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Case Report OMICS International

Stevens Johnson Syndrome and Toxic Epidermal Necrolysis Induced by Nevirapine among HIV-Infected Pregnant Women: Five Cases

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Abstract

Introduction: The nevirapine is the most widely accused drug in toxidermias in patients living with HIV. It is responsible for toxic epidermal necrolysis called Lyell syndrome or Stevens Johnson syndrome, severe during pregnancy. We report five cases in pregnant women who are HIV-positive.

Case reports: Five pregnant women aged 35 years on average with a mean gestational age of 29.6 weeks of amenorrhea were HIV1-positive.The mean CD4 count was 416/mm^3. They had severe toxidermia such as Lyell syndrome or Stevens Johnson syndrome. These toxidermias appeared on average 26 days after taking antiretroviral triple therapy including nevirapine as part of the prevention of mother-to-child transmission of HIV (PMTCT). The outcome was favorable after discontinuation of antiretrovirals. Nevirapine was substituted with lopinavir/ritonavir. Newborns had received antiretroviral prophylaxis and were not infected with HIV.

Conclusion: The nevirapine toxidermia is common during antiretroviral therapy. These toxidermia are severe during pregnancy related to maternal and fetal vital risks. The replacement of nevirapine with an anti-protease is a therapeutic alternative in our resource-limited countries.

Keywords: Toxidermia; HIV; Pregnancy; Nevirapine

Introduction

Antiretroviral therapy has greatly improved the mortality rate and risk of mother-to-child transmission of human immunodeficiency virus (HIV) infection in resource-limited countries [1]. However, studies have reported the frequency of some risk factors in the occurrence of toxidermia in patients living with HIV. These factors are female, CD4>250/mm^3 and viral load>10000 copies [2]. Nevirapine is the most widely accused drug in these toxidermia [2,3]. It is responsible for toxic epidermal necrolysis (TEN) called Lyell syndrome characterized by necrotic bullous eruption greater than 30% of body surface area and drug reaction with oesinophilia and systemic symptoms (DRESS) [2-4]. The occurrence of these medicinal side effects during pregnancy may involve the maternal and fetal prognosis [5]. We report five cases of toxidermia such as Lyell syndrome or Stevens Johnson syndrome (TEN/SJS) induced by nevirapine in HIV-positive pregnant women.

Case Reports

Case 1

A 35 year-old pregnant woman, with 34 weeks of amenorrhea of gestational age, was HIV1-positive with a CD4 count of 280/mm^3. It had a necrotic bullous eruption of more than 50% of the body surface, with involvement of the oral mucosa (Figure 1) and conjunctival hyperemia. This rash occurred 30 days after taking antiretrovirals (zidovudine 300 mg+lamivudine 150 mg and nevirapine 200 mg) as part of PMTCT. Leukocytes were at 7000/mm^3, hemoglobin at 13 g/dl, platelets at 250.000/mm^3, C-reactive protein was positive at 96 mg/l. Blood ionogram, urea, creatinine, hepatic transaminases and blood glucose were normal. Nevirapine was the incriminating drug. The outcome was favorable in 4 weeks with hyper pigmented scars (Figure 2). The newborn had received antiretroviral prophylaxis and was not infected with HIV. Nevirapine was substituted with lopinavir/ritonavir.

Case 2

A 35 year old pregnant woman with 34 weeks of amenorrhea of gestational age was HIV1-positive with a CD4 count of 400/mm^3. It had a necrotic bullous eruption at 28% of body surface area with oral mucosa and conjunctival hyperemia. This rash occurred 30 days after taking antiretroviral drugs (zidovudine 300 mg+lamivudine 150 mg+nevirapine 200 mg) as part of PMTCT. Anemia at 7.3 g/dl was noted and hepatic cytolysis. Nevirapine was the incriminated drug. The outcome was favorable in 3 weeks with hyper pigmented scars. The level of hemoglobin and transaminases had become normal. The newborn had received antiretroviral prophylaxis and was not infected with HIV. Nevirapine was substituted with lopinavir/ritonavir.

Case 3

A 21 year old pregnant woman with 30 weeks of amenorrhea of gestational age was HIV1-positive with a CD4 count of 500/mm^3. It had a necrotic bullous eruption of less than 10% of body surface area with oral mucosa and conjunctival hyperemia. This rash occurred 28 days after taking antiretrovirals (zidovudine 300 mg+lamivudine 150 mg and nevirapine 200 mg) as part of PMTCT. Biological explorations were normal. Nevirapine was the incriminating drug. The outcome was favorable in 3 weeks with hyper pigmented scars. The newborn

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Case	Age (Year)	GA (WA)	Type of HIV	CD4 (mm³)	Clinical form	Drug inducer	TO (Days)	Outcome	Substitution
Case 1	35	34	HIV1	280	TEN	NVP	30	Favorable	LPV/RTV
Case 2	35	34	HIV1	400	OS	NVP	30	Favorable	LPV/RTV
Case 3	21	30	HIV1	500	SJS	NVP	28	Favorable	LPV/RTV
Case 4	28	30	HIV1	400	SJS	NVP	21	Favorable	LPV/RTV
Case 5	26	20	HIV1	500	OS	NVP	21	Favorable	LPV/RTV

TEN: Toxic Epidermal Necrolysis; SJS: Stevens Johnson Syndrome; OS: Overlap Syndrome; NVP: Nevirapine; GA: Gestational Age; WA: Week of Amenorrhea; TO: Time of Occurrence; LPV/RTV: Lopinavir/Ritonavir

Table 1: Summary of cases.

