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IMPLANT FAILURE RESULTING IN AN UNINTENDED PREGNANCY IN A WOMAN LIVING WITH HIV: A CASE REPORT.

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ABSTRACT

Effective and safe contraception is crucial for women living with Human Immunodeficiency Virus (HIV) to prevent unintended pregnancy, mother-to-child transmission, disease progression and psychological impact. Anti-retroviral treatments (ART) are known to have many drug-drug interactions, causing a dilemma among physicians in choosing the most suitable contraception for women living with HIV (WLHIV). One of the suitable choices is the long-acting reversible contraceptive (LARC), such as contraceptive implants, but this method is not without issues. This case illustrates an Implanon failure that led to an unintended pregnancy in an HIV-positive woman on anti-retroviral treatment and suffered from depression. Contraceptive implant failure has been reported in co-administration with Efavirenz-based anti-retroviral therapy, with studies demonstrating a decline in serum concentrations of etonogestrel and levonorgestrel.

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ABSTRACT

Effective and safe contraception is crucial for women living with Human Immunodeficiency Virus (HIV) to prevent unintended pregnancy, mother-to-child transmission, disease progression and psychological impact. Anti-retroviral treatments (ART) are known to have many drug-drug interactions, causing a dilemma among physicians in choosing the most suitable contraception for women living with HIV (WLHIV). One of the suitable choices is the long-acting reversible contraceptive (LARC), such as contraceptive implants, but this method is not without issues. This case illustrates an Implanon failure that led to an unintended pregnancy in an HIV-positive woman on anti-retroviral treatment and suffered from depression. Contraceptive implant failure has been reported in co-administration with Efavirenz-based anti-retroviral therapy, with studies demonstrating a decline in serum concentrations of etonogestrel and levonorgestrel.

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INTRODUCTION

Unintended pregnancy among women living with HIV (WLHIV) is high, with prevalence ranging from 40.9% to 78%.[1,2] A previous report stated that as many as 60% of infants born to HIV-positive were unintended pregnancies.[1] Even though early initiation of ART in pregnancy has been a successful strategy to reduce the incidence of HIV infection among children,[3] effective contraception is an equally important and cost-effective strategy to reduce vertical HIV transmission.[4] Unfortunately, contraception use among WLHIV is low despite accessibility to various contraceptive methods, including the long-acting reversible contraception (LARC).[1,4] Unintended pregnancy could lead to poor maternal and foetal outcomes,[4] and thus, it is very important to prevent it with the use of effective contraception, such as subdermal implants.[4] However, there have been concerns about its contraceptive

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efficacy among WLHIV, whereby several studies demonstrated a decline in serum concentration of levonorgestrel and etonogestrel in co-administration with anti-retroviral therapy, especially Efavirenz.[5–7] This case illustrates a case of an Implanon failure leading to unintended pregnancy in a WLHIV on an Efavirenz -based anti-retroviral regime. The unplanned pregnancy worsened the patient's depressive symptoms.

CASE REPORT

SNS, a 32-year-old, was diagnosed with HIV in March 2021 during the early pregnancy of her 4th child. She contracted the infection through her husband, who became infected through unprotected sexual intercourse with a sex worker. SNS was on oral Tenofovir/ Emtricitabine one tablet and Efavirenz 600mg daily from the diagnosis with a baseline viral load of 173,000 copies and a Cluster of Differentiation 4 (CD4) count of 31 cell/mm³. Her viral load became undetected eight months after starting treatment and her CD4 count raised to 646 cell/mm³. When SNS was diagnosed with HIV, she began to have depressive symptoms as she could not accept her husband's infidelity. Since then, she has been taking T. Sertraline 50mg daily and received psychotherapy. Her symptoms improved with both treatments. Her husband was also on anti-retroviral treatment and his condition was stable; the latest viral load was undetected and CD4 count was 452 cells/ mm³.

Six weeks post-delivery, an Implanon was inserted upon her request and she was monitored regularly by a Family Medicine Specialist. The couple was also advised for dual contraception (Implanon with condom). Approximately 13 months after Implanon insertion, SNS became pregnant, and the couple admitted to not practising dual contraception for the past month as the husband denied high-risk behaviour. Due to the unintended pregnancy, her mood symptoms worsened as the couple were not ready for another child. Thus, SNS inquired whether the pregnancy could be terminated. Following a thorough assessment, SNS was found to be physically well and did not exhibit severe depressive symptoms. She had no suicidal tendencies and could still function in her daily activities. A discussion was held with the couple on the issue of termination of pregnancy and they agreed to think it over. During the consultation, her anti-depressant dose was optimised to 100 mg daily and a follow-up in 2 weeks was given.

SNS turned up at the clinic a month later and reported that she had just had a complete spontaneous miscarriage, for which she sought care at the nearest hospital. During this visit, she expressed concern about Implanon failure and requested a bilateral tubal ligation (BTL) as she did not want any more children. She was referred to the Obstetrics and Gynaecology team for BTL with Implanon removal. While waiting for BTL, she was given a short course of intramuscular Depo-Provera injection as contraception and the couple was advised for dual method of contraception. Her depressive symptoms also improved, as well as her HIV condition and her treatments were maintained.

