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Case Report

Co-trimoxazole induced Steven Johnson syndrome in HIV infected patient: things to consider

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ABSTRACT

Co-trimoxazole is a sulfonamide fixed dose combination antibiotic which is effective and widely use in treatment and prevention of opportunistic infections in people living with HIV/AIDS, but can be potentially associated with adverse drug reactions including drug hypersensitivity reactions such as Steven Johnson syndrome. PLWHA individuals have up to a 1000-fold increased risk of drug hypersensitivity reaction compared to the general population, which is associated with drug exposure, immune dysregulation, and concurrent infections. Here we present a case report of a 59-year-old man with HIV who experienced Stevens-Johnson Syndrome after taking co-trimoxazole for 18 days. Therefore, we would like to remind you to be more careful when giving cotrimoxazole to PLWHA because it can take time for a hypersensitivity reaction to occur, also in a few cases, it can occur immediately.

Keywords: People living with HIV/AIDS, Co-trimoxazole, Steven Johnson syndrome

INTRODUCTION

Co-trimoxazole is a sulfonamide class antibiotic, a combination of sulfamethoxazole and trimethoprim is useful in the treatment of various bacterial, fungal, and protozoan infections. The world health organization (WHO) has recommended the prophylactic use of co-trimoxazole in patients with HIV to prevent opportunistic infections.[1] However, the use of co-trimoxazole is associated with hypersensitivity reactions in 1-3% of the general population and a higher frequency of up to 34% in PLWH.[2] One form of hypersensitivity reaction to co-trimoxazole in PLWH is Steven Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).[3] The incidence of SJS and TEN in the world ranges from 0.4-6 cases out of 1 million people in a year with an estimated mortality rate of 5-12% for SJS, 30% for NET and 33.3% for SJS overlap NET. The incidence of SJS in patients with reactive HIV ranges from 1-2 cases out of 1000 people.[4]

Here we present a case report of a 59-year-old man with HIV who experienced Stevens-Johnson syndrome after taking co-trimoxazole for 18 days.

CASE REPORT

A 59-year-old man came to our hospital with a chief complaint of skin lesions in the form of blackish-red spots all over his body and feel pain. Initially, complaints began to appear with blackish-red spots appearing on the lips, then blisters and spread to the face, body, hands, and feet. Based on a detailed history, the patient was diagnosed as HIV positive 1 month and regularly takes Ternovofir+ Lamivudine+Dolutegravir 1×1 for Anti-retroviral therapy (ART), clindamycin, and co-trimoxazole. One month ago he was hospitalized with toxoplasma cerebri. He has no hypertension, diabetes mellitus, and no drug allergies. On examination, compos mentis state of consciousness, blood pressure 110/80 mmHg, regular heart rate 80/minute,

respiratory rate 20/minute, temperature 36.5°C, and oxygen saturation 99% in room air. There is no anemic and icteric conjunctiva. He had a blister on his lip. No persistent generalized lymphadenopathy was palpable. The cardiac, lung, and abdominal examinations were within normal limits. Capillary refill time is less than 2 seconds. Dermatological status on the face, lips, body, hands, and feet showed efflorescence in the form of hyperpigmented erythema, erosion, excoriation, crusting, and epidermolysis 10-30% of the body surface area (Figure 1).

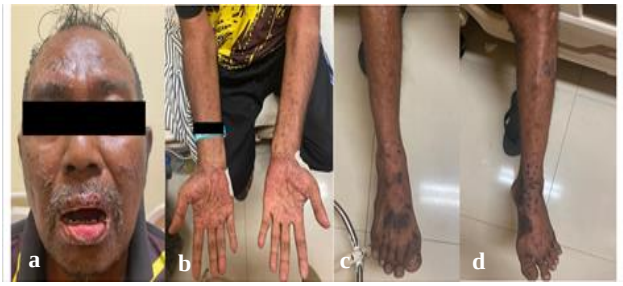

Figure 1: Epidermolysis 10-30% of the body surface area. (a) Forehead, cheek, lower and upper lips showing hyperpigmented erythema, erosion, excoriation, and crusting; (b) left and right hand showing hyperpigmented erythema, erosion, excoriation, and crusting; (c) right leg showing hyperpigmented erythema, and erosion; (d) left leg showing hyperpigmented erythema, and erosion.

