



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



ELSEVIER

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Immunological changes after COVID-19 vaccination in an HIV-positive patient

Changlin Gong, Xiaojing Song, Xiaoxia Li, Lianfeng Lu, Taisheng Li*

Department of Infectious Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China

ARTICLE INFO

Article history:

Received 7 June 2021

Revised 1 August 2021

Accepted 15 August 2021

KEYWORDS:

Coronavirus disease 2019

Vaccine

Human immunodeficiency virus

CD4+ T cells

ABSTRACT

Vaccination is an essential measure to stop the coronavirus disease 2019 (COVID-19) pandemic. We report a case of viral activation and CD4+ T cell loss in a treatment-naïve HIV-positive patient after receiving inactivated COVID-19 vaccine (Sinopharm). The vaccine should probably be given only to people living with HIV receiving antiretroviral therapy.

© 2021 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

Concerns regarding the safety of vaccination in people living with HIV (PLWH) remain. Although no unusual adverse effects have been found after vaccination in PLWH, there are still not enough data to definitively prove whether or not infection with HIV raises the risk of adverse events after vaccination (Su et al., 2018). More than a year into the pandemic of coronavirus disease 2019 (COVID-19), several vaccines based on different platforms have been developed, although no effective vaccine for HIV has yet been employed, probably due to the different mechanisms of infection (Haynes, 2021) [Au?1]. Vaccination against this newly emerged virus in PLWH has become of vital significance because of the potentially worse outcomes after infection in PLWH than in the general population (Eisinger et al., 2021, Tesoriero et al., 2021). However, to date, no large-scale study has been completed on the safety profiles of COVID-19 vaccines specifically within the population of PLWH.

Case report

We report the case of a 41-year-old HIV-positive male patient, with no other underlying chronic disease, who experienced a marked decline in CD4+ T cell count and increase in viral load after vaccination against COVID-19. He works as a medical profes-

sional and tested positive for HIV for the first time in 2015. The mode of HIV transmission was thought to be via sexual contact with another male; no history of intravenous drug abuse or blood transfusion was reported [Au?1]. Antiviral therapy (ART) was not initiated due to the patient's personal preferences. Follow-up visits were completed in the outpatient department of Peking Union Medical College Hospital (PUMCH), China.

Up until November 2020, the patient's CD4+ T cell count had been over 500/ μ l and his HIV viral load had been around 4.0 log₁₀ copies/ml. Immediately after the two doses of inactivated COVID-19 vaccine (Sinopharm), which were administered on January 10 and February 1, 2021, respectively, his CD4+ T cell count dropped to 285/ μ l (Figure 1, panel A). This was identified during follow-up as standard of care at another medical center in March 2021, although no other symptoms or signs were reported. No new sexual partners, new medications, or changes in lifestyle, diet, sleep, or work stress were reported. His viral load re-examined on April 1, 2021 at PUMCH had increased to 4.9 log₁₀ copies/ml (Figure 1, panel B).

The results of other laboratory tests obtained before and after vaccination were compared (November 25, 2019 and April 1, 2021, respectively). Within the CD4+ T cell population, the percentage of memory (CD45RA⁻) CD4+ T cells increased from 45.5% to 76.8%, and the percentage of naïve (CD45RA⁺) CD4+ T cells decreased from 54.5% to 23.2% (Figure 1, panel C). The blood counts and transaminases before and after vaccination were all within normal limits. Laboratory tests for hepatitis performed in April showed positivity only for hepatitis B surface antibody, but he was negative for all other hepatitis B antigens/antibodies and hepatitis C antibody.

* Corresponding author: Taisheng Li, Department of Infectious Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, 1# Shuai Fu Yuan, Beijing, China, 100730. Tel.: +86-10-69155086. Fax: +86-10-69155046

E-mail address: litsh@263.net (T. Li).

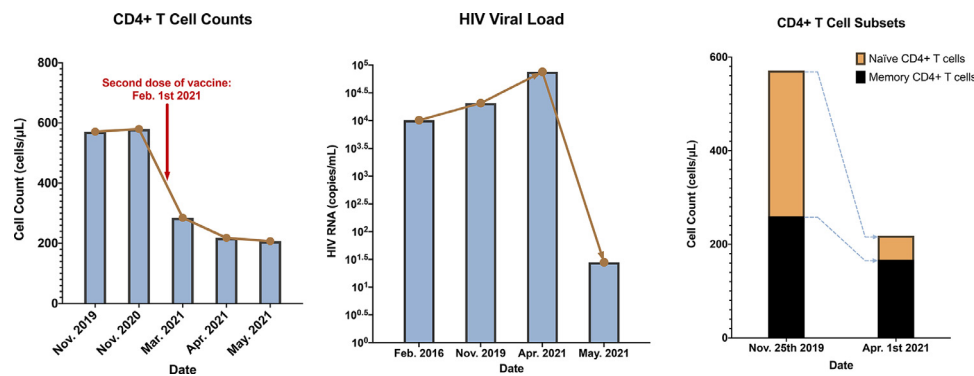


Figure 1. Virological and immunological changes in the patient after he had received the COVID-19 vaccine. (A) Changes in CD4+ T cell count after vaccination. (B) Changes in viral load after vaccination. (C) Changes in subsets of CD4+ T cells after vaccination.

