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Therapy Interruption in Patients with Human Immunodeficiency Virus Infection — Two Cases Report

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Authors' contributions

This work was carried out in collaboration between both authors. Author CML designed the protocol, provided these cases and reviewed the article. Author MCL wrote the article. Both authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Sustained use of combination antiretroviral therapy (cART) has been shown to decrease morbidity, mortality and human immunodeficiency virus transmission. However, incomplete adherence and treatment interruptions (TIs) have emerged as major challenges to the effectiveness of cART.
Currently clinical physicians at home and abroad still ask about the possibility of TIs for antiretroviral drugs and the effectiveness of resumptive treatment after TIs. This report provided experience sharing of two cases in our hospital for further discussions.
Both of these patients were young men diagnosed with HIV infection and their conditions were stabilized after cART with HIV viral load (VL) below 50 copies/ml (Roche Amplicor v1.5) and CD4

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counts as high as 600 cells/mm3. However, the patients inquired their physician to suspend their treatment due to quality of life concern. Their VL were significantly higher (>75 000 and 57 600 copies/ml) after their treatment were stopped four months and two months, respectively. Yet they started treatment again and their VL decreased rapidly to the instrument could not be detected (less than 400 copies/ml, Abbot Real Time) by the measured value of the situation 4 months later.
As "treatment as prevention (TasP)" has become the AIDS treatment guidelines, it's extremely important to not only minimize the occurrence of TIs but also be more active in dealing with the TIs issue.

Keywords: Human immunodeficiency virus infection; combination antiretroviral therapy (cART); treatment interruptions (TIs).

1. INTRODUCTION AND AIMS

The combination antiretroviral therapy (cART), cocktail therapy, has not only significantly improved the medical care quality of patients infected with human immunodeficiency virus (HIV) but also extended the patients' life since 1996 [1]. However, it should be noted that cART must be sustained and appropriate use to ensure the greatest benefits in the treatment of these drugs. Parts of the clinical patients due to poor tolerance to cART, side effects and toxicity lead to poor compliance and medication treatment interruptions (TIs) [2,3], which makes the efficacy of cART face a severe challenge.

Many observational studies and prospective clinical trials indicated whether planned TIs (structured) or unstructured TIs that mean patients with poor compliance, TIs have been shown to cause a rebound in viral load, a decrease in CD4 and an increased risk of opportunistic infections and death [4-6], even though the strategy of TIs can reduce treatment costs, decrease cART-related toxicity and improve the quality of life of patients. The strategy of TIs was not discontinued until the results of a large-scale cART (SMART) clinical trials was published by El-Sadr et al in 2006 [7]. Nevertheless, unstructured TIs continued to be found in subsequent literatures [8-10].

Currently clinical physicians at home and abroad still ask about the possibility of TIs for antiretroviral drugs and the effectiveness of resumptive treatment after TIs. This report provided experience sharing of two cases in our hospital for further discussion.

2. PRESENTATION OF CASE

A 22-year-old male had intermittent fever, sore throat, and mild headache two weeks before he was admitted to the hospital. He was sent to the ER of our hospital due to sudden loss of consciousness with tonic-clonic like seizure. He is diagnosed of HIV Ab positive with HSV-ⅠIgM:53.8 EU/ml、HSV-ⅡIgM:52.9 EU/ml. His cerebrospinal fluid analysis showed WBC: 210, L/N: 99/1. HIV infection, while herpes simplex virus meningoencephalitis was diagnosed. His HIV vial load (VL): 283100 copies/ml and CD_4 counts: 288 cell/ mm^3 were noted then.

After his clinical condition was stabilized, he was initially treated with cART by using zidovudine (AZT) (100 mg) 2 # tid, lamivudine (3TC) (150 mg) 1 bid, ritonavir (100 mg) 5# bid following up with continued outpatient. After three years and eight months of treatment, the patient's condition was stabilized with HIV VL < 50 copies/ml (by Roche Amplicor v1.5), CD_4 counts: 613 cell/mm^3.

As the model of antiretroviral drug treatment interruption began to be widely discussed internationally, the patient asked to temporarily stop cART but continue with outpatient follow-ups. Four months after discontinuing medication, his VL> 75000 copies/ml and CD_4 counts: 613 cell/mm^3 was noted. The physician recommended him to re-start cART treatment with the medication of combivir (3TC 150 mg & AZT 300 mg) 1 # bid, nelfinavir (250 mg) 4 # bid. Four months later, his HIV VL decreased to < 400 copies/ml (by Abbot Real Time with the lowest detectable level at that time) and CD_4 counts: 726 cells/mm^3. The drug sensitivity test showed no resistance to previous cART. The drug was readjusted to combivir (3TC 150 mg & AZT 300 mg) 1 # bid, efavirenz (600 mg) 1 # qhs. The treatment has gone on to this day, the patient's VL remains at less than 20 copies/ml (Roche Amplicor v2) and CD_4 counts always greater than 1000 cells/mm^3. This patient also has stable clinical condition with good quality of life.

