

Snake venom preparation for drug-resistant human immunodeficiency virus

Abdulrahman A. Alrajhi,^a Abdullah Almohaizeb^b

From the ^aSection of Infectious Diseases, Department of Medicine and ^bPharmacy Services, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

Correspondence and reprints: Abdulrahman A. Alrajhi · Department of Medicine, MBC 46, King Faisal Specialist Hospital and Research Centre · PO Box 3354, Riyadh 11211, Saudi Arabia · T: +966-1-442-7494 F: + 966-1-442-7499 · rajhi@kfshrc.edu.sa · Accepted for publication June 2008

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The effective control of human immunodeficiency virus type 1 (HIV-1) using antiretroviral therapy (ART) results in prolonged survival.¹ However, because of high rates of viral replication, along with other factors, resistance to antiretroviral drugs has become an important reason for therapy failure and progression to acquired immunodeficiency syndrome (AIDS).² The prevalence of drug-resistant strains is variable depending on location and use of ART; it is very high in treatment-experienced patients.^{3,4} Even in treatment-naïve patients, resistance rates can be up to 19%.⁵ Alternate therapies for extensively drug-resistant HIV are limited to recently introduced antiretroviral agents: darunavir, etravirine, maraviroc, and raltegravir. We report on a patient with multidrug-resistant HIV who had a remarkable response to a snake venom preparation. The patient signed a written informed consent to publish his case.

CASE

The patient was a hemophiliac male born in 1978 who was confirmed to be asymptomatic HIV positive in 1987. Zidovudine was started in 1990 for a CD4+ T-lymphocyte (CD4) count of less than 200/mm³. In 1997, the CD4 count was 24/mm³ and didanosine was added to his ART. In 2000, he was transferred to our facility. The initial viral load at that time was more than 500 000 copies/mL (Bayer Quantiplex bDNA System, detection range 50-500 000 copies/mL) and the CD4 count was 19/mm³. Highly active antiretroviral combination therapy, including a protease inhibitor, was started. Because of a persistently low CD4 count and high viral load, the ART was changed based on resistance genotyping (Roche Molecular Systems, Inc.) in 2002. Genotyping-based salvage therapy including enfuvirtide was started in 2004. However, the CD4 count continued to be low and viral load was more than 500 000 copies/mL. In March 2006, a new regimen of didanosine, tenofovir, and efavirenz was started based on genotyping.

Nevertheless, in November 2006, viral load remained high at 1 580 000 copies/mL (Abbott RealTime HIV assay, range 40-10 000 000 copies/mL). Repeat genotyping revealed resistance to all agents except tenofovir. The patient decided to take a preparation with the trade name *Samayz*, given to him by a friend. *Samayz* (formerly known as *Bioven*, and later *Autoimmune-5*; Equimune Research Corp., Coral Springs, FL, USA) is described in advertising material as "a combination of various components derived from snake venom". He took 0.1 mL subcutaneous injection daily for one month. Pre-injection viral load was 1 580 000 copies/mL and the CD4 count was 52/mm³. ART was unchanged. In March 2007, viral load was 3 279 copies/mL and the CD4 count increased to 232/mm³. In April, efavirenz was changed to lopinavir/ritonavir, and didanosine was changed to zidovudine due to adverse effects. The virus remained resistant to all these antiretroviral agents. He self-repeated the venom preparation course in April and July 2007. In November 2007, the viral load was 1 981 copies/mL, and the CD4 count was 345/mm³ (Figure 1). Repeat genotyping revealed the same resistance pattern. The specific mutations found were L74V, L100I, K103N, M184V, T215Y, K103N, I13V, K20R, D30N, L33I, M36I, I54L/V, I54V, L63P, A71T, N88D, L90M (Trugene HIV-1, Bayer HealthCare LLC). He continued to take zidovudine, tenofovir, and lopinavir/ritonavir as ART. The patient did not report any significant adverse effects related to the injections.