DISCUSSION

This case highlights the risk of contraceptive failure in women on concurrent contraceptive implants and anti-retroviral therapy. This imposed a dilemma for primary care physicians delivering reproductive healthcare and treating women with HIV. Pertaining to this case, we wish to highlight how contraceptive failure could have occurred in the first place. Subdermal implants are progestin-only contraception (etonogestrel or levonorgestrel), a highly effective LARC with a 99% effective rate.[8] The most common contraceptive implant in Malaysia is Implanon NXT, a single,

radiopaque implant containing 68mg of etonogestrel that is effective for up to 3 years.[8] Another available implant is Jadelle, a 2-rod levonorgestrel-releasing implant that is effective for up to 5 years.[8] Subdermal implants have been a favourable choice among physicians and patients as it is cost-effective, have long-term efficacy, and are easily inserted and removed with minimal complications.[8] The most common side effect and reason for discontinuing contraceptive implants is irregular menses, particularly heavy and abnormal frequency bleeding.[8] Other reasons for discontinuation are weight gain, emotional lability, depression, acne, and headache.[8]

The dilemma faced by the physician in choosing the best contraception for WLHIV is the drug-to-drug interactions, which are common with the concomitant use of ART and other medications. This is due to the shared metabolism of ART and certain medications through cytochrome P450 (CYP450), which may affect their efficacies.[7] In the case of SNS, she was on the first-line ART (Tenofovir, Emtricitabine, Efavirenz) and the Implanon was inserted post-delivery, around six months after ART initiation. However, she fell pregnant while on Implanon but ended in a spontaneous miscarriage. The unplanned pregnancy worsened her mental health, requiring an increased dose of anti-depressant.

The World Health Organization recommended the use of hormonal contraception without restriction (MEC 1) among HIV-infected women using NRTI, such as Tenofovir and Emtricitabine, as previous studies have demonstrated no significant interactions with hormonal contraception.[9] On the other hand, the use of subdermal implants among WLHIV on Efavirenz-based therapy was categorised as MEC category 2,[9] as there is a possible interaction between it and Efavirenz, which could reduce the efficacy of this contraception.[5–7] Efavirenz is a known potent CYP450 inducer,[7] and etonogestrel and levonorgestrel are mainly metabolised in the liver through the CYP450 system.[7] This may cause an increase in systemic clearance of etonogestrel and levonorgestrel when co-administered with Efavirenz.[7] Recent studies have documented a significant reduction of serum etonogestrel and levonorgestrel levels below the recommended levels to prevent ovulation when co-administered with Efavirenz.[5–7] The reduction of etonogestrel level below the required level for ovulation suppression could occur as early as 1-month post-insertion of the implant.[6] Additionally, a report indicates that unintended pregnancy could occur between 10 to 12 months post-levonorgestrel implant insertion.[5] However, in a large retrospective study, no significant time interval was found between the time of insertion and the occurrence of pregnancy to suggest that shortening the duration of contraceptive implant would improve its efficacy.[10]

A study by Roberts et al. found that lowering the Efavirenz dose to 400 mg did not optimise the levonorgestrel concentration, but doubling the levonorgestrel dose might be an effective strategy to maintain the contraceptive efficacy of levonorgestrel implants.[11] However, this finding was not observed in another study, and the possibility of more side effects with high-dose levonorgestrel should be considered.[12] Further research is warranted to address this issue. To date, there has not been any recommendation by the WHO to shorten the duration or increase the hormonal dosage of implants among WLHIV.[9] The current guidelines also have not recommended against using implants among WLHIV on ART as it is considered a suitable contraceptive method.[10,13] As such, healthcare providers should always discuss in detail with the woman and her partner when choosing the right contraceptive method. Apart from the subdermal implants, other hormonal contraceptives can also be considered for WLHIV with ART. One of these is the

progestogen-only injection (DMPA and NET-EN) and it is categorised as MEC Category 1,[9] as previous evidence showed no drug-drug interaction between depot medroxyprogesterone acetate (DMPA) and ART.[14] However, a recent retrospective longitudinal cohort study found that WLHIV on ART had a higher risk of unintended pregnancy with concomitant use of DMPA injectables than contraceptive implants.[13] Nevertheless, this retrospective study did not objectively assess compliance with DMPA injection, which is crucial in determining its efficacy.[13] This progestogen-only injection is reversible and highly effective, and there is no need to shorten the intervals between the treatments among women taking ART.[14] Thus, it can be considered for WLHIV.

Regarding copper or levonorgestrel intrauterine device (IUD), this method is suitable for women with asymptomatic or mild HIV clinical disease (MEC category 2), while those with severe or advanced HIV are generally advised against it (MEC category 3).[9] If women are asymptomatic or have mild disease, they must first be assessed for sexually transmitted infections (STI) and treatment instituted before inserting the IUD. Patients should also be counselled that IUD does not protect against STI. Therefore, dual protection with a condom should be used to reduce the risk.[15]

There have been recommendations and evidence stating that practising dual protection is the best choice for WLHIV to prevent unintended pregnancies.[15] Dual protection is the simultaneous use of an effective contraceptive method, such as intramuscular DMPA or implant, with consistent condom use.[15] It effectively reduces the risk of unintended pregnancy as well as transmission of HIV and STI when used correctly.[15] However, the uptake of dual protection has been low due to poor awareness, the unknown or positive HIV status of sexual partners, lower educational level, and the desire for fertility.[15] There is also a lack of consistency in using condoms among sero-concordant couples in the presence of another contraceptive method.[15] This can be improved with good counselling and partner involvement.[15]

CONCLUSIONS

Contraception in WLHIV requires careful consideration of many factors, including the disease stage, drug-drug interactions and the effectiveness of the chosen contraception. Contraceptive counselling for WLHIV and their partner should include discussing possible drug-drug interactions to improve compliance and reduce pregnancy risk. In women taking both implants and Efavirenz therapy, a high index of suspicion for pregnancy should be exercised whenever there is delayed menses or menstrual irregularity. Further research is needed to determine the efficacy of this method in women with concomitant Efavirenz -based therapy.

DISCLOSURE STATEMENT

The authors declare no conflict of interest.

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