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Case report

First description of past Hepatitis B Virus infection acute reactivation occurring in a Human Immunodeficiency Virus infected patient as manifestation of immune reconstitution inflammatory syndrome

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ABSTRACT

We report the case of an acute, self-resolving HBV-related hepatitis occurring in a HIV-infected patient carrying isolated anti-HBc antibodies. This acute HBV hepatitis may be considered as a clinical manifestation of a reactivation of HBV during an immune reconstitution inflammatory syndrome. Other hypotheses, even unlikely, are discussed.

1. Introduction

Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV) sharing the same transmission ways, co-infection is common. Reactivation is mostly described in co-infected patients with a positive HBs Ag (with 33% of them experienced a reactivation after withdrawal of combined Anti-Retroviral-Therapy (c ART) active on HBV [1], or because low CD4+ T cells count), but also in patients carrying isolated antibodies against HBV core antigen (anti-HBc) [2]. We report to our knowledge the first case of an acute HBV hepatitis in a HIV-infected patient presenting a serological profile of past HBV infection (Ag HBS -, anti-HBc ab +, anti-Hbs ab+). This acute HBV hepatitis may be considered as a clinical manifestation of a reactivation of HBV during an immune reconstitution inflammatory syndrome (IRIS). Other hypotheses, even unlikely, are discussed. This case report could have major consequences on medical supervision strategies in HIV-infected patients with past HBV infection following the introduction of c ART.

2. Case report

A 34 year-old man from Mali was diagnosed HIV-infected in 2008. When he came to France in November 2011, his CD4+ T cell count was 2 cells/μL, plasma viral load was 455,000 copies/mL (5.66 Log/mL). Serum testing showed anti-HBc repeatedly positive (index: 2.85; Architect®, Abbott, Rungis, France). He had no opportunistic infection; aminotransferases were within the normal range. ART combining tenofovir, emtricitabine [TRUVADA®], "boosted" atazanavir [REYATAZ®] was started.

In July 2012, the patient was admitted for cognitive impairment evolving for one month; an AIDS-related-encephalopathy was diagnosed. CD4+ T cell count was 162 cells/μL, HBV serological profile unchanged. HIV plasma viral load was 1406 copies/mL (3.12 Log/mL), allowing to perform genotyping for resistance testing. It showed resistance to lamivudine/emtricitabine, efavirenz/nevirapine, rilpivirine and lopinavir, with the mutations: 184V, 103N, 225H, 221Y. The treatment was switched to zidovudine

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[RETROVIR®], abacavir [ZIAGEN®], "boosted" darunavir [PREZISTA®], maraviroc [CELSENTRI®], according to the genotyping results and to the CHARTER score (CNS penetration-effectiveness of ART) [3], leading to a complete clinical recovery after two months. Until February 2013, the patient remained HBs Ag negative with normal aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. In February 2013, six months after combination of tenofovir + emtricitabine was switched, a biological routine control showed increased AST and ALT to 581 and 1184 UI/L respectively, without any change in prothrombin time or in bilirubin rate. Both HBs Ag and HBe Ag were positive. The patient was admitted 3 weeks later, he was asymptomatic and firmly denied any sexual or intravenous risk factor, nor any lack of adherence to c ART. Anti HBc IgM were slightly positive (index: 1.33; Architect®, Abbott) and the HBV DNA load level (COBAS® Taqman HIV-1 V2.0, Roche, France) was almost 6 Log UI/mL (812,000 UI/mL). Antibodies against hepatitis D virus and hepatitis C virus were negative, as testing for current or previous hepatitis A or E infection; testing for VZV, HSV, EBV, CMV and Parvovirus B19 by PCR were negative. An abdominal ultrasonography was normal. The HBV strain identified was genotype D without any genetic change conferring drug resistance (Fig. 1). Pre-S and S region were generated by aligning HBV sequences using ClustalW on MEGA version 4.0 and corrected manually by visual inspection on comparing the amino acid sequence of the index patient with the consensus sequence. The G145A mutation, a determinant immune escape variant found in

