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Unintended HIV-1 Transmission to a Sex Partner in a Study of a Therapeutic Vaccine Candidate

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We report a case of sexual transmission of human immunodeficiency virus (HIV) that occurred during treatment discontinuation in a therapeutic vaccine trial, following oral sex. Transmission occurred even though the index participant was an HIV/AIDS activist, particularly well informed about the risks and modalities of transmission. This case report highlights the risk of secondary transmission of HIV during cessation of treatment in HIV cure–related trials.

Keywords. HIV therapeutic vaccine; secondary transmission; oral sex; analytic treatment interruption.

We describe a case of unintended transmission of human immunodeficiency virus (HIV) during treatment interruption in a therapeutic vaccine trial among serodiscordant couples. The index participant was enrolled in the ANRS LIGHT VRI02 trial, a randomized, multicenter, double-blinded, placebo-controlled phase 2 therapeutic vaccine trial in France. This study aimed to evaluate the virological efficacy of therapeutic immunization, combining a recombinant DNA vaccine (GTU-MultiHIV B; 3 injections at weeks 0, 4, and 12) with a lipopeptide vaccine (LIPO-5; 2 injections at weeks 20 and 24) in HIV-1–infected patients who were receiving combination antiretroviral therapy (cART) and had had undetectable viral loads for at least 18 months (clinical trials registration NCT01492985).

Analytical treatment interruption (ATI) was planned between week 36 and week 48 of the trial (ie, 12 weeks after the last vaccine/placebo injection). During ATI, participants were followed up every 2 weeks, both clinically and biologically, with routine bioassays, $CD4^+$ T-cell count measurements, and HIV load testing. The following inclusion criteria were chosen to minimize the risk of clinical events during the ATI: (1) the absence of Centers for Disease Control and Prevention category C clinical events (1993 revised classification), including a history of cutaneous Kaposi sarcoma; (2) a nadir $CD4^+$ T-cell count of ≥ 300 cells/mm^3; (3) a $CD4^+$ T-cell count of ≥ 600/mm^3 at all measurements during the 6 months before their week 3 screening visit; and (4) a plasma HIV-1 RNA load of < 50 copies/mL at all measurements within the previous 6 months. Moreover, at each study visit, participants were advised to use condoms and were counseled on the risks of transmission, to preclude secondary transmission. The use of preexposure prophylaxis (PrEP) was not offered to the partners of the included participants because it had not been validated at the time the trial was conducted. Premature restart of cART (before week 48) was allowed for any of the following reasons: (1) a decrease in the $CD4^+$ T-cell count to ≤ 350 cells/mm^3, (2) evidence of disease progression, or (3) request from the participant or the physician, owing to concerns regarding the participant's health. One hundred and three participants were enrolled between 1 September 2013 and 4 May 2015 in 18 clinical sites in France. Ninety-eight participants received at least 1 injection of vaccine/placebo, and 93 received all vaccines (randomization was 2: 1) [1].

The index case was a 59-year-old heterosexual man who received a diagnosis of HIV infection in 2005, during the primary infection phase. Once he began cART, in 2005, he attained an undetectable HIV load. The discovery of his HIV status changed his relationship with the world and led him to become an activist, regularly attending meetings in his region. He, therefore, should be considered someone who is very familiar with HIV infection. Apart from HIV infection, he also had chronic depression (for which he refused to take treatment) and poorly managed diabetes mellitus. He was married in the past but had separated, and he no longer maintained a relationship with his previous wife. When he was enrolled in the trial, he was living with a new partner, who accompanied him to the trial consultations. This new partner was a 44-year-old woman with whom he had lived for the subsequent year. She had no medical history outside of depression, for which she did not report taking medication. Neither of them reported sexual relations with other partners.

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The index case was enrolled in the ANRS LIGHT VRI02 trial in mid-2014 and received 5 immunizations with vaccine or placebo according to the trial's protocol. He reported no adverse events related to those immunizations. On the day of his consultation, in the beginning of October 2014, corresponding to the date of treatment interruption, the physician noted the following in the patient's medical file: "The patient (in the presence of his partner) is perfectly informed i) of the need to protect all sexual intercourse by a physical means (condom) and ii) the possible risk of primary-infection-like syndrome in case of resumption of viral replication." One month after treatment interruption, the participant's viral load rose to 3.3 log copies/mL, with a zenith that did not exceed 4.2 log copies/mL at 6 weeks and a spontaneous return to a plateau at 3 log copies/mL after 2 months. The participant did not report any special symptoms.

At the beginning of November, the participant's partner presented with a clinical picture suggestive of primary infection associating fever, arthralgia and an erupting rash on the neckline that spontaneously resolved. A rapid HIV antibody test was performed 3 weeks later, and both the participant and his partner were consulted 1 week later. The partner's HIV infection was confirmed by enzyme-linked immunosorbent assay and Western blot, and secondary transmission was confirmed by a phylogenetic analysis of the viral strains obtained from the participant and his partner. ART was resumed in the participant and initiated in his partner. The couple reported having had unprotected oral sex (cunnilingus only) 2–3 times during the ATI.

This case highlights the risk of secondary transmission of HIV infection during treatment interruption, including among participants who have a good understanding of their HIV infection and its effects and whose level of viral rebound is low. This risk is undoubtedly in part enhanced by a lack of protective sexual practices among participants who have become accustomed to no longer needing them while receiving effective treatment and viral suppression. In the case reported here, transmission seems linked to the practice of cunnilingus, which is not considered a risky act. However, it cannot be ruled out that other sexual relations could have taken place and this case should not be reconsider the absence of risk related to this sexual act. Our case report shows that even well-informed patients/activists can harm themselves. Physicians have to make a checklist of all items that are associated with a risk of HIV transmission (eg, fellatio, penetrative sex, and route of penetration). It is, therefore, essential to continuously reinforce the risk of secondary transmission during clinical trials that include a treatment interruption in conversations with all study participants and to propose, whenever possible, the prescription of PrEP to study participants' partners. However, preventive treatment is associated with potential side effects and the PreP offer may be difficult to manage in practice if partners are multiple and casual (see the article by Lelièvre [2] elsewhere in this issue).

Notes

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