

Cutaneous Small Vessel Vasculitis Due to Dolutegravir: A Rare Side Effect of Dolutegravir Based HAART Regimen in PLHIV

Suvesh Singh, Bhavya Swarnkar*, Neetu Bhari and Akash Deep Chandra

Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi, India

Abstract

According to World Health Organization (WHO), Dolutegravir-based regimen is considered as first-line therapy for PLHIV and strongly recommended for all adults and children at the 10th International AIDS Society Conference on HIV Science (IAS 2019) held in Mexico City. Dolutegravir (integrase inhibitor) is pharmacokinetically favorable with a single daily dose, fewer drug interactions, superior potency against HIV-1, and potency against efavirenz-resistant virus. In 2020, NACO announced the phase-wise replacement of TLE regimen to TLD regimen.

Keywords: Cutaneous small-vessel vasculitis • Efavirenz-resistant virus • Cutaneous examination • Leukocytoclastic vasculitis

Introduction

The President's Emergency Plan for AIDS Relief (PEPFAR) promoted dolutegravir transition in 80-90% of patients by 2019, with the only concern being the lack of much data on the safety of dolutegravir [1,2]. Here, we present a case of Cutaneous Small-Vessel Vasculitis (CSVV), a rare side-effect of dolutegravir. A 41-year-old man, known case of retroviral disease positive, was found to have skin rash over extremities during his precheck-up for hernia surgery. He was referred to our dermatology OPD for evaluation of the rash. The patient was previously on TLE regimen for six years with no complaints and was shifted to TLD regimen on January 20, 2021 to comply with the newer WHO HAART regimen. After 15 days of TLD regimen, he developed mildly pruritic erythematous lesions present symmetrically over bilateral lower limbs, which progressed to involve buttocks, upper limbs, and lower abdomen over a period of five days. Consequently, the patient stopped the medications, following which, the cutaneous lesions improved, and no new lesions developed. There were no other systemic complaints. Also, there was no history suggestive of respiratory/gastrointestinal tract infections or any other drug intake.

Description

Cutaneous examination revealed multiple discrete-to-coalescent erythematous, non-blanchable, palpable papulo-plaques distributed symmetrically over bilateral lower limbs (more prominent) and few similar lesions over buttocks, lower back, lower abdomen, postero-

medial aspect of bilateral arms and forearms with relative sparing of upper trunk and face (Figure 1). Scalp, mucosae, nails, palms, and soles were normal. His routine investigations like complete blood count, liver, kidney function tests, urine routine microscopy, chest radiograph, and electrocardiogram were normal; however, erythrocyte-sedimentation rate was high (49 mm/hr). Hepatitis B, C and VDRL tests were negative. HIV viral load was 20 copies/mL. On histopathological examination, upper and mid dermis showed mild-to-moderate neutrophilic infiltrate with few perivascular eosinophils, extravasation of RBCs, and fibrin deposit in the wall of vessels, suggestive of leukocytoclastic vasculitis of small vessels. We started the patient on oral levocetirizine and topical steroid only, and TLD regimen was restarted since the cutaneous reaction was mild and there were no systemic features. After two weeks, he developed similar new lesions over the extremities, with sparing of upper trunk and face (Figure 1b). Based on temporal correlation *i.e.* worsening skin findings on dolutegravir rechallenge, absence of any other trigger, histopathological findings, Naranjo score of 7, and American College of Rheumatology 4 out of 5 criteria, diagnosis of dolutegravir-induced CSVV was made. Since the viral load was very low, retrovirus-induced CSVV was unlikely. He was advised to start topical steroid, oral levocetirizine, and indomethacin with follow-up in ART clinic for change of regimen. CSVV is a single-organ vasculitis mediated by immune-complex deposition in small vessels, and usually has good prognosis [3]. However, it may have frequent relapses and be deplorable to patients [4-6]. Dolutegravir has been previously suggested as a rare possible cause of CSVV in an earlier report. The worsening of disease on dolutegravir-rechallenge in our case suggests a definite

*Address to Correspondence: Bhavya Swarnkar, Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi, India; Email: swarnkarbhavya@gmail.com

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causation, and is a major highlight. Other side-effects of dolutegravir are neuropsychiatric symptoms and hyperlactemia, which were not present in our case. Nevertheless, the patient was referred to ART clinic for change of regimen, since CSVV frequently relapses, and could potentially show systemic involvement later [7-10].

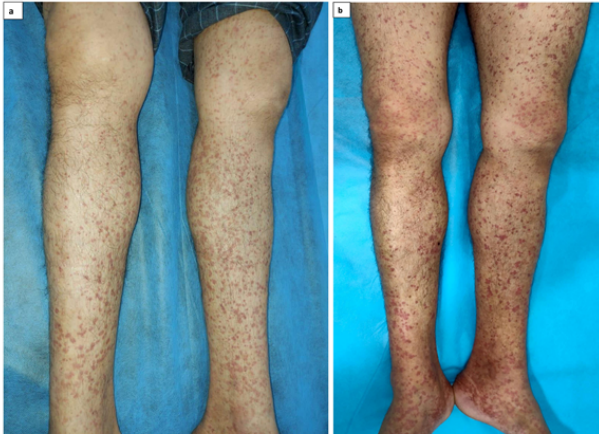


Figure 1. a) Discrete-to-coalescent erythematous palpable, non-blanchable purpuric lesions with symmetrical distribution over legs following dolutegravir-based HAART regimen; b) Findings worsening after 2 weeks of rechallenging dolutegravir.

Conclusion

With the increasing use of dolutegravir-based new HAART regimen worldwide, dermatologists need to be aware of this rare cutaneous adverse-effect of dolutegravir, and may advise a shift to an alternative regimen.

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