Case Report

A Case Report of Tenofovir Alafenamide Induced Alopecia in a Zambian Teenager: A call for Pharmacovigilance

Moonga Benedict[1], Mukumbuta M Jean[2], Malumani Malan[3,4]

[1]Department of Paediatrics and Child Health, Livingstone Central Hospital
[2]Department of Pharmacy, Pharmacovigilance Focal Point Person, Livingstone Central Hospital
[3]Dermatology and Venereology Unit, Department of Internal Medicine, Livingstone Central Hospital
[4]Mulungushi University, School of Medicine and Health Sciences

ABSTRACT

Adverse drug reactions continue to pose a global risk in the fight against HIV. In an attempt to attain the end AIDS pandemic by 2030, newer drugs are being formulated with better efficacy and fewer side effects. However, these new drugs still have Adverse Drug Reactions (ADRs), which may affect adherence and compliance. We present a rare case of Tenofovir Alafenamide (TAF) induced alopecia of a Zambian teenager in the context of pharmacovigilance as a tool to identify ADRs, which may or may not have been identified during clinical trials. This is a wake-up call to all health care workers to identify and report ADRs and use the established channels to affect policy change.

INTRODUCTION

Adverse Drug Reactions(ADR) and interactions are still a problem, especially In People Living with Human Immunodeficiency Virus (PLWHIV), ADRs are further amplified due to polypharmacy. Pharmacovigilance has been improved throughout most parts of the country due to the deliberate effort from the ministry of health-Zambia to ensure that all drug-related reactions are reported to the established task force team. The Zambia Medicines Regulatory Authority(ZAMRA) which has its surveillance personnel strategically placed country-wide.

ADRs have been a significant source of concern in PLWHIV from time immemorial, and this has been a considerable drawback to ease rollout of combination Antiretroviral Therapy(cART). Before initiating any drug, it undergoes toxicity profile. However, some of these ADRs may be missed or not observed during the trial phase. Some rare ADRs have been detected after a drug has been administered to many people over considerable periods.

Apart from TAF having a lesser toxicity profile of renal and bone adverse events[5] compared to Tenofovir disoproxil fumarate (TDF), it was found to have higher rates of HIV RNA suppression as evidenced by Hill et al.,2018.

Given the low toxicity levels of TAF coupled with a better outcome, the government of Zambia introduced Tenofovir Alafenamide (TAF) as the first-line HIV drug. TAF is co-formulated with Emtricitabine and Dolutegravir as one tablet known as TAFED.

We report the first case of TAF induced alopecia in a 13-year-old Zambian teenager at Livingstone Central Hospital.

Corresponding Author:
Malumani Malan,
Head of Dermatology and Venereology Unit, Department of Internal Medicine, Livingstone Central Hospital, Livingstone, Zambia. Mulungushi University, School of Medicine and Health Sciences-Honorary Lecturer.
Email: drmalumani@yahoo.com

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CASE PRESENTATION

A 13-year-old African female client living with HIV as a case of Mother to Child Transmission (MTCT) and has been on combined antiretroviral therapy for six years. She presented to our outpatient department with complaints of hair on her head falling out about seven days after being transitioned from Abacavir 300mg/Lamivudine 150mg/Efavirenz 200mg (ABC/3TC/EFV) based regimen to Tenofovir Alafenamide 25mg, Emtricitabine 2000mg, and Dolutegravir 50mg (TAFED) as a single tablet. The transition was necessitated by the prevailing Zambian Consolidated Guidelines for Treatment and Prevention of HIV Infection 2020. At the time of change, the client had no medical concerns and had no side effects to the drug. Her viral load was at less than 20 copies per milliliter, and CD4 count was at 442 cells per microliter at the time of transition.

The Guardian described hair loss as generalized, which would fall off while combing, bathing, and when a little tag was applied to it. They denied any history of change or use of any hair products or shampoos or visited any saloons in the recent past months. She had no record of any scalp rash, troublesome dandruff, or itchiness during this ordeal. The review of other systems was unremarkable. However, the teenager was sad about the situation but tried to be calm about the whole situation after counseling, reassuring her that her hair would grow back after dechallenging to her previous regimen.

She had no history of over the counter (OTC), herbal, or any other drug use. She reports that Efavirenz 200mg replaced nevirapine 200mg due to Nevirapine tablets' phasing about two years ago. The transition was uneventful. She has no known drug or food allergies and has no food restrictions. Her past medical and surgical history has been unremarkable. She had not yet reached the age of menarche.

On examination, her vitals were temperature 36.4^{O}C, a pulse of 98 per minute, and a respiratory rate of 19 breaths per minute. Her BMI was 17.9kg/m^2 at 43rd centile for age. She had curly pubic hair with slightly elevated breast buds. Local examination revealed alopecia totalis with other systems having normal findings. Full blood count and biochemistry results were within normal ranges as shown in table 1. The hair pluck test was not done as no hair samples could be sent for investigations on admission; however, the pluck test was negative on subsequent review.

