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LETTER TO THE EDITOR

Case of newly onset type 1 diabetes after highly active antiretroviral therapy against HIV infection

The survival of patients infected with human immunodeficiency virus (HIV) has been dramatically improved after the introduction of highly active antiretroviral therapy (HAART), the combination of multi-antiretroviral agents to decrease the replication of HIV type 1 (HIV-1). Although HIV-infected patients commonly show a low CD4-positive lymphocyte (CD4) count and a high CD8 count, HAART can effectively reduce the plasma HIV load, thus the CD4 count drastically increases, which is denoted as 'immune reconstitution'. It was reported that several autoimmune diseases could occur after immune reconstitution during HAART[1]. Here, we report a case of newly-onset type 1 diabetes after HAART against HIV infection.

A previously healthy 40-year-old Japanese man presented to Kawasaki Medical School (Kurashiki, Japan) in June 2009 for further examination of HIV-1 infection. HAART was started because of the low CD4 count and high titer of HIV ribonucleic acid. Then, the laboratory findings showed a total disappearance of HIV ribonucleic acid and increase of CD4 count with good clinical course (Figure 1). Around October 2011, however, the patient had nocturia and intense thirst with 6-kg weight loss. On admission, laboratory findings showed the elevation of glycated hemoglobin (12.5%) and glycoalbumin (30.8%) with mild ketosis. Endogenous insulin secretion was disturbed; serum C-peptide level was 0.6 ng/mL with plasma glucose level 242 mg/dL. Furthermore, anti-GAD antibody was positive (34.8 U/mL), but IA-2 antibody and anti-insulin antibody were negative. In addition, the patient had no obesity and/or diabetic family history, and human leukocyte antigen deoxyribonucleic acid typing of DRB1 and DQB1 was DRB1 *09:01-DQB1* 03:03, which is typical haplotype in Japanese type 1 diabetes. Thereby, we diagnosed the patient with newly-onset type 1 diabetes and introduced multiple daily injection, using insulin aspart and detemir. After that, his glycemic control was gradually improved, and he was discharged at day 19. It is likely that when the CD4 count is markedly increased, autoimmunity is stimulated by the CD4 dominant state. In the present case, the onset of type 1 diabetes and the marked increase of CD4 count around October 2011 were completely synchronized (Figure 1). To the best of our knowledge, there was only one report about the onset of type 1 diabetes after HAART[2]. According to the allele frequency net database (http://www.allelefrequencies.net)[3], human leukocyte antigen DRB1*09:03 is very rare or absent in Caucasians, but this is common in Japan. In fact, the difference in haplotypes associated with type 1 diabetes between Japanese and Caucasian populations has been reported, and it can be explained by the frequency of haplotypes in each ethnicity[4]. Although the mechanism of the onset of type 1 diabetes is not clear, we assume that after HAART, type 1 diabetes can be induced in Japanese rather than in Caucasians. Therefore, we believe that the present case report would call for attention from the clinical point of view, and that we should

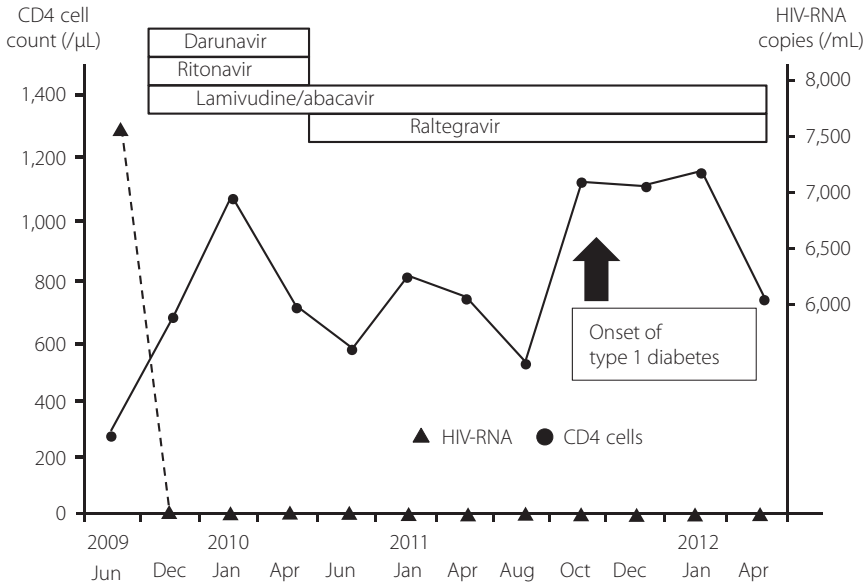

Figure 1 | Time-course of CD4 cell count and human immunodeficiency virus (HIV)-ribonucleic acid (RNA) copies after highly active antiretroviral therapy in an HIV-infected patient.

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consider the possibility of newly-onset type 1 diabetes when HAART is introduced against HIV infection, especially in Japanese patients.

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