Heliyon 10 (2024) e27219

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Case report

A case of multiple ART intolerance responds to Albuvirtide and Dolutegravir: Case report and literature review

Zhong Chen, Tan Si, Li Ying, Cao Guiying, Xiè Jiàn Píng, Min Wang *

The First Hospital of Changsha, China

ARTICLE INFO

Keywords:
HIV/AIDS
Antiretroviral therapy (ART)
Drug intolerance
Adverse reactions
Long-acting ART
Albuvirtide (ABT)
Dolutegravir (DTG)

ABSTRACT

Upon confirming an HIV diagnosis, patients need to start life-long antiretroviral therapy (ART) as soon as possible. During HIV treatment, ART drugs can cause intolerable adverse reactions, leading to poor medication compliance, treatment failure, and advancement of the HIV stage. Herein, we report a case of AIDS intolerant to multiple antiviral drugs due to side effects that we finally stabilized with the Albuvirtide (ABT) and Dolutegravir (DTG) combination. A 48 -year-old woman developed intractable nausea, vomiting and abdominal discomfort within one month of starting ART. Over the course of four years, she was switched to four different ART regimens due to her intolerance of severe adverse effects, mainly gastrointestinal symptoms, rash, and lethargy. Over four years, she failed to attain viral suppression due to poor drug compliance. After several ART changes, we started her on the Long-acting antiretroviral therapy (LA ART), Albuvirtide, combined with Dolutegravir, which she tolerated well. The patient's general condition improved significantly and attained marked virologic suppression. The patient's condition has been well controlled for nearly two years with good adherence. This case emphasizes the influence of ART treatment options on medication compliance and the outcome of HIV infection.

1. Introduction

Acquired Immunodeficiency Syndrome (AIDS) is a chronic, potentially life-threatening condition caused by the Human immunodeficiency virus (HIV), which destroys the body's immunity, thus impairing its ability to fight infections. AIDS is the late stage of HIV infection. With the promotion of ARTs, HIV/AIDS has developed into a chronic condition, and its complications are no longer primary concerns in well-resourced countries [1]. Due to effective antiviral drugs, HIV/AIDS patients' life span is significantly longer than in the past and close to the average level. However, some HIV-infected patients also suffer from ART adverse effects causing poor medication compliance and drug resistance during treatment, resulting in treatment failure [2,3].

More than 8000 people have received ART since 2003 when Changsha city began to provide free ART. Still, some patients have poor compliance to ART due to adverse drug reactions, drug interactions and other reasons, resulting in poor adherence. In recent years, better efficacy has been achieved due to the discovery of LA ART with fewer side effects [4,5].

Albuvirtide, a long-acting HIV-1 injectable fusion inhibitor developed in China. It is administered weekly through intravenous administration and has achieved good results in terms of effectiveness and safety [6]. It has a maximum half-life of 12 days [7]. Dolutegravir (DTG) is an oral HIV integrase inhibitor with a half-life of about 14 hours. It is quickly absorbed attaining the plasma maximum concentration in 0.5–2 hours [8]. Therapeutic DTG exposure levels were maintained for up to 72 hours [9], its safety and

* Corresponding author.
E-mail address: cswangmin0627@163.com (M. Wang).

https://doi.org/10.1016/j.heliyon.2024.e27219
Received 13 August 2023; Received in revised form 13 February 2024; Accepted 26 February 2024
Available online 12 March 2024

effectiveness have been proven, along with other advantages [10]. We report a case of HIV/AIDS intolerant to multiple antiviral drugs and finally stabilized with the Albuvirtide combined with Dolutegravir treatment.

2. Case presentation

A 48-year-old female was diagnosed with HIV infection eight years ago. The baseline investigations revealed; CD4+T cells of 181 cells/μL, liver and kidney functions were normal. 6 months after the diagnosis (December 2014), she was initiated on lamivudine (3TC) + tenofovir (TDF) + nevirapine (NVP).