DISCUSSION

The in vitro anti-HIV activity of snake venom has been reported.^{6,7} We believe this is the first case of an apparent in vivo effect of a snake venom preparation in controlling HIV. The peak viral load assay was not at a time of intercurrent illness. In fact, the preceding viral loads of 500 000 copies/mL were the maximum by the assay available at that time. When better assay tools became available, the viral load was more than a

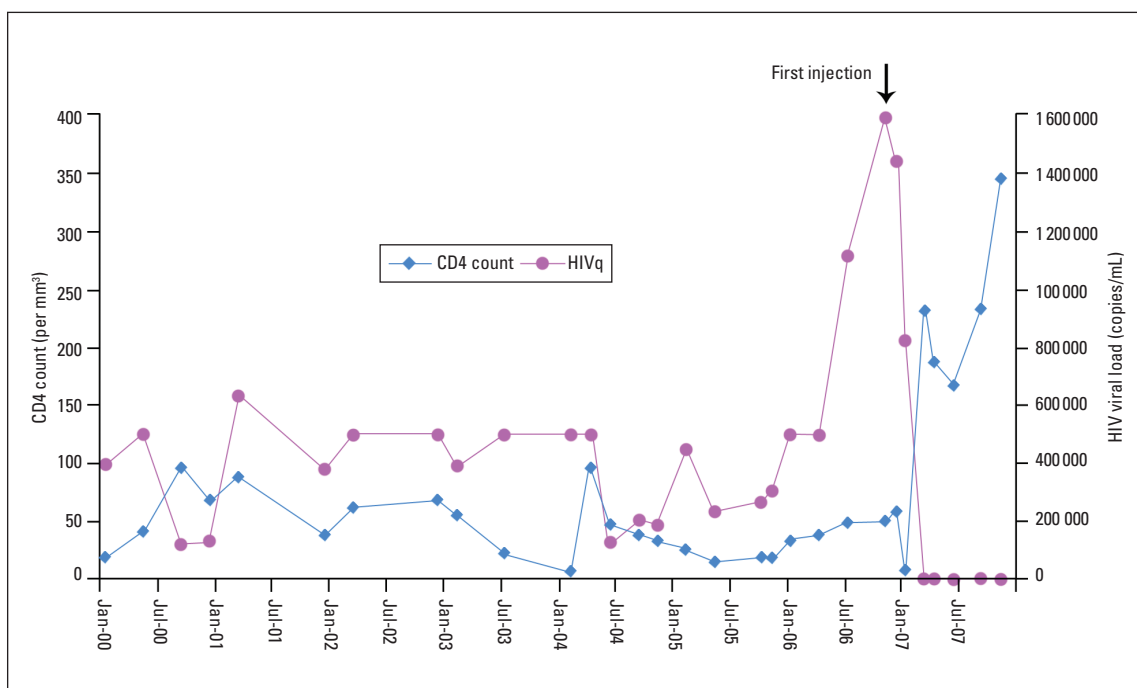


Figure 1. HIV viral load and CD4+ T-lymphocyte count over 8 years.

million. Although the patient was still using ART and genotyping revealed multidrug resistance, the dramatic drop in viral load and increase in CD4 count occurred only after use of the venom preparation. The evident change in viral load and CD4 count cannot be explained by the ART alone as the patient has been on the same regimen. Compliance with ART was suboptimal initially and probably improved after taking the venom preparation. Possibly, the interaction between the venom preparation and current ART worked to his advantage.⁸ Another possible explanation is the high

mutation rate of HIV, which may render the virus less fit, either through susceptibility to antiretroviral agents or an intrinsic defect.^{9,10} We believe that the response was related to the injectable snake venom preparation in the background of maintenance ART that the virus was resistant to on genotyping. Further research to confirm the effect and the exact mechanism of antiretroviral activity of the snake venom preparation is required. Phase II and III clinical studies using the preparation would hopefully establish its role as an adjuvant salvage therapy for multidrug-resistant HIV.

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