To prevent further deterioration of the infection, ART was initiated on April 12 with bicitgravir/emtricitabine/tenofovir alafenamide (B/FTC/TAF; Biktarvy, Gilead). Follow-up visits showed good viral control but less satisfactory CD4+ T cell counts, consistent with the usual course of disease in HIV management, where viral control may be achieved sooner than the normalization of CD4+ T cells.

Discussion

This appears to be the first reported case of a treatment-naïve HIV-positive patient experiencing a deterioration of HIV infection after receiving COVID-19 vaccine, raising concerns regarding vaccination in this population. A similar deterioration has been reported in a patient with immune thrombocytopenia, manifesting as depleted platelet counts (Jawed et al., 2021). The immunological profile of the patient presented here was remarkably altered after vaccination, manifesting as a substantially increased HIV viral load and decreased CD4+ T cell count, naïve CD4+ T cells in particular, which would not be expected otherwise in the natural course of HIV infection. With other common causes of lymphocytopenia being less likely, such as other chronic viral infections, immunological disorders, and hematological conditions, vaccination became the most likely trigger.

A decrease in CD4+ T cell count has also been observed in COVID-19 patients, and it seems reasonable to assume that some components in the vaccine might also have the same effect. However, if that was the case, there should also be an increased proportion of naïve CD4+ T cells, as observed in COVID-19 patients (Peng et al., 2020), contrary to the decreased proportion in the patient presented here. Therefore, activation of HIV infection might be a better explanation than immune reaction to the COVID-19 vaccine alone. Although many inactivated vaccines are considered safe in PLWH, negative influences have been reported, such as an increased HIV viral load after influenza, pneumococcus, and tetanus vaccinations (O'Brien et al., 1995, Katzenstein, 1997, Stanley et al., 1996). Despite the subsequent controversy, the case presented here raises the same concern. So, we propose that PLWH with unsatisfactory disease control are susceptible to vaccine-related HIV activation and CD4+ T cell loss, which might not be specific to COVID-19 vaccines.

Our hypothesis is that the activated HIV infection could result in accelerated destruction of CD4+ T cells directly. Moreover, inappropriate stimulation of the immune system by HIV further accelerates the turnover of CD4+ T cells, manifesting in this case as a lower percentage of naïve (CD45RA+) CD4+ T cells and a higher percentage of memory CD4+ T cells. The activation of CD4+ T cells by exogenous antigens might also contribute to the decreased percentage of naïve CD4+ T cells (Stanley et al., 1996, Rousseau et al.,

1999). These processes eventually lead to the loss of all subsets of CD4+ T cells, with naïve CD4+ T cells being the most severely affected.

In practice, different vaccination strategies are employed in different countries. According to the current guidelines in China, ART and stable viral control before COVID-19 vaccination in PLWH are emphasized (AIDS and Hepatitis C Professional Group 2021), which is consistent with our concerns in this patient. Considering that the vast majority of vaccines available in China are inactivated vaccines, with PLWH excluded from clinical trials (Al Kaabi et al., 2021, Tanriover et al., 2021), further evidence is needed to form a thorough vaccination strategy to safely provide immunization to as many people as possible. For all PLWH, we suggest ART be initiated as soon as possible, not only to preserve immune function and avoid secondary HIV transmission, but also to avoid the complicated interaction between HIV infection and other health conditions or procedures, such as vaccination in this case.

As per the United States Centers for Disease Control and Prevention, immunocompromised patients may receive the COVID-19 vaccines (Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States [Internet] 2021). In North America and Europe, mRNA vaccines and adenovirus vector vaccines are widely used, both of which allow the constant production of exogenous antigens, probably raising the same issue as in this case. While PLWH were included in the clinical trials of these vaccines, either good viral control or ART use was required in the criteria for eligibility (Baden et al., 2021, Polack et al., 2020, Ramasamy et al., 2021). Thus, more data are required to address this problem.

With regard to subunit vaccines, another major type of COVID-19 vaccine in China still in phase III clinical trials, PLWH were not involved in earlier studies (Yang et al., 2021). However, worsening of HIV infection after receiving other subunit vaccines, such as a varicella-zoster virus vaccine, has also been reported (Berkowitz et al., 2015). Therefore, the safety of all COVID-19 vaccines in ART-naïve PLWH requires further investigation.