She was adherent to her medication until January 30, 2015, when she got hospitalized because of persistent nausea and vomiting for two weeks. After physical examination and investigations, we admitted her with the diagnoses of HIV/AIDS and drug-induced hepatitis. We kept her on hepatoprotective therapy, antiemetics and continued her ART. One week later, we replaced her initial regimen with 3TC + TDF + Efavirenz (EFV) as we considered NVP-induced liver damage. Her general condition improved within a week. We discharged her with normal liver and kidney function test results. Three months later, she was seen with skin rashes at the outpatient clinic. Blood examination revealed elevated eosinophils, the liver and kidney functions were normal. After excluding other causes, we considered EFV the cause of the allergic rash and switched her to a 3TC + TDF + lopinavir/ritonavir (LPV/R). She remained on this regimen for a month before the complaints of persistent nausea, fatigue and abdominal discomfort. These symptoms gradually became worse and became intolerable. She requested a change of ART regimen. After through counselling and exclusion of other causes of these symptoms, we switched her to 3TC + TDF + RAL.

She stayed on this regimen until two years later (August 2018), when she was admitted again due to severe fatigue and joint pain. Laboratory and radiological examinations were normal. We managed her symptoms and kept her on osteo support therapy. She was discharged after ten days with an improved condition. She was re-admitted a year later due to severe fatigue and poor appetite. She reported having stopped ART five months earlier. Laboratory investigations revealed that; HIV-1 RNA was 51,200 copies/mL, $CD4^+$ −146 cells/μL, $CD8^+$ - 445 cells/μL, kidney and liver function tests were normal. We counseled her and resumed her on (3TC + TDF + RAL). We discharged her after two weeks in a stable state.

Four months later, she was seen at the outpatient clinic. Her general condition was stable. The laboratory test revealed; HIV-1 RNA load of 35,200 copies/mL and $CD4^+$ count of 238 cells/μL. She reported poor compliance due to economic concerns; thus, she requested to enroll for the national free ART drugs. We enrolled her for the free national ART and changed her regimen to 3TC + TDF + LPV/r.

During her routine follow-up as an outpatient, she complained of intermittent fatigue, persistent loss of appetite, diarrhea and abdominal discomfort since switching to 3TC + TDF + LPV/r. These symptoms were the major hindrance to her compliance. Laboratory examinations, were normal. We counseled her and switched the regimen to ABT + DTG. Since then (May 2019), she remained on this regimen with significant viral suppression, HIV-RNA (<50 cp/mL), good compliance and did not report any significant discomfort. Her viral load and $CD4^+$ T cell count trend are shown in Fig. 1a and b respectively.

3. Discussion

We report a case of AIDS with multiple ART intolerance, the clinical profile and management.

As a lifelong treatment, ART requires good compliance and adherence to attain viral suppression. While some ART drugs have been reported to have adverse side effects which cannot be tolerated, other reasons may lead to poor medication compliance, which leads to further immune suppression, viral rebound and progression to advanced stages. In this case, the compliance was compromised by ART adverse effects. The patient was hospitalized several times. She used multiple (five) regimes, most of which were stopped or changed

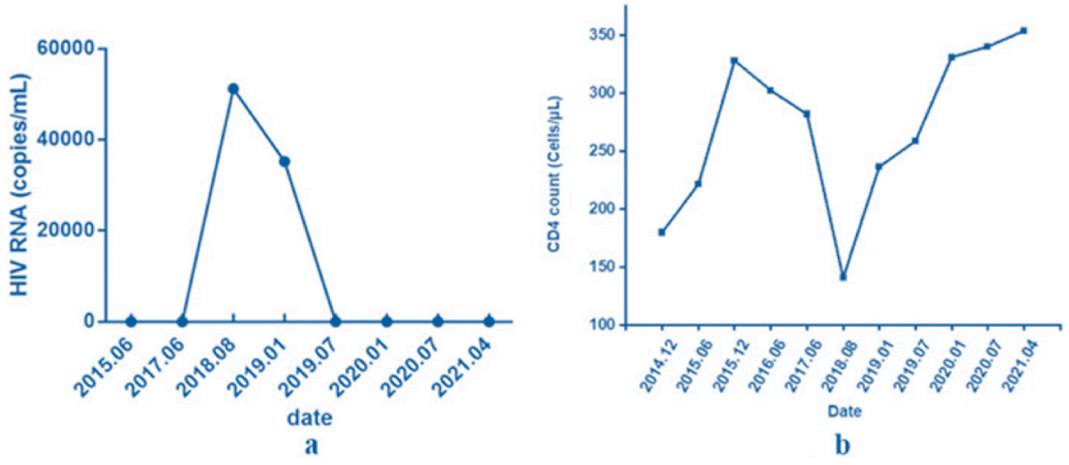

Fig. 1. Shows changes in HIV viral load (copies/mL of blood) (a) and $CD4^+$ T cells (cells/mm^3) (b) during the treatment course.

due to adverse side effects, notably fatigue, nausea, vomiting and rashes. Other causes of these conditions were ruled out.