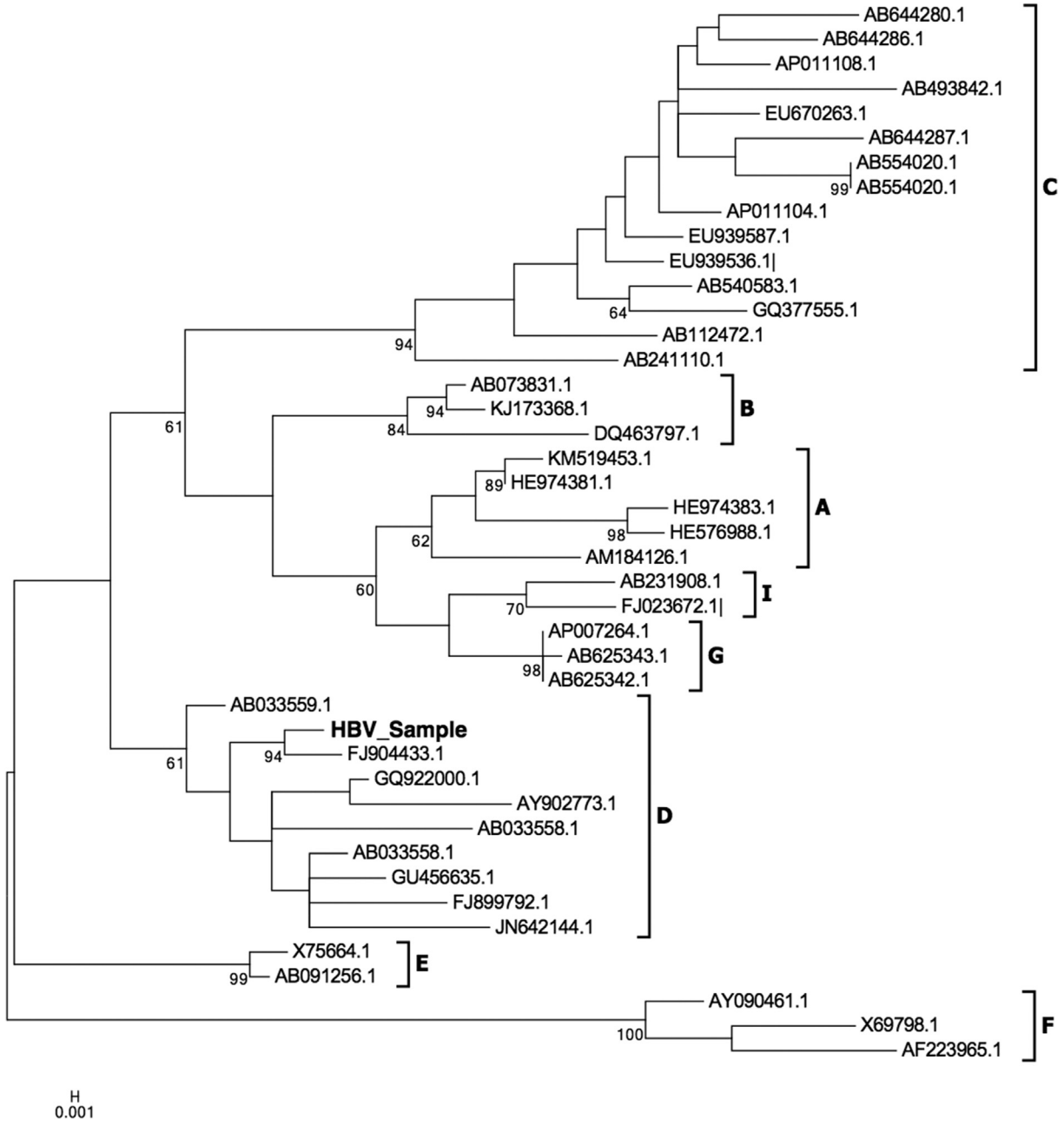

Fig. 1. Phylogenetic tree of HBV pol gene region (409 bp). Maximum likelihood analysis based on the Kimura 2 parameter model was carried out with patient HBV sequence (HBV sample) and other sequences from all HBV genotypes from GenBank, indicated by the accession number. Bootstrap support values (1000 Replicates) above 60% are shown at the respective branches.