A single case report is presented here. Well-controlled studies are needed to determine whether vaccination carries the risk of deterioration of HIV infection in patients with or without satisfactory disease control. In these studies, PLWH should also be further grouped according to their disease control, in order to make better adjustments to the current guidelines.

In conclusion, exogenous antigens might cause viral activation and CD4+ T cell depletion in PLWH. Thus, inactivated COVID-19 vaccines and likely similar vaccines should not be administered to treatment-naïve PLWH, but should be administered to patients with satisfactory disease control. Furthermore, all PLWH should receive ART as soon as possible.

Funding source

This work was supported by the Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences (CAMS-I2M) [2017-I2M-1-014].

Ethical approval

The patient described in this study gave consent to publish the history and laboratory test results anonymously.

Conflict of interest

No potential competing interest is reported by the authors.

Acknowledgements

We would like to extend our appreciation to all of the health-care workers and technicians working for the care of HIV patients at Peking Union Medical College Hospital.

References

- Su JR, Ng C, Lewis PW, Cano MV. Adverse events after vaccination among HIV-positive persons, 1990–2016. *PLoS One* 2018;13(6).
- Haynes BF. SARS-CoV-2 and HIV-1 - a tale of two vaccines. *Nat Rev Immunol* 2021;1–2 Jul 16.
- Eisinger RW, Lerner AM, Fauci AS. HIV/AIDS in the Era of COVID-19: A Juxtaposition of Two Pandemics. *J Infect Dis* 2021;jiab114 Apr 7.
- Tesoriero JM, Swain CE, Pierce JL, Zamboni L, Wu M, Holtgrave DR, et al. COVID-19 Outcomes Among Persons Living With or Without Diagnosed HIV Infection in New York State. *JAMA Netw Open* 2021;4(2) Feb 1.
- Jawed M, Khalid A, Rubin M, Shafiq R, Cemalovic N. Acute Immune Thrombocytopenia (ITP) Following COVID-19 Vaccination in a Patient With Previously Stable ITP. *Open Forum Infect Dis* 2021;8(7):ofab343 Jun 24.
- Peng X, Ouyang J, Isnard S, Lin J, Fombuena B, Zhu B, et al. Sharing CD4+ T Cell Loss: When COVID-19 and HIV Collide on Immune System. *Front Immunol* 2020;11 Dec 15.
- O'Brien WA, Grovit-Ferbas K, Namazi A, Ovcak-Derzic S, Wang HJ, Park J, et al. Human immunodeficiency virus-type 1 replication can be increased in peripheral blood of seropositive patients after influenza vaccination. *Blood* 1995;86(3):1082–9.
- Katzenstein TL. Pneumococcal vaccination of HIV-infected individuals: safety and efficacy. *AIDS Patient Care STDS* 1997;11(4):269–75.
- Stanley SK, Ostrowski MA, Justement JS, Gantt K, Hedayati S, Mannix M, et al. Effect of immunization with a common recall antigen on viral expression in patients infected with human immunodeficiency virus type 1. *N Engl J Med* 1996;334(19):1222–30.
- Rousseau MC, Moreau J, Delmont J. Vaccination and HIV: a review of the literature. *Vaccine* 1999;18(9–10):825–31.
- AIDS and Hepatitis C Professional Group. Chinese Society of Infectious Diseases. Expert recommendation for novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination in patients with HIV infection. *Chin J Intern Med* 2021;60(7):615–18.
- Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, et al. Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial. *JAMA* 2021;326(1):35–45 Jul 6.
- Tanriover MD, Doğanay HL, Akova M, Güner HR, Azap A, Akhan S, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. *Lancet* 2021 Jul 8:S0140-6736(21)01429-X.
- Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States [Internet]. US: Centers for Disease Control and Prevention; [updated 2021 Apr 27; cited 1 May 2021]. Available from: <https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>.
- Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med* 2021;384(5):403–16 Feb 4.
- Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med* 2020;383(27):2603–15 Dec 31.
- Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2021;396(10267):1979–93 Dec 19.
- Yang S, Li Y, Dai L, Wang J, He P, Li C, et al. Safety and immunogenicity of a recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) against COVID-19 in adults: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials. *Lancet Infect Dis* 2021;S1473-3099(21):00124–7 Mar 24.
- Berkowitz EM, Moyle G, Stellbrink HJ, Schürmann D, Kegg S, Stoll M, et al. Safety and immunogenicity of an adjuvanted herpes zoster subunit candidate vaccine in HIV-infected adults: a phase 1/2a randomized, placebo-controlled study. *J Infect Dis* 2015;211(8):1279–87 Apr 15.