The patient had a baseline $CD4^+$ T cell count of less than 200 cells/μL, indicating that she already had AIDS at diagnosis. After proper counselling, she was initiated on ART. Her immune status improved steadily until when, she started experiencing a series of ART side effects that were intolerable. This compromised her drug adherence but she was never disengaged in care. Several self-withdrawals during treatment resulted in viral rebound and decreased $CD4^+$ T cell count. After trying several ART regimens, the Albuvirtide combined with DTG regimen resulted in good tolerance and was finally selected to better maintain medication compliance. Together with the patient requirements, its tolerability, and the subsequent impacts of COVID-19 were considered since Albuvirtide has a half-life of up to 12 days [7]. We kept the patient on Albuvirtide infusion (320 mg) every two weeks and daily oral DTG (50 mg). She started this treatment in May 2019, achieved viral suppression in 3 months (VL < 50 copies/mL) and maintained it (Fig. 1a) and her $CD4^+$ cell count improved gradually as seen in (Fig. 1b).

LA ART provide new options for HIV treatment. With fewer side effects, LA ART are expected to improve compliance and benefit more patients [5]. Albuvirtide is a HIV fusion inhibitor with regulatory approval in China for treatment of HIV. It has a maximum half-life of 12 days in the blood circulation and has good anti-HIV activity [11]. Phase III clinical trials demonstrated that HIV-1 patients with viral replication after antiviral treatment tolerated a once-weekly injection of Albuvirtide combined with LPV/r therapy well. Its effectiveness was not inferior to second-line regimens recommended by the WHO. It is documented to have fewer adverse reactions and is safe [6]. Dolutegravir is a second-generation integrase inhibitor with many advantages over other oral anti-HIV drugs, such as a longer half-life, fewer side effects, highly effective in viral load reduction, with fewer drug interactions. It is safe and recommended for all populations, including pregnant women [8,10,12,13].

The patient did not complain of any particular discomfort, had good compliance and attained virological suppression (<50 cp/mL) under this regimen. She has remained on the same regimen for three years without any complaint and she perceived that this medicine tolerable and helpful. The HIV has been significantly suppressed during this time, with undetectable viral road and improved $CD4^+$ count.

4. Conclusion

This case report shows that Long-acting antiretroviral therapy; Albuvirtide, in combination with Dolutegravir was tolerated well in a patient who could not tolerate the side effects of most conventional ARTs. So, this implies good tolerability and viral suppression by the two drugs in a case with poor drug tolerability hence improving the long-term compliance.

Introducing ART drugs with fewer side effects and long-term action is critical to improving patient compliance and quality of life. Combining Albuvirtide with the integrase inhibitor Dolutegravir can effectively suppress the virus. This regimen should be considered in patients with HIV with multiple ART drug intolerance. We also recommend more comprehensive studies using these drugs in patients with HIV experiencing multiple ART intolerance.

However, the patients need proper counselling about frequent hospital visits as self-medication is impossible for intravenous administered drugs. Furthermore, counselling in patients with HIV should be a continuous process, and a shared-decision treatment approach should be prioritized.

Ethics approval statement

We obtained written informed consent to publish the clinical details and images from the patient.

Data availability statement

The data associated with this study has not been deposited into a publicly available repository because the data was included and referenced in article.

Funding statement

This article was supported by the First Hospital of Changsha. Award number: (2018ZX10302104-001-002).

CRediT authorship contribution statement

Zhong Chen: Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Data curation, Conceptualization. **Tan Si:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Li Ying:** Writing – original draft, Data curation, Conceptualization. **Cao Guiying:** Writing – original draft, Data curation, Conceptualization. **Xiè Jiàn Píng:** Writing – original draft, Conceptualization. **Min Wang:** Writing – review & editing, Writing – original draft, Supervision, Resources, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] J.P. Chou, C.M. Ramirez, J.E. Wu, R.B. Effros, Accelerated aging in HIV/AIDS: novel biomarkers of senescent human CD8+ T cells, PLoS One 8 (2013) e64702, https://doi.org/10.1371/journal.pone.0064702.

