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International Journal of Current Research
Vol. 7, Issue, 12, pp.23944-23946, December, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

NEVIRAPINE-INDUCED STEVENS-JOHNSONS SYNDROME / TOXIC EPIDERMOLYSIS NECROLYSIS OVERLAP IN AN HIV PATIENT

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ARTICLE INFO

Article History:
Received 25th September, 2015
Received in revised form
19th October, 2015
Accepted 15th November, 2015
Published online 30th December, 2015

Key words:

Steven- Johnsons syndrome,
Nevirapine, Highly Active Antiretroviral Therapy, Follicular eruptions.

ABSTRACT

Nevirapine (NVP) a Non Nucleoside reverse transcription inhibitors (NNRTI) commonly used in Highly Active Antiretroviral Therapy (HAART) regimens for treatment of HIV infections in National Aids Control Organisation because of its efficacy and good tolerability. Stevens- Johnson syndrome may occur 0.3% with nevirapine, 0.1% with efavirenz. We are here with submitting a case report of nevirapine induced Stevens- Johnson syndrome in a HIV patient who was on zidovudine + lamivudine + nevirapine, which has resolved completely after changing the regimen and with supportive treatment.

Citation: Dr. Siddeswari, R., Dr. Suryanarayana, B., Dr. Srinivasa Rao, N., Dr. Prabhu Kumar, C.H. and Dr. Madhavi, P. 2015. "Nevirapine-Induced Stevens-Johnsons Syndrome / Toxic Epidermolysis Necrolysis Overlap in an HIV Patient", *International Journal of Current Research*, 7, (12), 23944-23946.

INTRODUCTION

Nevirapine NVP) was the first Non Nucleoside reverse transcription inhibitors (NNRTI) to be developed .It is highly specific for HIV –RT and does not interfere with human DNA polymerases. It directly binds to the RT which leads to conformational change which inactivates the HIV-RT enzyme. It is readily absorbed after oral administration. It crosses placenta and is also found in breast milk. It is metabolized via cytochrome P450 pathway. (Alaka Despande *et al*., 2006) Other NNRTIs are Efavirenz, Etraverine and Delavirdine. Hypersensitivity rash and hepatitis are the major class-specific side effects. The rash is usually mild and self limiting but Stevens- Johnson syndrome may occur 0.3% with nevirapine, 0.1% with efavirenz. (Wilkins, 2010) In 1997, nevirapine became the first NNRTI available for the treatment of HIV infection. Its efficacy was established both for the treatment of naive patients and in oversimplification strategies. (Negredo *et al*., 2002) Nevirapine-based regimens of highly active antiretroviral therapy (HAART) have been widely used in resource-restricted countries because of their efficacy, accessibility and comparatively low cost. (Sabbatani *et al*., 2005)

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World Health Organization (WHO) recommends nevirapine and efavirenz (EFV) as one of the first-line drugs. The drug is widely available and is less costly than EFV; however, a higher incidence of rash is associated with it than with EFV. The most serious toxic effects associated with nevirapine are skin reactions and liver dysfunction; both are generally mild to moderate and usually an early phenomenon, occurring during the first 6-8 weeks of therapy. (Carr and Cooper, 1996)

Case report

A 50 year old female diagnosed as HIV positive with CD4 count 86 cells/mm^3 , was started on zidovudine 300mg +lamivudine 150mg+nevirapine 200 mg twice daily 20 days back. She presented with fever, generalised rash all over the body with itching and follicular eruptions. On examination extensive skin necrosis with peeling over the trunk, involvement of eye lids, oral mucosa with crusting lesions and bulla over the palms and soles and genital mucosa. Bil congestion of conjunctiva present. Cornea is clear shown in Figure 1.

Investigations

Complete blood picture is within normal limits ;Renal parameters, Liver function tests and serum electrolytes are

normal.CD4 count 126 cells/$mm^{3.}$ Stevens- Johnson syndrome was diagnosed based on clinical presentation and by

