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Case Report Full Proceeding Paper

NEVIRAPINE INDUCED MACULOPAPULAR RASH

K.Venkateswarlu[1]*, K. Supriya[2], G.Sarah Marlyn[2], Sharadha Srikanth[3], Konde Abbulu[4]

[1] Assistant Professor, Department of Pharmacy Practice, CMR College of Pharmacy, Kandlakoya, Medchal, Hyderabad, Telangana, INDIA.

[2] Pharm D, Department of Pharmacy Practice, CMR College of Pharmacy, Kandlakoya, Medchal, Hyderabad, Telangana, INDIA.

[3] HOD, Department of Pharmacy Practice, CMR College of Pharmacy, Kandlakoya, Medchal, Hyderabad, Telangana, INDIA.

[4] Department of Pharmacy Practice, Principal, CMR college of Pharmacy, Kandlakoya, Medchal, Hyderabad, Telangana, INDIA.

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ABSTRACT

Nevirapine has a serious adverse effect of causing Maculopapular Rash .Here we report a case of 6 yrs old female patient with Chief complaints of,erythomatous rash present all over the body since 5days after taking Nevirapine for 10 days, itching and pain with a past history of Retroviral Disease on Medication Nevirapine.Patientwasmanaged with drugs like Dexamethasone, Chlorpheniramine Maleate, Multi Vitamins and Calamine Lotion.

KEYWORDS: *Nevirapine, Adverse Drug Reaction, Maculopapular Rash, Retro Viral Disease.*

INTRODUCTION

Nevirapine (Viramune) belongs to the pharmacological class of non-nucleoside reverse transcriptase inhibitors (**NNRTIs**) and a therapeutic class of anti-retroviral drugs[1]. It acts by binding directly to reverse transcriptase (RT) thereby blocking the RNA-dependent and DNA-dependent DNA polymerase activities by causing a disruption of the enzyme's catalytic site[2]. The commonly associated ADRs include edema, hepatotoxicity, Toxic Epidermal Necrosis (TEN), Steven Johnson's Syndrome (SJS), erythema nodosum, insomnia, nausea, pulmonary infiltrates, vertigo, vomiting, and weight decrease, with most common adverse reaction is rash (maculopapular)[3].

In accordance with animal and human trials, the mechanism of nevirapine induced maculopapular rash involves the following variations in the body. Thetotal T cells, orpurified CD4+ T cells in some cases, are capable of transferringsusceptibility, which the CD8+ T cells are not capable of[4].

The depletion of CD8+ T cells appear to worsen the reaction, that partial depletion of CD4+ T cells do not completely prevent the rash, and CD4+ T cells cannot consistently transfer sensitivity to the rash. Splenocytes, total T cells, or CD4+ T cells, but not CD8+ T cells are collectively found to be causative[5].

Importantly, CD4+ T cells have also been implicated in the mechanism of nevirapine-inducedskin rash in humans. In fact, nevirapineshould not be initiated in women withCD4 cell counts >250 cells/mm 3 and men withCD4 counts >400 cells/mm 3 unless the benefitoutweighs the risk. Nevirapine-specific T cellshave also been identified ex vivo in HIV-positivecases[6].

Microscopic and immune histochemical evaluation of skin illustrated significant inflammatorycell infiltrates in the skin.. T cells and macrophages werethe predominant cell types, and cells were observedin the dermis, epidermis, and at the dermal-epidermal junction. Similar expression patterns of T-cell receptor, CD4, and CD8 were observed, and thus it is believed that the inflammatoryinfiltrate contained both CD4+ and CD8+ T cells[7].

Lesions of satellite-cell necrosis,i.e., apoptotic cells (likely keratinocytes) adjacentto mononuclear cells are responsible for changes occurring within. The lesions also may represent immune-mediatedkeratinocyte cell death[8].

Risk factors to develop skin rash with nevirapine include Age (both children and adults), Nevirapine dosing given alone (not in combination with lopinavir, ritonavir,HIV positive, HBsAg positive, CD4 cells >300, Previous opportunistic infections (Tuberculosis, Pneumocystis pneumonia, cryptococcosis, penicilliosis), Concurrent medications (Cotrimoxazole, fluconazole, isoniazid, rifampicin, ethambutal, pyrazinamide, dapsone)[9, 10].

***Corresponding author:**

K. Venkateswarlu

Assistant Professor,

Department of Pharmacy Practice,

CMR College of Pharmacy,Kandlakoya,Medchal,

Hyderabad,Telangana, INDIA.

Case:

Case report:The patient is female, 6 years old and has complaints of Erythematous rashes all over the body (since 5 days) after taking nevirapine for 10days. She also complaints of itch and pain associated with the rash. She is diagnosed with RVD (Retro Viral Disease) for the past 10 days. On examination, she was concious & coherent, her BP was 110/70mmHg, Pr was 70/min, CVS-S1S2+, R/S-BAE+ all all other virals were normal. She was provisionally diagnosed as Nevirapine induced drug rash as she was on the anti-retroviral therapy. She was adviced with complete Urine examination, Complete Blood Picture, Serum biochemistry, & Liver funtion Tests.

