



SEVERE SKIN RASH WITH LAMIVUDINE IN HIV INFECTED PATIENTS; SOME UNUSAL CASE REPORTS

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ABSTRACT

With an alarming increase in the incidence of Human immunodeficiency virus (HIV) infections, use of antiretroviral drugs has been playing a vital role in improving quality of life and disease-related condition of these patients. HIV-infected patients are at an increased risk of developing mucocutaneous drug reaction. Nearly 80% patients experienced adverse drug reaction at some time during treatment either from immune dysregulation or altered drug metabolism. The severe skin rashes caused due to Lamivudine seen in our cases was observed between 7 to 11 days of starting antiretroviral therapy (ART) and re-exposure to Lamivudine triggered the reaction within 1–2 days.

Key words: Antiretroviral Therapy, HIV, Adverse Drug Reaction.

Access this article online		
Home page: http://www.mcmed.us/journal/ijacr DOI: http://dx.doi.org/10.21276/ijacr.2020.7.1.1	Quick Response code 	
Received:25.11.19	Revised:12.12.19	Accepted:15.01.2020

INTRODUCTION

With an alarming increase in the incidence of Human immunodeficiency virus (HIV) infections, use of antiretroviral drugs has been playing a vital role in improving quality of life and disease-related condition of these patients. However, on the other side of its benefits are a number of adverse effects including dermatological reactions most commonly Nevirapine is responsible for cutaneous reactions, Lamivudine Nucleoside Reverse Transcriptase Inhibitor (NRTI) can also cause severe skin reactions including toxic epidermal necrolysis (TEN), which necessitates its discontinuation and prevent its

reintroduction. We report a total of two cases where skin rashes developed after Lamivudine therapy. [1]

CASE REPORTS:

CASE 1

Severe maculopapular, pruritic rash, with conjunctival redness and mucosal involvement of the oral cavity and genitalia were observed on the 10th day of antiretroviral (ARV) initiation with Zidovudine, Lamivudine, and Nevirapine in a 32-year-old female with CD4 count of 25 cells/ μ L. She was found to be allergic to Co-Trimoxazole earlier and the attempts at desensitization had failed. She was diagnosed with Steven-Johnson syndrome (SJS). Her laboratory parameters were normal. She improved following discontinuation of all the drugs and symptomatic management. ART was re-initiated with Lopinavir/Ritonavir, Zidovudine, and Lamivudine. However, she was admitted again with desquamation of

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skin of more than 30% of total body area, and a diagnosis of toxic epidermal necrolysis (TEN) was made. All medicines were stopped and she recovered gradually in the next 4 weeks. Two months later, antiretroviral therapy (ART) was re-started with Tenofovir, Zidovudine, and Lopinavir/Ritonavir, presuming Lamivudine to be offending drug. She continued the drugs without any further adverse effects.

CASE 2

In a 38-year-old male patient diagnosed to be HIV positive for last 6 years, antiretroviral therapy (ART) was started with Zidovudine, Lamivudine, and Nevirapine when his CD4 count dropped to 223/ μ L. He was admitted with pruritic, erythematous, maculopapular rash with blisters over genitalia, and multiple ulcers in buccal mucosa [Figure 1] along with constitutional symptoms like fever and myalgia on the 7th day of starting ART. All medications including co-Trimoxazole were stopped. On examination, he was febrile with maculopapular rash, patchy areas of desquamation, [Figure 2] and multiple ulcers over oral and genital mucous membrane. Steven-Johnson syndrome (SJS) was diagnosed. His kidney and

liver functions were normal. He was managed symptomatically in the hospital with disappearance of the rash by 7th day. Following complete resolution of rash, ART was re-started with Lopinavir/Ritonavir along with Zidovudine and Lamivudine. However, similar but more severe rash re-appeared after the first dose. All medicines were withdrawn. Antiretroviral therapy was subsequently restarted with Tenofovir, Zidovudine, and Lopinavir/Ritonavir after complete recovery of rash. He tolerated the drugs well and rash did not re-appear. Two months later Lopinavir/Ritonavir was substituted with Efavirenz which was well-tolerated by the patient.

CASUALTY ASSESSMENT

The reaction seen in our cases was observed between 7 to 11 days of starting ART and re-exposure to Lamivudine triggered the reaction within 1–2 days. As per the World Health Organization-The Uppsala Monitoring Centre (WHO-UMC) standardized case causality assessment criteria, these events can be considered as a “certain” reaction due to Lamivudine. The Naranjo's Adverse Drug Reaction (ADR) probability, also confirmed this causality as “definite” reaction due to Lamivudine. [2].



DISCUSSION

HIV-infected patients are at an increased risk of developing mucocutaneous drug reaction. Nearly 80% patients experienced adverse drug reaction at some time during treatment either from immune dysregulation or altered drug metabolism. In severe cases like Stevens-Johnson syndrome/Toxic Epidermal Necrolysis (SJS/TEN), Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) are never re-introduced and alternate agents like protease inhibitors are started (Ritonavir-boosted Atazanavir or Lopinavir) An extensive literature search revealed only a few case reports of drug allergy to Lamivudine alone. The first is a case of an anaphylactoid reaction, 30 minutes after the first dose of Lamivudine (150 mg) in a 49-year-old man, a full recovery was observed within the next 24 hours. Since Lamivudine has

been an effective, safe, and widely used antiretroviral drug, clinicians must be aware of such severe adverse reactions to Lamivudine, which may require treatment discontinuation so that swift treatment can be given in such patients. [3, 4]

CONCLUSION

The severe skin rashes caused due to Lamivudine seen in our cases was observed between 7 to 11 days of starting antiretroviral therapy (ART) and re-exposure to Lamivudine triggered the reaction within 1–2 days. The temporal relation between appearance of rash and Lamivudine initiation, rapid regression after its discontinuation, relapse following its re-introduction, and tolerance to Lamivudine sparing regimens, it was revealed only a few case reports of drug allergy to Lamivudine alone. [5]

ACKNOWLEDGEMENT

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Cite this article:

Nancy Kavya D, Ruthu Kumari D, Dhanalakshmi E, Ivy Muya Henry Jackson, Mani Sekhar C. Severe Skin Rash With Lamivudine In Hiv Infected Patients; Some Unusal Case Reports. *International Journal of Advances In Case Reports*, 7(1), 2020, 1-3. DOI: <http://dx.doi.org/10.21276/ijacr.2020.7.1.1>



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