LETTER TO EDITOR
Year: 2018 I Volume: 1 I Issue:3 I Page: 87-88

LAMIVUDIN INDUCED DRUG RASH- A RARE ENTITY

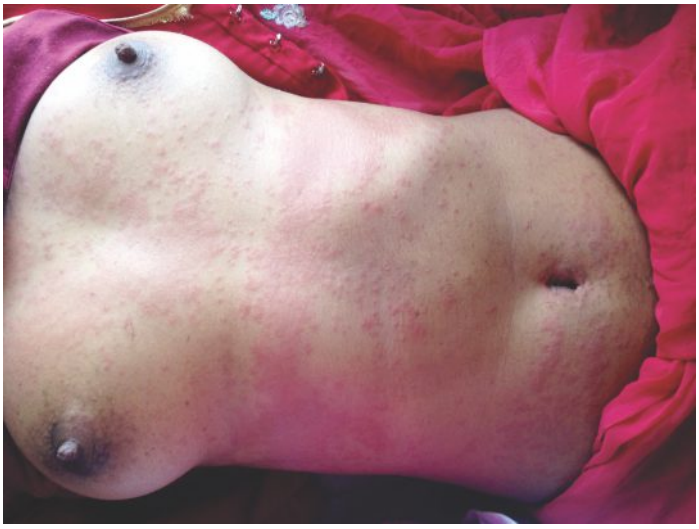
Dr. Chestha Agarwal
Consultant Dermatologist
Email: hesskmc@yahoo.com

Sir,

The use of highly active antiretroviral therapy (HAART) has had an important impact on the course and treatment of disease and disease-related morbidity of HIV-infected patients, increasing their lifespan and quality of life.[1] However, these advantages have been accompanied with a marked increase in the number of adverse drug reactions, both minor and serious cutaneous adverse drug reactions[2]. Of all the drugs nevirapine is commonly responsible for cutaneous reactions and Lamivudine is considered relatively safer[3]. We are here present a case with cutaneous adverse drug reaction in a female patient with lamivudin.

A 40 year old immunocompromised female, receiving 1st line anti retroviral therapy i.e zidovudine, lamivudine & nevirapine (ZLN),within 10 days of initiation of therapy, she developed diffuse erythematous maculopapular pruritic rash which was first noticed by the patient on the abdomen then progressed to involve the chest, extremities and back (Fig. 1).

Figure 1: diffuse erythematous maculopapular pruritic rash



Mucosa was however spared and there were no constitutional symptoms. Systemic examination was also unremarkable. Laboratory investigations including complete hemogram, liver and renal function tests, urine examination were normal. Because of significant itching, all medications were stopped and she was given antihistamines like cetirizine and topical mid potent steroid with emolients. Within 1 week, patient became comfortable and rash disappeared. Two weeks later, zidovudine, lamivudine & efaverinz (ZLE) was initiated at the ART centre assuming nevirapine to be the offending agent, but within 48 hrs, patient redeveloped similar type of rash. Again ART was stopped and antihistamines were given. Once the rash completely subsided (within 2 weeks) we decided to hospitalize the patient for oral drug provocation test to find the offending agent. We suspected zidovudine and lamivudine to be the culprit drugs as they were common in both the regimen. Using the method described by Ramam et al[4] the patient was provocated first with half dose of Zidovudine followed by full dose on the next day. There was no reaction. On giving half dose of Lamivudine, she developed itching and faint rash over trunk within 12 hours and on giving full dose on the next day she developed diffuse maculopapular pruritic rash over trunk and extremities. Biopsy from the representative lesion showed sparse to moderately dense perivascular lymphocytic infiltrate in upper dermis, no eosinophils and interface changes. Spongiosis and parakeratosis were seen. The histopathology was suggestive of superficial perivascular dermatitis. Routine laboratory investigations were normal. There were no mucosal and systemic symptoms. But due to severe itching lamivudine was withdrawal and antihistamines were introduced leading to subsidence of rash with in 2days. Because the grade of the reaction was mild and controlled with antihistamines, she was continued on the same regimen i.e ZLE along with antihistamines. Patient is doing well since then.

