International Journal of Infectious Diseases 117 (2022) 230–232

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

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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.

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 professional 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/μl and his HIV viral load had been around 4.0 $\log_{10}$ 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/μl (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 $\log_{10}$ 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.

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https://doi.org/10.1016/j.ijid.2021.08.039

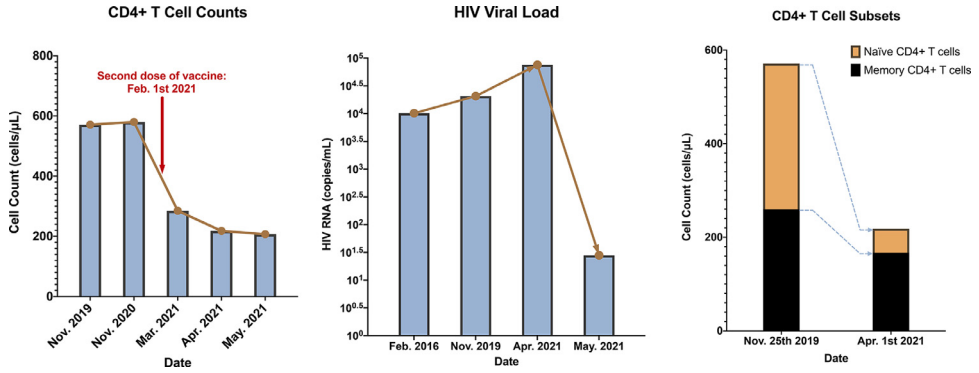

Figure 1. Virological and immunological changes in the patient after he had received the COVID-19 vaccine. (A) Changes in CD4+ T cell count after vaccination. (B) Changes in viral load after vaccination. (C) Changes in subsets of CD4+ T cells after vaccination.

To prevent further deterioration of the infection, ART was initiated on April 12 with bictegravir/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.

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