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Short Communication

Transient increase in plasma HIV RNA after COVID-19 vaccination with mRNA-1272

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Dear Editor,

The latent viral reservoir is the main obstacle preventing HIV eradication, as the virus persists, integrated in long-lived quiescent cells. Immune stimulatory by their nature, vaccines have been evaluated as possible agents for 'shock and kill' strategies, which rely on using latency-reversing agents to activate HIV transcription and virion production in order to purge the reservoir.

Due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, unprecedented efforts towards public health interventions have been made globally, and a constantly growing proportion of individuals have received various vaccines against coronavirus disease 2019 (COVID-19), including those developed using the novel mRNA technology (Polack et al., 2020; Baden et al., 2021). Despite having shown good efficacy and safety in people living with HIV (PLWH), and being recommended by national and international HIV societies, the effect of such compounds on HIV latency has yet to be evaluated (BHIVA, DAIG, EACS, GESIDA 2021) https://www.eacsociety.org/home/eacs-statement-15-january-2021/.

Here, we report the case of a man living with HIV who, having previously achieved stable viral suppression, experienced a transient period of non-suppressible viremia after receiving a dose of COVID-19 vaccine.

The patient, a 65-year-old heterosexual male, was diagnosed with HIV infection in March 2020, during a diagnostic workup for chronic liver disease due to former alcohol abuse. At diagnosis, his plasma HIV RNA (viral load, VL) was 5 780 000 copies/ml and his CD4+ count was 44/µl (3.6%; CD4/CD8 0.1%). No co-infections were diagnosed. Antiretroviral treatment (ART) with tenofovir alafenamide (TAF)/emtricitabine (FTC)/bictegravir (BIC) was started 2 weeks after diagnosis, and was well tolerated; adherence was optimal, as assessed through visit interviews. Three months after ART initiation, his VL was below 200 copies/ml and his CD4+ count was >200/µl. Six months after initiation (October 2020) the patient achieved VL suppression (<50 copies/ml), confirmed by three subsequent determinations.

In April 2021, the patient, by then suppressed for more than 6 months, with a negative clinical history and negative anti-N antibodies for SARS-CoV-2, received the first dose of mRNA-1273 vaccine (Moderna Biotech) in the context of the Italian vaccination campaign. The vaccine was also well tolerated; the patient did not report any systemic side effect. Twenty-eight days later, before receiving his second dose of vaccine, which was scheduled on the same day, blood samples were acquired in the outpatient HIV clinic

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for quarterly routine bloodwork. The patient's HIV VL was 1790 copies/ml; he was asymptomatic and blood chemistry was normal. Counseling was arranged. Questioned, the patient once again reported optimal adherence. Potential drug–drug interactions were screened and ruled out. Adherence to ART was indirectly confirmed by therapeutic drug monitoring, showing tenofovir trough concentrations (21 ng/l) within the expected range for TAF (10–25 ng/ml) on a leftover blood sample obtained on the same day viremia was assessed (Cattaneo et al., 2020). Fourteen days after the increase (and the second vaccine dose), a new bloodwork was obtained and his VL was suppressed again.

Previous studies have found transient increases in HIV VL after vaccination for influenza, *Streptococcus pneumoniae*, and hepatitis B virus among others, whereas others have shown no effect (Brichacek et al., 1996; Cheeseman et al., 1996; Glesby et al., 1996; Tasker et al., 1998; Viganò et al., 1998). When observed, most VL increases occurred 7–14 days after vaccination (Yek et al., 2016). A recent randomized controlled trial compared the effects of several vaccination schedules versus placebo in suppressed PLWH and did not find effects on plasma RNA, but showed an increase in HIV cell-associated RNA, CD4+ and CD8+ T-cell activation markers, as well as HIV-specific CD8+ responses (Yek et al., 2016). The most likely mechanism explaining the increased HIV transcription observed in the context of standard vaccines administered to ART-suppressed PLWH is a generalized inflammatory response with cytokine production, able to activate bystander cells harboring latent HIV, rather than activation of infected vaccine-specific T-cells (Posthouwer et al., 2004; Yek et al., 2016). Furthermore, a recent work showed CD4+ T-cell cross-reactivity between seasonal coronaviruses and SARS-CoV-2 in vaccine recipients (Woldemeskel et al, 2021). However, the interplay of mRNA vaccines, the immune system, and latent HIV infection is yet to be thoroughly understood. Of note, C-reactive protein quantification was negative in the case presented here; however, we might have documented the descending phase of a curve, as VL determination was at 28 days.

