60% within 12 to 36 months after drug withdrawal. Although recent clinical guidelines suggest that some patients may discontinue nucleos(t)ide analogs before achieving hepatitis B surface antigen serum clearance, sensitive and reliable biomarkers for identifying patients with low recurrence risk have not yet been established (Liu, et al., 2019) (Xu, et al., 2021) (Hall, et al., 2022)

Hepatitis B virus recurrent is a common event following the discontinuation of nucleos(t)ide analogs and can be categorized into virological recurrent and clinical recurrent. Most studies define virological recurrent as hepatitis B virus DNA levels exceeding 2000 IU/mL. When this is accompanied by alanine aminotransferase levels at least twice the upper limit of normal, it is classified as clinical recurrent. A systematic review by Papatheodoridis et al. reported virological recurrent rates of 51.4% and 38.2% at one and three years, respectively,

after nucleos(t)ide analog discontinuation. The incidence of virological recurrent was higher in hepatitis B e antigen-negative patients compared to hepatitis B e antigen-positive patients, with rates of 56.3% versus 37.5% at one year, and 69.9% versus 48.5% at three years (Kaneko, et al., 2021) (Wang, et al., 2020) (Moussa, et al., 2022)

While virological recurrent commonly occurs after stopping nucleos(t)ide analogs, it may not always have a clinically significant impact. In some patients, virological recurrent can be transient, with a spontaneous decline in viral replication due to an immune response. However, clinical recurrent can be more problematic, potentially necessitating the initiation of retreatment and, in severe cases, leading to hepatic flare and liver failure (Dimond, et al., 2021) (Smolders, et al., 2020) (Inoue, et al., 2021).

These findings underscore the complexity of managing chronic hepatitis B and the need for careful consideration before discontinuing antiviral therapy. They highlight the importance of ongoing monitoring and the potential need for retreatment to prevent severe clinical outcomes. Therefore, as illustrated in the case report where the patient discontinued treatment on his own accord, it resulted in significant adverse health impacts. The decision to halt antiviral therapy prematurely can lead to severe consequences such as virological recurrent, clinical recurrent, and progression to hepatic decompensation (Höner, et al., 2017) (Tan, et al., 2021) (Saw, et al., 2020). This case report is written to demonstrate the critical importance of adhering to the prescribed treatment regimen until completion and ensuring continuous patient monitoring throughout the treatment process. It aims to underscore the necessity of a structured and vigilant follow-up plan to detect any signs of recurrent early and to intervene promptly. By showcasing the adverse outcomes in this particular case, we emphasize the broader implications for patient education and clinical practice. It is crucial for healthcare providers to communicate effectively with patients about the risks of discontinuing treatment prematurely and to implement robust monitoring protocols to safeguard against such detrimental health outcomes.

CONCLUSION

This case report illustrates the severe consequences of discontinuing hepatitis B treatment. Chronic hepatitis B is a significant health concern, potentially leading to cirrhosis and hepatocellular carcinoma. Long-term nucleoside and nucleotide analog therapy has been crucial in controlling the virus and reducing liver disease risk. However, premature discontinuation can result in virological and clinical recurrence, leading to severe health deterioration, including hepatic flare and liver failure. This case underscores the importance of adhering to antiviral therapy and the need for continuous monitoring. It highlights the role of healthcare providers in educating patients about the risks of stopping treatment prematurely and the importance of vigilant follow-up to prevent severe outcomes.

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