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Open access Case Report

Three-Class Drug Resistance in a HIV Treatment-Naive Individual: A Case Report

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ABSTRACT

This report describes a patient who was newly diagnosed with HIV and was found to have resistance to drugs from three major classes of Antiretroviral Therapy (ART), which is the first case of three-class HIV drug resistance reported in treatment-naive individuals amongst the Gulf Cooperation Council Region, to the best of our knowledge.

Keywords: Transmitted drug resistance; HIV; AIDS; Resistance-associated mutations; Antiretroviral therapy; Viral transmission

INTRODUCTION

Drug resistance is a major concern when it comes to treating HIV, particularly in treatment naive patients. The Transmission of Drug-Resistant (TDR) strain poses a challenge for the control of the HIV-1 epidemic. It occurs when a person who have never received antiretroviral therapy before, get infected with a strain of HIV that is resistant to one or more drugs used to treat the virus. Such infection can be harder to treat effectively and make HIV management much more challenging.

CASE REPORT

We reported a case of 48-year-old Saudi woman, living in Kuwait who was diagnosed with HIV after undergoing a hematological work-up for leucopenia. She is treatment naive and claims to have contracted the virus either through a salon procedure or from her ex-husband. The initial viral load is noted to be quite high at 279581 copy/ml and the CD4 cell count is also low at 182 cell/ml.

At diagnosis, she was offered a counselling and a series of blood tests and found to be eligible for same day HIV treatment initiation, which is the current practice in Kuwait, and she was offered a Single Tablet Regimen (STR) that is a combination of three drugs: Bictegravir (BIC) Emtricitabine (FTC) and Tenofovir Alafenamide Fumarate (TAF).

Three weeks later, her HIV sequencing through viral RNA extraction from plasma sample showed HIV-1 subtype CRF01_AE with high similarity with sequence from Thailand, and the following result:

Protease Inhibitors (PI) shows no major or accessory mutations, but minor mutations: L10I, I13V, K14R, I15V, E35D, N37D, N37S, R41K, H69K, L89M and the drugs in this class are susceptible. And the sequence includes PR: Codons 1-99. Of note that L10I/V is polymorphic, PI selected mutations that might increase the replication of the virus.

For Nucleoside (NRTI) and Non-Nucleoside (NNRTI) reverse

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transcriptase inhibitors Ad the sequence included RT: Codons 1-560

And it shows the following:

NRTI mutations: D67N, K70E, K219R

NNRTI mutations: A98G

With many other minor mutations resulting in a resistant to all class medication with different resistance degree:

- Abacavir (low level resistance)
- Zidovudine (low level resistance)
- Stavudine (intermediate resistance)
- Didanosine (low level resistance)
- Emtricitabine (potential low level resistance)
- Lamivudine (potential low level resistance)
- Tenofovir (low level resistance)
- Doravirine (low level resistance)
- Efavirenz (low level resistance)
- Etravirine (potential low level resistance)
- Nevirapine (intermediate level resistance)
- Rilpivirine (low level resistance).

For integrase strand transfer inhibitors the sequence included codons was 1-288 and it shows major mutation E138K with multiple other minor mutations resulted in resistance to:

- Bictegravir (potential low level resistance)
- Cabotegravir (potential low level resistance)
- Dolutegravir QD (potential low level resistance)
- Elvitegravir (low level resistance)
- Raltegravir (low level resistance)

While Dolutegravir BD was susceptible.

She was tolerating the TAF/FTC/BIC regimen very well, but due to an unfavorable genotype result, it was recommended that she switch to twice-daily Dolutegravir at 50 mg along with co-formulated Darunavir and Cobicistat at 800/150 mg daily. Following the switch, her viral load became undetectable and her CD4 count showed a notable improvement.

RESULTS AND DISCUSSION

HIV transmitted drug resistance can pose a challenge for HIV treatment and prevention efforts because it restricts a range of drugs that can be used to manage the infection and increase risk of treatment failure and disease progression.

It's crucial that countries take proactive measures to monitor and identify the emergence of drug-resistant strains of HIV, especially given the potential for this problem to spread to different regions of the world. Hopefully, with the right monitoring and prevention strategies in place, we can continue to effectively manage the infection and reduce the risk of treatment failure and disease progression. It's always important to stay vigilant and take action to protect public health.

World Health Organization (WHO) issued a warning about HIV drug resistance and the concern that it may spread to different regions in the world. They recommend countries to look at Early Warning Indicator (EWI) and implement monitoring system which is designed to identify and track the emergence of HIV drug resistant strains [1].

To the best of our knowledge, based on the available resources at our disposal, this is the first case of three-class HIV drug resistance reported in treatment-naive individuals in Kuwait and the Gulf Cooperation Council countries (Saudi Arabia, Oman, United Arab Emirates, Bahrain, Kuwait and Qatar), and it might be considered to be a warning indicator.

HIV associated mutations (RAM) confer resistance to single class in treatment naïve was reported previously in Kuwait [2]. While two-class resistance was reported previously in treatment naïve in Saudi Arabia in cases with mutations conferring resistance to both NRTI and NNRTI or PI [3,4].

Globally, few cases of resistance to three classes of antiretroviral drugs have been reported among treatment naive individuals living with HIV, specifically the NRTIs, NNRTIs and PIs. In a study by Agwu et al., 12 out of 130 treatment-naive subjects with HIV transmitted drug resistance among youth, 2 of the 12 (16.7%) had triple class resistance against NRTIs, NNRTIs, and PIs. However, screening genotypes were not evaluated for integrase inhibitors. No significant factors were associated with the identification of transmitted drug resistance.

HIV-1 CRF01_AE is predominant in Southeast Asia and East Asia and it is believed to have originated in Thailand. It is a recombinant form of HIV that is mix of clades A and E. This strain is known to be highly virulent and can rapidly progress to full blown Acquired Immune Deficiency Syndrome (AIDS) and can develop resistance to antiretroviral therapy through the accumulation of mutations in the virus [5].

CONCLUSION

It is crucial for healthcare providers and policymakers to collaborate and establish an early warning monitoring system to prevent the spread of drug-resistant HIV strains. Additionally, ensuring the availability of effective second and third-line treatment options for HIV.

HIV genotyping is an essential tool even in same-day initiation approach that uses first-line recommended medications with high genetic barrier. It provides crucial information about the individual's specific viral strain.

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CONFLICT OF INTEREST

The Authors declare that there is no conflict of interest.

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