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B형 간염 환자에서 Lamivudine과 Adefovir 병용처방으로 유발된 이명의 증례보고

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Lamivudine- and Adefovir-Induced Tinnitus in a Patient with Hepatitis B: A Case Report

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Lamivudine and adefovir are medications used to treat hepatitis B. We observed the occurrence of tinnitus after administering lamivudine and adefovir to a 49-year-old hepatitis B patient for two months. The patient had no comorbidities and no history of ear diseases, including tinnitus, and was not taking any other medications. In general, neither lamivudine nor adefovir are known to induce tinnitus as an adverse reaction. A literature search revealed that this is the first case in which tinnitus occurred after lamivudine and adefovir were administered to a hepatitis B patient. Therefore, we believe that this case is clinically valuable and decided to report it.

□ Key words - adefovir, lamivudine, tinnitus, adverse reactions

INTRODUCTION

Lamivudine is an antiviral drug that is effective against human immunodeficiency virus (HIV) and hepatitis B virus (HBV) infections.[1,2] Lamivudine is a nucleoside reverse transcriptase inhibitor (NRTI) that is phosphorylated in liver cells into its active form, a 5-triphosphate metabolite, hindering DNA synthesis by impeding the DNA polymerase of HBV. This drug also displays antiviral activities after it is inserted into the viral DNA.[3,4] Lamivudine is known to exhibit outstanding potency, but the dose has to be customized to the patient because the blood content of lamivudine is increased in moderate and severe nephropathy patients whose creatinine clearance is less than 50 mL/minute.[5] Occasionally, severe hepatomegaly accompanied by lactic acidosis and lipidosis has been reported as a serious adverse reaction induced by lamivudine when administered alone or in combination with another antiretroviral drug. Headaches, fatigue, insomnia, nausea, vomiting, diarrhea, pancreatitis, intranasal symptoms, and coughing are some of the other common adverse reactions that have been reported to occur at a frequency of more than 10%.[3,6,7] Adefovir acts as a competitive inhibitor of viral DNA polymerase and reverse transcriptase and is therefore used for the sustained suppression of HBV replication and remission of liver disease in hepatitis B patients.[8,9] Similar to lamivudine, adefovir requires a

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dose adjustment for patients whose creatinine clearance is less than 50 mL/minute. Headaches, stomachaches, diarrhea, asthenia, and hematuria are some of the commonly reported adverse reactions of adefovir.[10] Based on a literature search, this is the first case in which tinnitus occurred after lamivudine and adefovir were administered to a hepatitis B patient, and thus, we decided to report it.

CASE REPORT

The patient in this case was a 49-year-old Asian (Korean) male with a height of 176 cm and a weight of 101 kg. Based on the findings of a regular physical exam performed in October 2009, the patient was referred to this hospital with elevated levels of aspartate aminotransferase (AST; 64 U/L), alanine aminotransferase (ALT; 89 U/L), and gamma guanosine triphosphate (g-GTP; 224 U/L), nodules in the right lobe of the liver, and a gallbladder stone. The patient had a family history of hepatitis B; two out of his four siblings were diagnosed with liver cancer, and one of them died from it. Other than hepatitis, the patient did not have any diseases and was not taking any medications. At the time of the hepatitis diagnosis, his HBV DNA real-time PCR result was 661,000 IU/ml, and his hepatitis B e antigen (HBeAg) and hepatitis B e antibody (HBeAb) responses were both positive. When nodules that were suspected to be liver cancer were found in the liver during a computed tomography (CT) scan conducted in November 2009, the patient received transarterial chemoembolization (TACE). Afterwards, CT scans and tumor marker tests were conducted regularly until his ALT levels were found to be elevated to 85 U/L in March 2010. The patient then began taking 30 mg of clevudine once daily. The patient was prescribed clevudine at outpatient visits every two months and took the medication. However, he did not show good drug compliance, and at some of his visits, it was discovered that he had not taken the medication. In June 2011, the patient's HBV DNA real-time PCR result and the number of HBV copies were found to be radically elevated from the previous examinations (2335 IU/ml and 7964 copies/ml, respectively), and a drug resistance test identified resistance against clevudine. Thus, on June 30, 2011, clevudine administration was discontinued, and in its place, 100 mg of lamivudine and 10 mg of adefovir were administered in combination. The patient began to suffer from tinnitus two months after the change in his medication. Prior to that, the patient had not experienced tinnitus and had no history of ear diseases. His kidney function was also normal. No special measures were taken to treat his tinnitus, but his symptoms improved slightly over time and were reported to be tolerable. Lamivudine and adefovir continue to be administered to the patient, and the tinnitus persists.

DISCUSSION

Of the major antiviral drugs used to treat hepatitis B, lamivudine and adefovir are known to exhibit superior potency. Based on a literature search, there has never been a reported case of tinnitus occurring in a hepatitis B patient after lamivudine and adefovir administration. However, there has been one reported case in which tinnitus occurred when lamivudine and another NRTI were administered in combination to a patient infected with HIV.[11] The patient in this case report, who had no history of ear diseases, experienced tinnitus after lamivudine, efavirenz, stavudine, trimethoprim, and sulfamethoxazole were concurrently administered for four months. The results of recent studies that compared the effects of interferon-only treatment and the combined administration of interferon and lamivudine on patients' auditory function have shown that tinnitus occurs more often in the group administered interferon alone than in the group administered interferon in combination with lamivudine.[12] However, our literature search did not yield any information regarding the effects of lamivudine-only treatment on tinnitus. Furthermore, nothing has been reported regarding tinnitus either when lamivudine and adefovir are administered in combination or when adefovir is administered alone. Auditory function was not evaluated before administering the medications

because the results of studies on tinnitus or ototoxicity induced by lamivudine and adefovir are poorly documented. Therefore, this study is limited in its ability to objectively confirm whether there is a definitive relationship between tinnitus in the patient in this study and the administration of lamivudine and adefovir. Nevertheless, given that the patient suffered from tinnitus after taking lamivudine and adefovir for two months, despite having no history or symptoms of ear diseases before changing medications, and that the symptom continues to persist as the patient continues to take the medication, it is very likely that lamivudine and adefovir influenced the patient's tinnitus.

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