It appears that this is the first report of a plasma HIV RNA increase after vaccination with an mRNA COVID-19 vaccine in a patient with documented adherence, possibly reflecting induced proviral transcription. Peculiarities of the case were advanced HIV infection with a high baseline VL set-point (6.7 $\log_{10}$) before a relatively recently started ART, which may reflect a larger reservoir size, which could have contributed to the observed transient increase in VL upon generalized stimulation.

In the context of mass vaccination, this observation might be of use to guide the clinical practice of other physicians observing unexplained VL increases in ART-adherent PLWH. Further studies are needed to evaluate whether novel mRNA vaccines have the potential to perturb the latent HIV reservoir, which would be beneficial for the design of future eradication strategies.

Author contributions

GB was involved in the patient's care and conceived and drafted the present work. AL and SL were involved in clinical decisions and contributed to the writing of the manuscript. LM and DC performed laboratory work and contributed to the writing of the manuscript. AM, AB, and AG took part in the multidisciplinary group discussion and revised the manuscript critically for important intellectual content. All authors revised the existing literature and approved the final version of the manuscript.

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Ethical approval

Written informed consent was obtained from the patient for publication of their clinical details.

Conflict of interest

None related to the content of the manuscript.

References

Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med 2021;384(5):403–16 Feb 4. doi:10.1056/NEJMoa2035389.

BHIVA, DAIG, EACS, GESIDA, Polish Scientific AIDS Society and Portuguese Association for the clinical study of AIDS (APECS) - Statement on risk of COVID-19 for people living with HIV (PLWH) and SARS-CoV-2 vaccine advice for adults living with HIV. Friday, 15 January 2021. https://www.eacsociety.org/home/eacs-statement-15-january-2021/(accessed 21 July, 2021).

Brichacek B, Swindells S, Janoff EN, et al. Increased plasma human immunodeficiency virus type 1 burden following antigenic challenge with pneumococcal vaccine. J Infect Dis 1996;174(6):1191–9 Dec. doi:10.1093/infdis/174.6.1191.

Cattaneo D, Baldelli S, Cozzi V, et al. Impact of Therapeutic Drug Monitoring of Antiretroviral Drugs in Routine Clinical Management of People Living With HIV: A Narrative Review. Ther Drug Monit 2020;42(1):64–74 Feb.

Cheeseman SH, Davaro RE. Ellison RT 3rd. Hepatitis B vaccination and plasma HIV-1 RNA. N Engl J Med 1996;334(19):1272 May 9.

Glesby MJ, Hoover DR, Farzadegan H, et al. The effect of influenza vaccination on human immunodeficiency virus type 1 load: a randomized, double-blind, placebo-controlled study. J Infect Dis 1996;174(6):1332–6 Dec. doi:10.1093/infdis/174.6.1332.

Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med 2020;383(27):2603–15 Dec 31. doi:10.1056/NEJMoa2034577.

Posthouwer D, Voorbij HA, Grobbee DE, et al. Influenza and pneumococcal vaccination as a model to assess C-reactive protein response to mild inflammation. Vaccine 2004;23(3):362–5 Dec 2. doi:10.1016/j.vaccine.2004.05.035.

Tasker SA, O'Brien WA, Treanor JJ, et al. Effects of influenza vaccination in HIV-infected adults: a double-blind, placebo-controlled trial. Vaccine 1998;16(9-10):1039–42 May-Jun. doi:10.1016/s0264-410x(97)00275-2.

Viganò A, Bricalli D, Trabattoni D, et al. Immunization with both T cell-dependent and T cell-independent vaccines augments HIV viral load secondarily to stimulation of tumor necrosis factor alpha. AIDS Res Hum Retroviruses 1998;14(9):727–34 Jun 10.

Woldemeskel BA, Garliss CC, Blankson JN. SARS-CoV-2 mRNA vaccines induce broad CD4+ T cell responses that recognize SARS-CoV-2 variants and HCoV-NL63. J Clin Invest 2021;131(10) May 17. doi:10.1172/JCI149335.

Yek C, Gianella S, Plana M, et al. Standard vaccines increase HIV-1 transcription during antiretroviral therapy. AIDS 2016;30(15):2289–98 Sep 24. doi:10.1097/QAD.0000000000001201.