Tables and figure:

Table 1: Investigations done on an adolescent with TAFED induced alopecia

Laboratory test	Results	Reference value
Full blood count	White blood cell counts 5.3 X 10^9/l Haemoglobin 12.0g/dl	4.00–10.00
	Red blood cell count 4.7 X $10/l^{12}$	12.1–16.3
	Platelet count 365 X $10/l^9$	4.13–5.67
	HCT 34.4%	150–400
	MCV 83.3 fl	35–47.0
	MCH 31.3pg	79.1–98.9
	MCHC 35.1g/dl	27.0 32.0
	Neutrophils 69.4% 3.68 X $10/l^9$	32.0–36.0
	Lymphocytes 23.1%l.9 X $10/l^9$	2.00–7.50
	Monocytes 7.5% 0.4 X 10^9	1.00–4.00
		0.00–0.80
Renal function test	Creatinine 52.4 umol/l	23.0 58.0
	Urea 2.83 mmol/l	1.40–5.40
CD4	442cells/mm^3	
Viral load	20copies/mL	

A causality assessment was done, and there was no history of other medicines nor herbal medicines taken known to cause alopecia in the last 28 days. The same day the child was assessed, the TAFED was stopped as it was the only identifiable new drug combination that was introduced prior to presentation. We dechallenged the TAFED with the child's previous ABC/3TC/EFV regimen. The recipient of care was monitored weekly after discontinuing the medication to ascertain whether there was resolution of the suspected ADR and also if the time to recovery was consistent with the action taken. No other medications were given. The suspected ADR was reported to ZAMRA.

The outcome of the Dechallenge: One month later, the client experienced a positive dechallenged, as shown in figure 1B. Figure 1C shows the client's hair at 3months after switching back to the previous ABC/3TC/EFV regimen.

Ethical consideration: Consent was obtained from Guardian for using their pictures, and none of the patient information was used in the document.

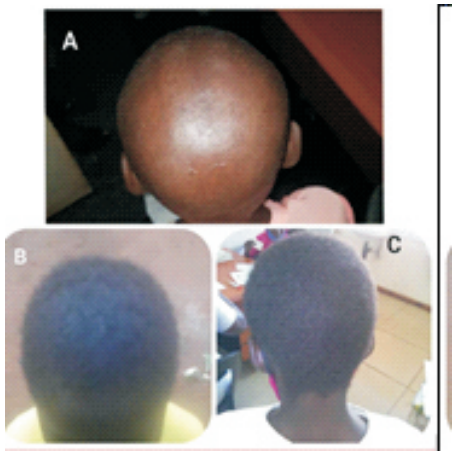

Figure 1 (A) Scalp of the teenager at Seven days post being on TAFED. (B) At One-month post dechallenging TAFED on ABC/3TC/EFV regimen (C) Hair growth at three months after stopping TAFED, the client was not on any hair growth products.

DISCUSSION

This single case report TAF-induced alopecia is an eye-opener and calls all healthcare workers vigilant to all drugs, especially to these newly introduced therapeutic agents.

In 2004 the Zambian government enacted the Pharmaceutical Act No 14 of 2004; this was necessitated by the discrepancy and a low number of Adverse Drug Reactions. As a result of the efforts in reporting ADRs, Zambia became the 97th member of the WHO became a full member (97th full member) of the WHO Programme for International Drug Monitoring. Despite these efforts, Zambia's target ADRs reporting was at less than 2% of the target in 2019.

Pharmacovigilance is the science and its activities related to the detection, assessment, understanding, and prevention of adverse effects or other medicine-related problems. It is a crucial component of comprehensive client care safety in the use of medicines. This is because all drugs have the potential to cause harm during their usage. Inability or failure to monitor, understand and manage these events leads to poor clinical outcomes, poor adherence to medications, unnecessarily prolonged exposure to serious adverse effects, and the emergence of drug resistance and treatment failure. These have the potential to erode public confidence in the healthcare system.

Further, adverse events associated with the use of medicines have considerable social and economic consequences. For instance, as is the case with our teenager, the change of anti-retrovirals (ARVs) in the future should there be a need to change regimen will be met with hostility and maximum resistance due to the ADR she went through. Therefore, it is imperative for provider-initiated regimen change, especially newer drugs on the market, that patients be informed and educated on the known and undocumented ADRs.

Reporting of Adverse drug reactions is very beneficial because it helps identify rare ADRs as is with our case; it helps prevent medicine tragedies. It leads to the improvement of information in labeling and contributing to the development of a database on ADRs that would serve as a useful and relevant educational source for the country and medical fraternity at large.

Not all medicine effects are known during clinical trials; hence it calls for all health workers to be vigilant in Pharmacovigilance and educate the clients both on the documented and undocumented ADRs.

People react differently to drugs and hence the need to actively look out for the ADRs as they can lead to death, hospitalization, permanent impairment, and stopping of treatment.

The mechanism in which tenofovir alafenamide induces alopecia is not yet understood. However,

NRTIs have been shown to inhibit the mitochondrial polymerase γ, leading to inhibition of mitochondrial DNA replication, thereby causing alopecia in mouse models.

CONCLUSION

Adverse drug reactions continue to occur and can lead to non-adherence and resistance to medications. However, this calls for all health workers to be extremely alert and vigilant even as we prescribe, dispense, or rather administer the drugs to our clients.

Recipients of care need to be adequately monitored, educated on side effects, and adverse drug reactions. How to identify them and what to do whenever one experiences something unusual.

Early detection of ADRs can help reduce drug-related morbidities, mortalities, lack of adherence to medications, prevention of medicine tragedies like the thalidomide disaster. The authors propose that Pharmacovigilance should be emphasized in healthcare workers' curriculum during their training.

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