

A synopsis of cutaneous adverse effects of Tenofovir

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Introduction

Tenofovir is a nucleotide reverse transcription inhibitor. It is widely used for the treatment of HIV and Hepatitis B. The most common side effect of the drug is gastrointestinal which is usually mild.^{1,2} Other side effects include hepatic, nephrological, pancreatitis, Fanconi's anemia, diabetes insipidus, and pneumonia.^{2,3} The incidence of cutaneous adverse effects ranges from 5% to 18%. However, they have not been well documented.^{4,5} Tenofovir is the least suspected drug for cutaneous side effects as there are many other antiviral medications used for the treatment of HIV with well-documented adverse effects. Only two cases of Leukocytoclastic vasculitis due to tenofovir have been reported to date. Here, we present a third case and also review the cutaneous side effects of tenofovir.

Case History

A 34-year-old lady was diagnosed with HIV and started on Anti-retroviral therapy with regimen TDF (Tenofovir disoproxil fumarate) +3TC(Lamivudine)+NVP(Nevirapine). After three months of medications, the patient noticed multiple reddish lesions on bilateral legs associated with itching and pain. There were no systemic complaints. Initially, NVP was thought to be the cause of the rash and thus the drug was stopped. The patient was prescribed tapering doses of oral steroids that relieved her lesions. After 2 weeks of stoppage of oral steroids, she again developed similar new lesions with similar progression, for which she visited our OPD.

Cutaneous examination showed multiple purpura and petechiae distributed symmetrically on bilateral legs extending up to mid-thigh (Fig 1). Systemic examination did not reveal any abnormalities.

Methods

Blood investigations including complete blood count, renal function test, liver function test, urine routine microscopic examination, ESR, and ASO were within normal limits. Biopsy with histopathological evaluation showed features consistent with Leukocytoclastic vasculitis (LCV) (Fig 2). Tenofovir was suspected as the cause of cutaneous eruption and was stopped. The patient was prescribed tapering doses of oral steroids for 4 weeks which caused the resolution of her symptoms. There was no recurrence of the rashes in 1-year follow-up.

Discussion

American College of Rheumatology has defined LCV as the presence of three or more of the following five criteria: 1) age > 16 years, 2) history of taking a medication at onset, 3) the presence of palpable purpura, 4) the presence of maculopapular rash, and 5) a biopsy demonstrating granulocytes around an arteriole or a venule (LCV)⁶. In our patient, four out of the five criteria were met and hence the diagnosis of LCV was

made. It is usually difficult to find the cause of LCV. It is idiopathic (in approximately half of cases) or secondary to drugs or infections⁷. In our case, the patient had no history of fever and the investigations didn't show any possibility of infection. The stoppage of tenofovir resolved the vasculitis. Hence, tenofovir was suspected as the etiological agent.

Studies show that the occurrence of cutaneous adverse effects due to tenofovir ranges from 5% to 18% which includes maculopapular rash, urticaria, pustules, pruritus, vesiculobullous rash^{4,5} However, they are under-reported in the literature. The reported cutaneous adverse events from the use of tenofovir are summarized in Table 1.

Conclusion

Tenofovir is a drug that is suspected less as a culprit drug during cutaneous eruptions as there are only limited reported cases. Tenofovir-induced LCV has been reported in 2 cases before this case report. Though cutaneous vasculitis is a less common adverse effect due to tenofovir, clinicians should be aware of this because timely diagnosis helps in the proper management of the patient.

Reference:

