Case Report

First report of primary tenofovir resistance in a hepatitis b viral hepatitis patient from India without human immunodeficiency virus co-infection

Abstract

Tenofovir confers potent and durable HBV-DNA suppression; we do not know the best strategy in case of resistance of HBV to reverse transcriptase inhibitor Tenofovir. Levels of Tenofovir resistance in individuals with viral failure ranged from 20% in Europe to more than 50% in sub-Saharan Africa. Here we are doing case reporting of a rare case of resistance to Tenofovir in a patient with Hepatitis B related hepatitis without HIV co-infection. No past history of exposure, strict compliance was there, HIV and HCV were negative. Any systemic diseases that might have been able to explain the drug inefficacy and pharmacological history excluded a possible drug-drug interaction.

Keywords: virus, hepatitis, tenofovir resistance, mutation, nucleos(t)ide analogue

Introduction

Nucleos(t)ide analogs such as Tenofovir, Lamivudine or Emtricitabine work well against both HBV and HIV. Tenofovir confers potent and durable HBV-DNA suppression but the best strategy in case of resistance of HBV to reverse transcriptase inhibitor Tenofovir remains unknown. New tests are being developed to study HBV resistance. Levels of Tenofovir resistance in individuals with viral failure ranged from 20% in Europe to more than 50% in sub-Saharan Africa. It is likely that 7-17% of individuals given Tenofovir plus cytosine analogue plus Efavirenz will develop Tenofovir resistance within 1 year of treatment initiation under present practices in sub-Saharan Africa. One study has reported HBV genotypes quasi species diversity and drug resistance mutations in antiretroviral treatment naive and treatment experienced HIV-HBV co-infected patients, apart from case reports of prolonged and intermittent treatment of HIV with Lamivudine and Tenofovir and development of resistant to Lamivudine and Tenofovir, while HIV-RNA remained constantly suppressed. Here we are reporting a case of resistance to Tenofovir in a patient with Hepatitis B virus related hepatitis without HIV co-infection.

Patient and method

Patients were 59 years old female, which consulted Gastroenterologist, baseline Hepatitis B Viral DNA level was 5,49,1000IU/ml and transaminase were more than two times normal. Fibroscan was done to grade and stage fibrosis, her kPa score was 8.6, Alpha fetoprotein level was 3.79IU/ml and HBsAg level was 111.64. Patient was started on Tenofovir disoproxil fumarate 300mg, one tablet daily (Brand Name Tanvir, Cipla Limited, which is one of the largest pharmaceutical companies in India, well known for cost effective high efficacy antiviral and other medicines). After one month of Tenofovir treatment first HBV DNA level was 3210 IU/ml. Patient continued same treatment and was on regular follow up at outpatient department. After 6 months HBV DNA level was 674000IU/ml, on further history taking patient was on regular follow up, patient regularly purchased medicine from hospital pharmacy, patient confirmed that she took medicine regularly every single day, no history of any other medicine intake which could decrease efficacy of Tenofovir or increase its metabolism or we excluded any drug-drug interaction thoroughly. Clinical evaluation and laboratory findings excluded the presence of systemic diseases that might have been able to explain the drug inefficacy, resistance to medicine and/or rapid loss of medicine from body, there was no past history of exposure to Tenofovir, as patient was highly motivated, educated, college professor she was having all the records of regular visits, pharmacy shop purchase record were also available. On testing HIV and HCV were negative. We suspected possible resistance to Tenofovir. Patient consented for further high cost testing. First patients serum sample was sent for mutation study and genotyping and tablet Tenofovir was stopped, Tablet Entecavir (Brand name Entavir from Cipla Limited) 1mg once daily was started, which was well-tolerated. Report of mutation study and genotyping revealed A181T/V mutation with A194T and M204V/I, these mutations are associated with resistant to Lamivudine, Adefovir, Tenofovir and development of resistant to Lamivudine and Tenofovir, while HIV-RNA remained constantly suppressed. Here we are reporting a case of resistance to Tenofovir in a patient with Hepatitis B virus related hepatitis without HIV co-infection.
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Conclusion

This is a First report from India of occurrence of Tenofovir mutation A181T/V, A194T and M204V/I in a non HIV infected patient with HBV hepatitis, without any prior irregular Tenofovir treatment and without drug-drug interaction.

Acknowledgements

None.

Conflict of interest

Author declares that there is no conflict of interest.

References