A complete blood examination found WBC 3,260/µl, hemoglobin 10.7 g/dl, hematocrit 30.1%, and thrombocyte 215,000/µl. Electrolyte examination found sodium 127 mmol/l, potassium 4.0 mmol/l, and chloride 93 mmol/l. In the clinical chemistry examination, blood sugar was found to be 93 mg/dl, urea 40 mg/dl, creatinine 1.3 mg/dl, SGOT 32 µ/l, SGPT 34 µ/l, and albumin 2.9 gr/dl. Toxoplasma serology was sent, and IgG was reactive: 156.8 IU/ml. Dermatology was consulted and Steven Johnson syndrome-toxic epidermal necrolysis. Overlapping was the leading diagnosis at presentation, given physical examination findings.

The patient was treated with intravenous NaCl 0.9% solution, methylprednisolone 62.5 mg IV BID, Gentamycin 80 mg IV BID, Loratadine 10 mg once daily, topical desoximetasone+gentamicin, and continued ARV drugs. He was advised to stop taking co-trimoxazole. He was discharged after eleven days of admission; the skin lesions had dried and there were no complaints of skin pain.

DISCUSSION

SJS or TEN are epidermal necrolysis differentiated based on the extent of skin detachment, which is limited to less than 10% of the body surface area in SJS, 10%-30% of the body surface area in SJS/TEN overlap, and greater than 30% of the body surface area in TEN.[5] These are categorised as type IV cell-mediated delayed hypersensitivity reactions with release of various cytotoxic signals activated by cytotoxic T lymphocytes and natural killer cells.[6] A majority of patients will have symmetrical scattered skin lesions on the face, body and proximal extremities and at least two lesions on the mucosa (oral, genital, or conjunctival). Lesions in the form of erythema macules, dusky red, irregularly shaped purpura, target lesions can be found then the lesions become necrotic, and bullae with Nikolsky sign positive.[5] Sulfonamide class antibiotics such as co-trimoxazole often cause drug-induced reactions (ADR) in patients with HIV/AIDS.[4] Co-trimoxazole is a universal antibiotic that is available at low cost and is effective for the treatment of various bacterial, fungal, and protozoa. Co-trimoxazole is widely use in treatment and prevention of opportunistic infections in (PLWHA). The prevention therapy has been shown to reduce mortality, morbidity, and hospitalization among PLWHA.[7] [8] However, PLWHA have a higher potential for experiencing ADRs which have a significant impact on the management of opportunistic infections.[2] The increased risk of PLWHA can be 1000-fold compared to the general population of experiencing SJS or TEN, several factors that cause this are exposure to drugs such as nevirapine and trimethoprim-sulfamethoxazole, immune dysregulation and concurrent infections.[9] In this case, co-trimoxazole is the drug that has the greatest possibility of being a suspect drug compared to other drugs that have been consumed by the patient. He took this medicine for 18 days, on the 19th day blackish-red spots began to appear, then blisters appeared on his lips and spread to his body, hands, and feet, feeling sore and painful. Early recognition of drug reactions, discontinuation of use of suspected drugs and supportive care provision of treatment are critical in the management of SJS. Administration of corticosteroids is effective in the early stages, but can have bad consequences such as increased risk of infection and delayed wound healing, especially in the event of bullous eruption or mucosal erosion. Administration of short-term corticosteroids pulse therapy, especially during the initial phase of SJS/TEN, may be beneficial in reducing mortality rates. [10] In this case, after discontinuation of use of suspected drugs and being treated for 11 days with intravenous fluid, corticosteroids, and oral antihistamines, his complaints improved. SJS and TEN are potentially fatal severe cutaneous adverse reactions that affect multiple organs and systems. Co-trimoxazole has been implicated as a trigger for these adverse drug reactions. The resulting hypersensitivity reaction should occur approximately 2 to 7 weeks after the first exposure. However, in several recent studies, it could take usually takes up to 8 weeks.[5] The history of SJS should be considered when prescribing antiretroviral therapy and prophylaxis if indicated.[1]

CONCLUSION

Patients with HIV infection are very vulnerable to adverse drug reactions. It is necessary to monitor clinical changes periodically because hypersensitivity reactions

can occur immediately or takes time. Therefore, we would like to remind you to be more careful when giving cotrimoxazole to PLWHA.

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