A 35-years-old male, who was an user of illegal drug injection, tested to be HIV Ab positive with

CD_4 counts: 348 cell/mm^3 and VL< 400 copies/ml. He was diagnosed as HIV infection and started cART treatment by using AZT (100 mg) 2# tid, 3TC (150 mg) 1# bid, ritonavir (100 mg) 6# bid. He was stabilized after undergone the treatment for 3 years and 2 months with VL <50 copies/ml and CD_4 counts: 792 cell/mm^3.

The patient asked to stop the treatment but followed up his condition with outpatient. However, his VL reached 57600 copies/ml and CD_4 counts: 314 cell/mm^3 two months later with cervical lymphadenopathy. The largest lymphadenopathy (2x1.5 cm) is on his right neck while one lymph node on his left neck was enlarged to 2x1 cm. The patient was highly suspected to have developed tuberculous lymphadenopathy based on the results of his clinical and pathological reports. So he began cART again after stopping the treatment for 4 months. The drug sensitivity test showed no resistance to previous cART. He was treated with combivir* (3TC 150 mg & AZT 300 mg) 1# bid, nelfinavir (250 mg) 5# bid in addition to ethambutol (400 mg) 2# qd, and isoniazid (100 mg) 1# qd. Two months after the treatment, the sizes of the swelling lymphatic glands on his right side of the neck were significantly reduced, while the swelling lymphatic gland on the left side was almost disappeared. After nearly four months of continuous cART treatment, the patient's VL decreased to <400 copies/ml (by Abbot Real Time with the lowest detectable level at that time) and CD_4 counts: 537 cells/mm^3. Since Nelfinavir withdrew from the market, his medication was re-adjusted to combivir (3TC 150 mg & AZT 300 mg) 1# bid, atazanavir (150 mg) 2# qd, ritonavir (100 mg) 1# qd. The patient was stabilized under the drug therapy and the VL is still lower than 20 copies/ml up with CD_4 counts always greater than 700 cell/mm^3. Patient also has stable clinical condition with good quality of life. Unfortunately, this patient died of arteriole-venous malformation rupture in the brain about two years ago.

3. DISCUSSION

Both of these patients were young men diagnosed with HIV infection and their conditions were stabilized after cART with HIV VL below 50 copies/ml and CD4 counts as high as 600 cells/mm^3. However, the patients inquired their physician to suspend their treatment due to quality of life concern. Their VL were significantly higher (>75 000 and 57 600 copies/ml) after their treatment were stopped four months and two months, respectively. Yet they started treatment again and their VL decreased rapidly to the instrument could not be detected by the measured value of the situation 4 months later (less than 400 copies/ml). These two patients initially used AZT + 3TC + Ritonavir in the treatment and then used AZT+3TC+Nelfinavir after they were re-administered back into the treatment. These two patients were not tested drug resistance for the virus before re-entering cART treatment since there was no such test available during that time.

A study published by Samji et al. in 2015 found that as many as 1860 (24.5%) of the 7633 patients treated with cART had experienced TIs. The TIs in this study were defined as having at least one interruption of cART treatment. The number in this study showed that TIs are still quite common [11]. Fortunately, the proportion of patients discontinued cART treatment declined over time after the first year of the study [11], the result was consistent with the previous study by Moore et al. [12]. These studies confirm that clinical caregivers urgently need to communicate with patients about the importance of continuing medication and lifelong treatment to reduce morbidity, mortality, and virus transmission, so to achieve the greatest benefit in the treatment of cART.

However, the side effect of cART is the main reason that causes TIs, which means that the reduction of the toxicity associated with cART can significantly improve patient tolerance to the drug [13,14]. This was also demonstrated in the Samji et al. [11] study, and it noted that the risk of developing TIs was high in patients receiving older drugs such as AZT at the outset [11]. In contrast, the two patients in this report were also using AZT while inquired their physicians to use TIs. In addition, the study also indicated that choosing a once-a-day compact fixed dose or single tablet regimen (STR) as a first-line treatment would help to reduce the proportion of patients with TIs in the first year [15]. This is one of the domestic AIDS treatment options so far has always been recommended by Taiwan CDC.

4. CONCLUSION

As "treatment as prevention (TasP)" has become the AIDS treatment guidelines [16], it's extremely important to minimize the occurrence of TIs. Other than working on the revision of AIDS treatment guidelines constantly, the World Health Organization (WHO) has been calling on at least

50% of global AIDS infected come out to receive proper treatment [17]. The WHO has also proposed the "90-90-90" goal in the past two years that advocates 90% of all HIV-infected people can be found and diagnosed by 2020, 90% of these people can receive treatment, and 90% of these people whom undergo treatment will achieve effective control of HIV [18]. This not only provides us with a more urgent goal, but also be more active in dealing with the TIs issue.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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