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HIV drug resistance test harbouring the RT M184V mutation in a PrEP (Pre Exposure Prophylaxis) administered sex worker

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Introduction

Pre-Exposure Prophylaxis (PrEP) is considered one of the most important recent biomedical advances in HIV prevention. Although its effectiveness is well established in the literature, compliance and retention of individuals using PrEP in reference services is challenging, especially in vulnerable populations.

Case presentation

A 41-year-old Brazilian transgender sex worker who has been living in Italy for 20 years presented to the II Infectious Diseases Division of ASST Fatebenefratelli Sacco due to persistent fever, fatigue and bilateral cervical lymphadenopaty in August 2023.

The patient had a history of recurring genital condylomatosis and several plastic surgery interventions.

She had been regularly taking tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) as PrEP from 2020 until the middle of 2022 with time scheduled serological follow-up tests (the last negative HIV 1/2 Ab screening test was in May 2022). Thereafter, for unclear reasons, the administration of PrEP was both self-managed and not adherent to the schedule according to the national guide-lines.

At the diagnosis of HIV infection on 10th August 2023 after three months of persistent clinical symptoms, patient's viremia was 29.000 cp/mL with HIV-1/2 Western – Blot test positive for all HIV-1 bands and a CD4+ cell count of 368 cell/microL (21%); in addition both HCV-Ab and HBsAg were negative.

Methods

Next-Generation Sequencing HIV drug Resistance Test was performed on a plasma sample, using the HIV-1 Solution v2 kit (Arrow Diagnostic) on Miseq platfom (Illumina). The interpretation of NGS results was performed using the HIVdb Stanford tool (version 9.5.0 - 20230822) and SmartVir software (Arrow Diagnostics). Subtyping was assigned using the COMET HIV-1 (COntext-based Modeling for Expeditious Typingt) online tool.

Results

HIV drug Resistance Test revealed a B subtype virus harbouring the 3TC/FTC signature mutation RT-M184V as major *quasispecie* (86%) with only polymorphisms detected on protease (PR-L10V) and integrase (IN-M50I) regions. According to the current strategy "test and treat" bictegravir/TAF/FTC regimen was promptly administered: despite the low baseline viral load probably due to the presence of the mutation RT-M184V affecting viral replication capacity, virological undectability resulted just 5 months after with an optimal immunological recovery (CD4+ 1000 cell/microL, 36%).

Drug resistance interpretation: RT

NRTI Mutations:	**M184MV** V: 86%, M: 11% cov=3,065
NNRTI Mutations:	None
abacavir (ABC)	Low-Level Resistance
zidovudine (AZT)	Susceptible
stavudine (D4T)	Susceptible
didanosine (DDI)	Potential Low-Level Resistance
emtricitabine (FTC)	High-Level Resistance
lamivudine (3TC)	High-Level Resistance
tenofovir (TDF)	Susceptible

Conclusion

We reported a case of a HIV-1 infection in a transgender sex worker with a PrEP associated mutation. The presence of RT-M184V alone at high frequence (86%) without any other drug resistance mutations can be reasonably attributed to a suboptimal administration of PrEP rather than to the result of a mutated virus transmission. The consolidated strategy "test and treat" and the use of the two-drug regimen, dolutegravir plus lamivudine, for initial treatment highlights the importance of adherence counselling and monitoring: PrEP users should constantly be reminded of the importance of adequate drug levels and possibility of drug-resistant HIV. Implementation strategies for PrEP administration in different risk populations, especially in fragile setting, are needed.

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