HAART is effective and had lead to significant reduction in mortality and morbidity from HIV[5]. However each of these drugs has a potential to cause adverse cutaneous reactions including both minor and serious side effects. Skin reactions are the most common manifestation of drug hypersensitivity. These may present with exanthem without systemic symptoms or drug hypersensitivity syndromes typically manifesting as an erythematous, maculopapular confluent rash with constitutional features[6]. It is routine to consider the NNRTI component as the culprit agent when the patients are initiated simultaneously with zidovudine/stavudine, lamivudine, and nevirapine/efavirenz and cutaneous reaction appears. Nevirapine can cause skin rash in 17% to 32% of patients,13% of these are mild rashes.[7] Efavirenz can cause mild skin rash, with severe eruptions such as SJS, TEN and erythema multiforme being reported in 0.1% of patients[8]. However, the next common drug group suspected are the NRTIs. Zidovudine and lamivudine have been reported to be associated with skin rash very rarely. An extensive literature search revealed only a few case reports of drug allergy to lamivudine alone. Reaction of lamivudine was first reported in a 49 year old man, who developed an anaphylactoid reaction within 30 minutes of the first dose of lamivudine (150 mg). Withdrawal of the drug was followed by full recovery within the next 24 hours.[9] A case of contact dermatitis has been reported in a

healthcare worker taking lamivudine for post exposure prophylaxis.[10] There is another reported incident of severe skin eruption caused by lamivudine that needed discontinuation in a patient with chronic hepatitis B.[11] A case series of four patients has recently been published in which two patients developed SJS/TEN and other two developed maculopapular purpuric rash with Lamivudine.[3]

Since lamivudine is an effective, safe, and widely used antiretroviral drug, clinicians must be aware of the possibility of such severe adverse reactions to lamivudine, which requires drug cessation and administration of supportive treatment. Also, because lamivudine constitutes a part of all the first line ART regimens in India, a reaction to lamivudine warrants for higher centre referral and 2nd line medications which are associated with severe systemic side effects.

How to cite this article:
Agarwal C. Lamivudin induced drug rash- a rare entity. JDA Indian Journal of Clinical Dermatology 2018;1:87-88.

References

1. Crum NF, Riffenburgh RH, Wegner S, et al. Comparisons of causes of death and mortality rates among HIV-infected persons: analysis of the pre-, early, and late HAART (highly active antiretroviral therapy) eras. J Acquir Immune Defic Syndr 2006;41:194-200.
2. González-Martín G, Yañez CG, González-Contreras L, et al. Adverse drug reactions (ADRs) in patients with HIV infection. A prospective study. Int J Clin Pharmacol Ther 1999;37:34-40.
3. Modak D, Guha SK. Severe skin rash with lamivudine in HIV infected patients: some unusual case reports. Indian J pharmacol 2013;45:298-300
4. Ramam M, Kumar U, Bhat R, Sharma VK. Oral drug provocation test to generate a list of safe drugs: Experience with 100 patients. Indian J Dermatol Venereol Leprol 2012;78:595-8
5. Palella FJ, Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, Aschman DJ, Holmberg SD. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators.N Engl J Med. 1998;338:853–60.
6. Seth D, Kamat D, Montejo J. DRESS syndrome: a practical approach for primary care practitioners. Clin Pediatr (Phila) 2008;47:947–52.
7. Warren KJ, Boxwell DE, Kim NY, Drolet BA. Nevirapine-associated Stevens-Johnson syndrome. Lancet. 1998;351:567.
8. Bossi P, Colin D, Bricaire F, Caumes E. Hypersensitivity syndrome associated with efavirenz therapy. Clin Infect Dis. 2000;30:227–8.
9. Kainer MA, Mijch A. Anaphylactoid reaction, angioedema and urticaria associated with Lamivudine. Lancet. 1996;348:1519.
10. Smith KJ, Buckley R, Skelton H. Lamivudine (3TC)induced contact dermatitis. Cutis. 2000;65:227–9.
11. Kim SB, Seo PJ, Baik du S, Yun SY, Kim BH, Shin JE, et al. A case of severe skin eruption caused by lamivudine in a patient with chronic hepatitis B. Korean J Gastroenterol. 2006;48:281–5.