1. Van Bommel F, Wunsche T, Schurmann D, Berg T. Tenofovir treatment in patients with lamivudine-resistant hepatitis B mutants strongly affects viral replication. *Hepatology*. 2002; 36:507–508.
2. Nelson MR, Katlama C, Montaner JS, et al. The safety of tenofovir disoproxil fumarate for the treatment of HIV infection in adults: the first 4 years. *AIDS*. 2007; 21:1273–1281.
3. Verhelst D, Monge M, Meynard JL, Fouqueray B, Mougnot B, Girard PM, et al. Fanconi syndrome and renal failure induced by tenofovir: A first case report. *Am J Kidney Dis*. 2002;40:1331–3
4. J. Borrás-Blasco, A. Navarro-Ruiz, C. Borrás, E. Casterá. Adverse cutaneous reactions associated with the newest antiretroviral drugs in patients with human immunodeficiency virus infection. *Journal of Antimicrobial Chemotherapy*, Volume 62, Issue 5, November 2008,879–888
5. Staszewski S, Gallant J, Pozniak AL, Sulieman JMAH, De Jesus E, Koenig E, et al. Efficacy and safety of tenofovir disoproxil fumarate (TDF) versus stavudine (d4T) when used in combination with lamivudine (3TC) and efavirenz (EFV) in HIV-1 infected patients naive to antiretroviral therapy (ART): 48-week interim results. In: *Program and abstracts of the XIVth International AIDS Conference*. Barcelona, Spain, 7–12 July 2002.
6. Calabrese LH, Michel BA, Bloch dA, Arend WP, Edworthy SM, Fauci AS, et al. The American College of Rheumatology 1990 criteria for the classification of hypersensitivity vasculitis. *Arthritis Rheum* 1990 Aug;33(8):1108-1113.
7. Sais G, Vidaller A, Jugla A, Gallardo F, Peyri J. Colchicine in the treatment of cutaneous leukocytoclastic vasculitis. Results of a prospective, randomized controlled trial. *Arch dermatol* 1995 dec;131(12):1399-1402.
8. Said A. Al-Busafi, Abdulatif Al-Suleimani, Aysha Al-Hamadani and Wasif Rasool Tenofovir-induced Leukocytoclastic Vasculitis. *Oman Medical Journal*.2017;32(5):429-431.
9. Solay AH, Eser FC, Tutuncu EE, Gencler B, Onder EO. A Leukocytoclastic Vasculitis Case Due to Tenofovir Use. *Journal of Clinical and Analytical Medicine*.2017;8 (suppl 3):187-191.
10. WoolleyIJ, VeitchAJ, HarangozoCS, MoyleM, KormanTM. Lichenoid drug eruption to tenofovir in an HIV/hepatitis B virus co-infected patient. *AIDS*. 2004; 18:1857–1858.
11. Virath R, Balai M, Gupta LK. Blaschkoid Lichenoid Drug Eruption Due to Tenofovir. *Indian Dermatol Online J*. 2020;11(5):826-827.
12. Pankaj Jain.A Case of Cutaneous Reaction with Tenofovir Disoproxil Fumarate. *Journal of clinical and experimental hepatology*. 2013;3(3):254-255.
13. Lockhart SM, Rathbun RC, Stephens JR, Baker DL, Drevets DA, Greenfield RA, et al. Cutaneous reactions with tenofovir disoproxil fumarate: A report of nine cases. *AIDS*. 2007; 21:1370–3
14. Obadah Aqtash, Aman Naim Ajmeri, Brent A Thornhill, Elise Anderson and et. al. A unique case of tenofovir induced DRESS Syndrome associated with Raynaud's of the tongue. *International Journal of General Medicine* 2019;12 .

15. Verma R, Vasudevan B, Shankar S, Pragasam V, Suwal B, Venugopal R. First reported case of tenofovir-induced photoallergic reaction. *Indian J Pharmacol.* 2012; 44:651–3.
16. Khanijao Suchit, Kitchloo Karishma, Kamath Anisha, Dancy Leah and et. al. Tenofovir-induced bullous lesions. *Allergy and airway.* 2016;150(4)

S.N.	Cutaneous adverse effects	Comment
	Lichenoid eruptions	A case was reported by Woolley IJ and et.al. ¹⁰ A case of blaschkoid lichenoid drug eruption was reported by Gupta Mrinal and et. al. ¹¹
	Hypersensitivity reaction	10 cases have been reported, 1 by Pankaj Jain and 9 by Lockhart SM and et. al. ^{12,13}
	Photoallergic reaction	A case reported by Verma R and et. al. ¹⁴
	Tenofovir-induced bullous lesions LCV	A case has been reported. ¹⁵ 2 cases have been reported. ^{8,9}

Table 1: Reported cutaneous adverse effects due to tenofovir

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