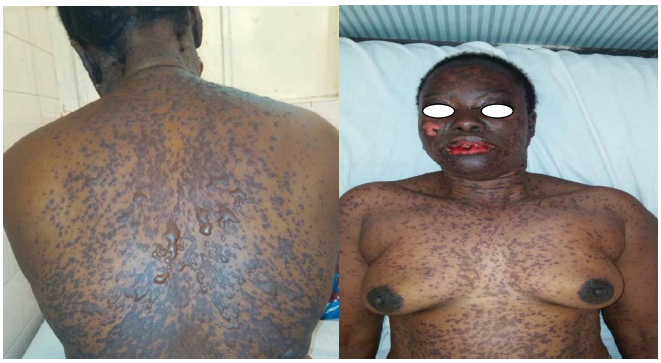

Figure 1: A necrotic bullous rash of more than 50% of the body surface, with mucosal involvement.

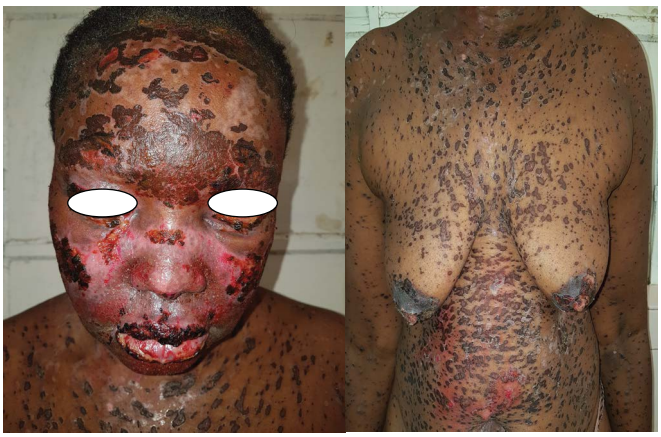

Figure 2: Hyper pigmented macula of trunk and face.

had received antiretroviral prophylaxis and was not infected with HIV. Nevirapine was substituted with lopinavir/ritonavir.

Case 4

A 28 year old pregnant woman with 30 weeks of amenorrhea of gestational age was HIV1-positive with a CD4 count of 400/mm³. It had a necrotic bullous eruption of less than 10% of body surface area with involvement of the oral mucosa and conjunctival hyperemia. This rash occurred 21 days after taking antiretrovirals (zidovudine 300 mg+lamivudine150 mg and nevirapine 200 mg) as part of PMTCT. Biological explorations were normal. Nevirapine was the incriminating drug. The outcome was favorable in 3 weeks with hyper pigmented scars. The newborn had received antiretroviral prophylaxis and was not infected with HIV. Nevirapine was substituted with lopinavir/ritonavir.

Case 5

A 26 year old pregnant woman with 30 weeks of amenorrhea of gestational age was HIV1-positive with a CD4 count of 500/mm³. It had a necrotic bullous eruption of less than 28% of the body surface with oral mucosa and conjunctival hyperemia. This rash occurred 21 days after taking antiretrovirals (zidovudine 300 mg+lamivudine 150 mg and nevirapine 200 mg) as part of PMTCT. Nevirapine was the incriminating drug. The outcome was favorable in 3 weeks with hyper pigmented scars. The newborn had received antiretroviral prophylaxis and was not infected with HIV. Nevirapine was substituted with lopinavir/ritonavir.

Discussion

We report 5 cases of toxidermia characterized by their occurrence in young pregnant women who are HIV positive with an average CD4 count of 416/mm³. They had severe clinical forms such as Lyell syndrome and Stevens Johnson syndrome. Nevirapine was the most implicated drug. The outcome was favorable under symptomatic treatment and discontinuation of antiretrovirals with newborns not infected with HIV (Table 1). Nevirapine toxicity is common [6,7]. Control studies have reported that pregnancy is a risk factor for TEN/SJS when HIV-positive women are treated with a combination of nevirapine with an odds ratio of 14.28 (p=0.006), a 95% confidence interval (1.54-131.82) [8]. All women had taken antiretroviral triple therapy as part of mother-child prevention of HIV transmission with an average CD4 cell count at 416/mm³, viral load was not available. The maculopapular exanthema is the predominant clinical form during the nevirapine toxidermia; the severe forms represent 4 and 9% [2]. The imputability of nevirapine by the French method was very likely [9]. The favorable outcome in all our patients could be related to the young age, the absence of factors of co morbidities, the stoppage of the ARV and the multidisciplinary early management (between dermatologist and obstetricians). We did not observe fetal complications to the type of prematurity that is reported by some authors [10-12]. Anti-proteases were used as a therapeutic alternative in the antiretroviral treatment protocol because nevirapine toxidermia is associated with a 10% cross-reactivity risk with efavirenz.

Conclusion

The Nevirapine is the most widely accused drug during antiretroviral. These toxidermias are severe during pregnancy with high maternal and fetal mortality and a risk of prematurity in the newborn. The replacement of nevirapine with an anti-protease is a therapeutic alternative in our resource-limited countries.

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