Fig. 1. (A) At that time of admission

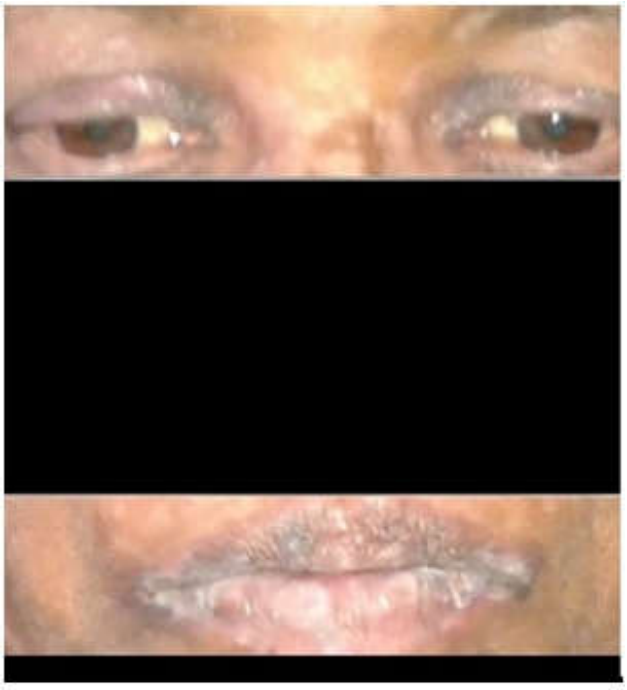

Fig. 2. (B) After Treatment

dermatologist and ophthalmologist opinion. Treatment was changed to zidovudine 300mg,lamivudine 150 mg bid and efavierenz 600mg OD excluding nevirapine. Patient improved in 10 days with steroids, anti histamines, local application of 1% gentian violet, fucidic acid and beclamethasone dipropionate ointment, Hydroxyl propyle methyl Cellulose eye drops Intravenous fluids, and with antibiotics shown in Figure 2.

DISCUSSION

First described in 1922 by Stevens and Johnson, Stevens - Johnson syndrome (SJS) is an immune complex hypersensitivity reaction that can be caused by many factors such as infections, drugs and malignancies. Recent reports have linked SJS to the use of drugs rather than other etiologic factors. Antibiotics e.g. sulphonamides are the most common cause of SJS, followed by analgesics, cough and cold medication, nonsteroidal anti-inflammatory drug (NSAID), psycho-epileptics, and antigout drugs. (www.emedicine.com/oph/topic268.htm-90k, 2005) Nevirapine has also been implicated in the pathogenesis of SJS (Fagot *et al*., 2001; Leichty *et al*., 2005). Erythema multiforme (EM) is an acute, self-limiting, usually mild, often recurrent inflammatory syndrome characterised by symmetrically distributed erythematous papular, urticarial and typical iris/target shaped lesions. This classic form of EM is currently defined as EM minor. The more severe variant with extensive mucous membrane involvement and constitutional symptoms is called EM major (Stevens - Johnson syndrome) (Jaiswal *et al*., 2012). Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis *SJS* and *TEN* are characterized by blisters and mucosal/epidermal detachment resulting from full-thickness epidermal necrosis in the absence of substantial dermal inflammation. The term *Stevens-Johnson syndrome* describes cases with blisters developing on target lesions, dusky or purpuric macules in which mucosal involvement is significant, and total body surface area blistering and eventual detachment in <10% of cases. The term *Stevens-Johnson syndrome/toxic epidermal necrolysis overlap* is used to describe cases with 10–30% detachment, and Ten is used to describe cases with >30% detachment.

Patients with SJS, SJS/TEN, or TEN initially present with acute Drugs that most commonly cause SJS or TEN are sulphonamides, nevirapine (1 in 1000 risk of SJS or TEN), allopurinol, lamotrigine, aromatic anticonvulsants, and NSAIDs, specifically oxicam. Frozen-section skin biopsy may aid in rapid diagnosis. The best results come from early diagnosis, immediate discontinuation of any suspected drug, supportive therapy, and paying close attention to ocular complications and infection. Systemic glucocorticoid therapy (prednisone 1–2 mg/kg) may be useful early in the evolution of the disease, but long-term systemic glucocorticoid use has been associated with higher mortality. Cyclosporine may be a possible therapy for SJS/TEN. Intestinal and pulmonary involvement is associated with a poor prognosis, as are a greater extent of epidermal detachment and older age. (Kanade Shinkai *et al*., 2015) Manifestations of hepatic toxicity may range from reversible mild to moderate elevation in liver enzymes (Prakash *et al*., 2001) to fulminant hepatic failure (Buyse *et al*., 2006).

Conclusion

Nevirapine, a non-nucleoside reverse transcriptase inhibitor (NNRTI), is widely prescribed as a part of the combination therapy of human immunodeficiency virus (HIV) infection because of its efficacy and good tolerability. The most serious toxic effects associated with nevirapine are skin reactions

(Steven Johnsons Syndrome) and liver dysfunction; both are generally mild to moderate and usually an early phenomenon, occurring during the first 6-8 weeks of therapy. The best results come from early diagnosis, immediate discontinuation of any suspected drug, supportive therapy, and paying close attention to ocular complications and infection.

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