CASE REPORT ON NEVIRAPINE INDUCED DRESS SYNDROME

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ARTICLE INFO

ABSTRACT

Nevirapine-induced drug reaction with eosinophilia and systemic symptom (DRESS) is uncommon but a potentially life-threatening condition, with significant morbidity and mortality rates due to multiple-organ involvement. DRESS syndrome has also been reported with a number of other drugs including allopurinol, minocycline, terbinafine, sulfonamides, azathioprine and dapsone. It was earlier referred to by various names such as Dilantin hypersensitivity syndrome and anticonvulsant hypersensitivity. It is a severe adverse drug reaction characterised by skin rash, fever, lymph node enlargement, hepatic dysfunction and internal organ involvement. Here we are going to describe a rare case of nevirapine-induced dress syndrome that was successfully treated with systemic steroid.

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INTRODUCTION

The Drug Reaction with Eosinophilia and Systemic Symptom (DRESS) is a severe adverse drug-induced reaction. The estimated incidence of this syndrome ranges from 1 in 1000 to 1 in 10,000 drug exposures. The clinical manifestations usually appear 2–6 weeks after the initiation of therapy and include a diffuse maculopapular rash, multi-organ involvement, eosinophilia, atypical lymphocytosis, and hepatic dysfunction. The pathogenesis of DRESS syndrome is partially understood. Different mechanisms have been implicated in its development, including detoxification defects leading to reactive metabolite formation and subsequent immunological reactions, slow acetylation, and reactivation of human herpes, including Epstein-Barr virus and human herpes virus (HHV)-6 and -7. The detection of HHV-6 reactivation has even been recently proposed as a diagnostic marker for DRESS.

The diagnosis involves 3 criteria; 1) Drug induced skin eruption 2) Absolute eosinophil count (AEC) >1500/dL or atypical lymphocytosis 3) One of the following enlarged lymphnodes at least 2 cm in diameter, hepatitis, interstitial nephritis, interstitial lung disease or myocarditis.

Nevirapine is an Anti-Retro viral drug comes under the category of Non-Nucleoside Reverse Transcriptase inhibitors (NNRTs) used for the treatment of HIV because of efficacy, good tolerability and comparatively low cost. It binds directly to reverse transcriptase and blocks RNA dependent and DNA dependent DNA polymerase activity, causing destruction of the enzyme’s catalytic site. The NNRT’s are indicated in combination regimens for HIV. Even though out of its effective therapeutic outcome it has certain side effects like skin rashes, nausea, headache, fever, rises in liver enzymes and hepatotoxicity.

Nevirapine-induced DRESS syndrome is uncommon but a potentially life-threatening condition, with significant morbidity and mortality rates due to multiple-organ involvement. Nevirapine-induced DRESS is relatively rare condition and extensive web-based search revealed <10 cases. The mainstay of management includes withdrawal of the culprit drug and corticosteroids. However, the use of intravenous immunoglobulin in the management of nevirapine-induced DRESS has also been reported.

We report a patient who was on nevirapine for HIV-1 infection who developed DRESS syndrome.

CASE REPORT

A 36-year-old with a known case of pulmonary tuberculosis since December 1994, on antituberculosis therapy from 20 years was detected to have HIV in January 2014. He was admitted to the Hospital on February 2014 after 1 month of his ART (zidovudine, nevirapine, lamivudine) with the complaints of fever, vomiting, right hypochondrium pain, jaundice, and muculopapular rash all over the body.

Routine investigations showed progressive anemia (Hemoglobin 10.7 gm %), eosinophil count 60%, high bilirubin level (4.5mg/dl), direct and indirect bilirubin 4.2 mg/dl and 7.8mg/dl respectively. And also SGOT was found to be 396 U/L and SGPT was 244 U/L. Urinalysis, renal function and serum chemistries were normal. Direct Coombs test was positive.

The patient was diagnosed to have DRESS syndrome. Therefore, nevirapine was identified as the culprit drug and it was stopped along with a known case of pulmonary tuberculosis since December 1994, on antituberculosis therapy from 20 years exposure. Nevirapine-induced DRESS syndrome.

The patient was diagnosed to have DRESS syndrome. Therefore, nevirapine was identified as the culprit drug and it was used with a dose of 200mg once daily. Patient was managed by stopping nevirapine and putting him on alternate ART regimen. He was also started on injection hydrocortisone 100 mg twice daily for the treatment of DRESS syndrome. Rechallenge with nevirapine was never performed but an alternative ART regimen was started with efavirenz 200mg instead of nevirapine. The patient was managed aggressively with parenteral antibiotics, laxative, proton pump inhibitor, and nutritional supplements. He was resolved completely after 6 days and no recurrence of rash and impairment of hepatic function were recorded on subsequent follow up.

DISCUSSION

Nevirapine is an oral medication that is used in combination with other antiretroviral agents for the treatment of human immunodeficiency virus disease. It belongs to a class of drugs known as nonnucleoside reverse transcriptase inhibitors. The drug exerts a virustatic effect by acting as a specific, noncompetitive HIV-1 reverse transcriptase (RT) inhibitor. The drug binds directly to heterodimeric HIV-1 RT and inhibits the RT activity by disrupting the catalytic site of the enzyme. Rash is the most frequent adverse event associated with nevirapine therapy. Nevirapine-induced DRESS was first reported in 1988. And since then there have been less than ten case reports found during literature search. The first reported case was managed with methylprednisolone and withdrawal of nevirapine.

In this patient it was identified that after intake of HAART which contains Nevirapine is the major cause for DRESS. Although our patient was not re-challenged with nevirapine, the signs and symptoms of this patient were most consistent with nevirapine induced dres syndrome. There is no evidence on lamivudine and zidovudin -induced dres syndrome. The causality assessment of dres syndrome with nevirapine using Naranjo's Causality Assessment Scale showed a score of seven indicating a probable relationship between the drug and occurrence of adverse drug reaction. WHO Uppsala Monitoring Centre (UMC) Causality Assessment Criteria also indicated a probable association with nevirapine in our patient.

This report highlights the importance of considering nevirapine-induced DRESS among the spectrum of cutaneous side effects of nevirapine, which can range from drug rash, Steven Johnson Syndrome, toxic epidermal necrolysis. Stopping nevirapine and administration of steroids remains the mainstay of management of this condition.
CONCLUSION

In conclusion, DRESS syndrome is potentially life-threatening, with significant morbidity and estimated mortality of 10%. In many studies it was found that use of a 2-week lead-in dose of 200 mg per day followed by 200 mg twice a day may reduce the overall risk of rash. With the increasing use of nevirapine the incidence of DRESS among patients infected with the HIV-1 virus is likely to increase which is the major challenge for HIV-1-infected individuals. We conclude that early detection, discontinuation of the suspected drug, and administration of systemic corticosteroids are the key steps in management of DRESS syndrome.

REFERENCE