On the second day of admission, her vitals were normal, PR: 76/min. On day 3, she was concious/coherent, Bp: 110/70mmHg, PR: 76/min. On day 4 all her vitals were normal and she was advied with a high protein diet. On day 5 all her vitals were normal and PR: 88/min. Based on her complaints of rash (maculopapular in nature), past history of RVD, and her laboratory findings of a high urea level (26 gm/dl), low Hb (11gm/dl) and abnormal urine examination (pus ceels +, epithelial cells +, RBCs +), she was confirmed with Nevirapine induced maculopapular rash.

Here, the ADR in this patient can be confirmed by:

i) The disappearance of the reaction progressing after stopping the administration of the suspected drug (Nevirapine)

ii) Recovery of the patient on withdrawal on the drug with other drugs given for the reaction developed

Case Analysis:The possible risk factors in this child include a young age (6 years), Retro viral disease and depletion in CD4 cell count (Due to RVD). The naranjo scale assessment of ADR is probable (5-8), WHO severity assessment is possible.

DISCUSSION

The patient is a known case of RVD and due to this she is immune compromised, where her CD4 and CD8 cell counts deplete. On depletion, the CD4 cells, do have the capacity to transfersusceptibility to the skin rash. Also, the Total T cells and purified CD4 cells are responsible for such a reaction. These cells, along with other inflammatory infiltrates and macrophages reach the dermis, epidermis and dermal-epidermal junction where they exhibit their properties to cause a skin reaction. This results in the apoptosis of the cells leading to necrosis, and the skin appears as a raised erythematous rash over the affected part of the body. The keratinocytes subjected to necrosis can be present when the skin lesion is examined histopathologically. Since the child is 6 years diagnosed with retro viral disease her immunity is bound to be in a compromised state along with the body's lack of complete organ functionality owing to her age and other possible opportunistic infections like with the urinary tract (increased pus cells and blood urea revelations from her laboratory data) might have led to accumulation of the drug in the body or excess protein binding of drug. Also taking nevirapine alone for RVD has potency to cause the reaction in the patient.

To overcome this reaction in the patient the suspected drug (nevirapine) is to be discontinued, and a once daily dosing schedule for 2 weeks followed by escalation to twice daily dosing with other anti-retro viral drugs that can reduce the risk for toxicity. Since the drug can cause hepatotoxicicity, monitoring of AST and ALT levels is recommended. Avoid this drug if the CD4 counts exceed 250cells/mm^3. Also, do not reintroduce the drug or use another drug of the same class when reintroducing retro viral therapy after discontinuation of the suspected drug.

CONCLUSION

On developing the erythmetatous rash asscociated with itching and pain, nevirapine has shown to cause maculopapular rash in the patrient owing to the possible higher protein binding of drug, or other posiible infections and nevirapine given without a combination of the other two drugs (lopinavir, ritonavir). Since the child is on the therapy, it took 5 days to develop the reaction which aims at a dosing shedule of an initial once daily regimen and then increasing it to twice daily. The suspected drug (nevirapine) is to be discontinued and replaced with other NNRTIs like delavirdine, etravirine.

REFERENCES:

1. Patel SS, Benfield P. "New drug profile: nevirapine". Clinical Immunotherapeutics. **1996**;6(4):307–317.
2. Schauer Grant D, Huber Kelly D, Leuba, Sanford H. Sluis-Cremer Nicolas. "Mechanism of allosteric inhibition of HIV-1 reverse transcriptase revealed by single-molecule and ensemble fluorescence". Nucleic Acids Res **2014**;42(18):11687–11696.
3. Alternative First-Line ART operational guidelines by NACO, Government of India: Ministry of health and family welfare,**2010**; p. 8-9.
4. JM. Shenton, M. Popovic, JP. Uetrech. Department of Pharmaceutical Sciences, University of Toronto, Toronto, Ont. , Canada; b Department of Immunotoxicology, Bristol-Myers Squibb Co., Syracuse, N.Y. , USA; Department of Investigative Toxicology, Novartis Pharma AG, Basel , Switzerland Pichler WJ (ed): Drug Hypersensitivity. Basel, Karger, **2007**; pp 115–128.
5. Antinori A, Baldini F, Girardi E, Cingolani A, Zaccarelli M, Di Giambenedetto S, Barracchini A, De Longis P, Murri R, Tozzi V, Ammassari A, Rizzo MG, Ippolito G, De Luca A. Female sex and the use of anti-allergic agents increase the risk of developing cutaneous rash associated with nevirapine therapy. AIDS **2001**;15:1579-1581.
6. Chen X, Tharmanathan T, Mannargudi B, Gou H, Uetrecht J. A study of the specificity of lymphocytes in nevirapine-induced skin rash. J PharmacolExp Therapy, Fast Forward,**2009**.
7. MarijaPopovic, Jeff L. Caswell, Faculty of Pharmacy, University of Toronto, Toronto,Department of Pathobiology, Ontario,Canada, Department of Immunotoxicology, Pharmaceutical Research Institute, Bristol-Myers Squibb Company, East Syracuse, New York. *Chem Res Toxicol* **2006**;*19*(9):1205–1214
8. Palella FJ Jr, Delaney KM, Moorman AC et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med **1998**;338:853–860.
9. Ferrer E, Santamarina E, Domingo P et al. Nevirapine-containing regimens in HIV-infected naive patients with CD4 cell counts of 200 cells/microl or less. AIDS **2004**;18:1727–1729.
10. Clarke S, Harrington P, Barry M, Mulcahy F. The tolerability of efavirenz after nevirapine-related adverse events. Clin Infect Dis **2000**;31:806–807.

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