[2] E. Aharonovich, E. Greenstein, A. O'Leary, B. Johnston, S.G. Seol, D.S. Hasin, HealthCall: technology-based extension of motivational interviewing to reduce non-injection drug use in HIV primary care patients – a pilot study, AIDS Care 24 (2012) 1461–1469, https://doi.org/10.1080/09540121.2012.663882.

[3] H. Li, G. Marley, W. Ma, C. Wei, M. Lackey, Q. Ma, et al., The role of ARV associated adverse drug reactions in influencing adherence among HIV-infected individuals: a systematic review and qualitative meta-synthesis, AIDS Behav. 21 (2017) 341–351, https://doi.org/10.1007/s10461-016-1545-0.

[4] S.H. He, H.X. Liu, Y. Yao, Y. Wang, R.F. Zhou, L. Cai, Clinical efficacy of Albuvirtide regimen in patients with severe AIDS, Sichuan Medical Journal 41 (2020) 893–897.

[5] A.I. Rana, J.R. Castillo-Mancilla, K.T. Tashima, R.L. Landovitz, Advances in long-acting agents for the treatment of HIV infection, Drugs 80 (2020) 535–545, https://doi.org/10.1007/s40265-020-01284-1.

[6] B. Su, C. Yao, Q.-X. Zhao, W.-P. Cai, M. Wang, H.-Z. Lu, et al., Efficacy and safety of the long-acting fusion inhibitor albuvirtide in antiretroviral-experienced adults with human immunodeficiency virus-1: interim analysis of the randomized, controlled, phase 3, non-inferiority TALENT study, Chinese Med J 133 (2020) 2919–2927, https://doi.org/10.1097/CM9.0000000000001273.

[7] H. Zhang, R. Jin, C. Yao, T. Zhang, M. Wang, W. Xia, Combination of long-acting HIV fusion inhibitor albuvirtide and LPV/r showed potent efficacy in HIV-1 patients, AIDS Res. Ther. 13 (2016) 8, https://doi.org/10.1186/s12981-016-0091-1.

[8] M.L. Cottrell, T. Hadzic, A.D.M. Kashuba, Clinical pharmacokinetic, pharmacodynamic and drug-interaction profile of the integrase inhibitor dolutegravir, Clin. Pharmacokinet. 52 (2013) 981–994, https://doi.org/10.1007/s40262-013-0093-2.

[9] E. Elliot, A. Amara, A. Jackson, G. Moyle, L. Else, S. Khoo, et al., Dolutegravir and elvitegravir plasma concentrations following cessation of drug intake, J. Antimicrob. Chemother. 71 (2016) 1031–1036, https://doi.org/10.1093/jac/dkv425.

[10] S.J. Snedecor, M. Radford, D. Kratochvil, R. Grove, Y.S. Punekar, Comparative efficacy and safety of dolutegravir relative to common core agents in treatment-naïve patients infected with HIV-1: a systematic review and network meta-analysis, BMC Infect. Dis. 19 (2019) 484, https://doi.org/10.1186/s12879-019-3975-6.

[11] H. Chong, X. Yao, C. Zhang, L. Cai, S. Cui, Y. Wang, et al., Biophysical property and broad anti-HIV activity of albuvirtide, a 3-Maleimimidopropionic acid-modified peptide fusion inhibitor, PLoS One 7 (2012) e32599, https://doi.org/10.1371/journal.pone.0032599.

[12] F. Raffi, A. Rachlis, H.-J. Stellbrink, W.D. Hardy, C. Torti, C. Orkin, et al., Once-daily dolutegravir versus raltegravir in antiretroviral-naive adults with HIV-1 infection: 48 week results from the randomised, double-blind, non-inferiority SPRING-2 study, Lancet 381 (2013) 735–743, https://doi.org/10.1016/S0140-6736(12)61853-4.

[13] S. Walmsley, A. Baumgarten, J. Berenguer, F. Felizarta, E. Florence, M.-A. Khuong-Josses, et al., Brief report: dolutegravir plus abacavir/lamivudine for the treatment of HIV-1 infection in antiretroviral therapy-naive patients: week 96 and week 144 results from the SINGLE randomised clinical trial, JAIDS Journal of Acquired Immune Deficiency Syndromes 70 (2015) 515–519, https://doi.org/10.1097/QAI.0000000000000790.