

Toxic Epidermal Necrolysis caused by Cotrimoxazole in a Patient with Human Immunodeficiency Virus Infection

Ramakant Dixit, Sidharth Sharma

Department of Respiratory Medicine & Tuberculosis, J. L. N. Medical College, Ajmer, India

Abstract

Toxic epidermal necrolysis (TEN) is a rare but a very serious dermatologic disorder. We present a case of TEN in a 45-year-old human immune deficiency virus (HIV) infected man due to cotrimoxazole therapy. Increased risk of drug reactions and possible mechanism among patients with HIV infection/AIDS are also discussed.

Key words: Toxic epidermal necrolysis, Cotrimoxazole, HIV infection

INTRODUCTION

Toxic epidermal necrolysis (TEN) or Lyell's syndrome is a rare but very serious dermatologic disorder attributed to a drug reaction. It is characterized by sudden development of constitutional symptoms like malaise, lethargy and fever followed by vesiculobullous eruptions involving the face, hands, feet with extensive peeling of skin, ulceration of buccal mucosa, ocular lesions mainly conjunctivitis and genital involvement¹.

In general population, the incidence of TEN has been found to be 1.17-1.89 patients per million inhabitants per year in one of the studies². This disorder is more common in HIV infected persons^{1,3}. We present a case of TEN in a HIV infected person caused by cotrimoxazole therapy.

Address for correspondence: Dr Ramakant Dixit, Assistant Professor, 381/26, Ramganj, Ajmer-305001. Phone no. 91-0145-2691542. E-mail: dr.ramakantdixit@gmail.com
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CASE REPORT

A 45-year-old previously known HIV sero-positive male patient presented with skin manifestation and fever following cotrimoxazole therapy for urinary tract infection. He developed severe itching with generalized maculopapular and purpuric rashes over face, trunk and extremities, six hour after consuming cotrimoxazole tablet. Subsequently, these eruptions became necrotic, surrounded by rim of erythema with blister formation. Soon he developed vesiculobullous lesions over back and extremities. He also had conjunctivitis and stomatitis. Nikolsky's sign was positive. There was rupture of cutaneous blisters followed by sloughing of skin exposing an intensely erythematous and exudative base over lower limbs. He was febrile with normal other vital parameters. His general physical and systemic examination was otherwise unremarkable.

Routine investigations of blood i.e. hemoglobin, total and differential leukocyte count, bleeding profile,



Fig 1. Photographs of patient showing epidermal necrolysis. extensive lesions of toxic

ESR etc. were normal. Skiagram chest, urine examination including culture, liver function tests and renal function tests were within normal limits. Peripheral blood film smear examination was normal and antinuclear antibody test was also negative. Skin biopsy could not be taken. ELISA test for HIV-1 and HIV-2 was positive with two different kits after the episode of present illness.

Patient was treated with injection dexamethasone 16 mg intravenously, then 8 mg six hourly, tablet roxithromycin 300mg twice daily, pheniramine maleate 25 mg eight hourly daily along with local soothing agents, cold sponging and paracetamol for fever. Fever and erythema surrounding the lesions disappeared within 12 hour; bullous lesions started healing and became inactive by 7th day. Oral and ocular lesions healed completely within two weeks.

DISCUSSION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) represent severe form of cutaneous drug reactions. TEN is defined as > 50% body surface area (BSA) involved with a vesiculobullous reaction and confirmed by biopsy. SJS is defined as < 50% BSA involved with iris and bullous lesions and mucosal involvement. Such types of severe cutaneous drug reactions are more common among HIV infected persons³.

In India, drugs are perhaps the commonest cause of TEN. The various drugs known to cause TEN includes sulfonamides, anti-convulsants, nonsteroidal anti-inflammatory drugs, anti-tubercular drugs (particularly thiacetazone, PAS, streptomycin, rifampicin and isoniazid), allopurinol, erythromycin, valproic acid, fluconazole and anti-retroviral drugs (particularly nevirapine) etc.⁴⁻⁶

Sulfonamides are the most common drugs responsible for TEN and were found to be the cause of TEN in 25% cases in the general population in France. This drug is also a commonest cause of TEN among HIV infected individuals with a prevalence of 12 cases per 1500 persons (0.8%) with AIDS^{4,7}. Hypersensitivity reactions were reported in 78% of AIDS patients treated with trimethoprim-sulphamethoxazole for *Pneumocystis carinii* in one series⁸. Rash was the common reaction with other manifestations including fever, leucopenia, thrombocytopenia and hepatitis. Since sulfa drugs are commonly used to treat central nervous system toxoplasmosis and *Pneumocystis carinii* pneumonia, there may be a higher incidence of TEN in HIV-infected persons having such diseases very commonly.

The exact pathogenesis of TEN is unknown, although there is evidence to suggest development of TEN linked to genetic differences in patients metabolic reactions to drugs such as sulfonamides¹. Multiple prior cutaneous drug reactions or a prior reaction to a specific drug is also found to be a risk factor for the development of TEN in HIV infection. Increased occurrence of hypersensitivity reactions among AIDS patients might be related to defects of both T and B cells. AIDS patients have increased number of abnormal polyclonally activated B cells that are defectively activated and secrete immunoglobulins.

This leads to formation of circulating immune complexes and auto-immune phenomena⁹. Therefore, in any patient developing severe cutaneous drug reaction i.e. TEN, HIV should always be suspected and care must be used in subsequent drug therapies, especially with the drugs that caused the previous reactions or with sulfonamides particularly. A high index of suspicion should be observed while dealing such type of patients (HIV & AIDS), as evolution of any drug rash is expected to be severe and response to treatment is unpredictable with high mortality.

REFERENCES

1. Decker DS. Toxic epidermal necrolysis. *Lancet* 1998; **351**: 1417-20.
2. Rzamy B, Mockenhaupy M, Baur S, et al. Epidemiology of erythema: Exsudativum multiforme majus, stevens Johnson syndrome and toxic epidermal necrolysis in Germany (1990-92). Structure and results of a population based registry. *J Clin Epidemiol* 1996; **49**: 769-73.
3. Porteous DM, Berger TG. Severe cutaneous drug reactions (stevens Johnson syndrome and toxic epidermal necrolysis) in human immunodeficiency virus infection. *Arch Dermatol* 1991; **127**: 740-41.
4. Guillaume JC, Roujenu JC, Revuz J, et al. The culprit drugs in 87 cases of toxic epidermal necrolysis (Lyell's syndrome). *Arch Dermatol* 1987; **123**: 1166-70.
5. Jain VK, Mathur KC, Shukla SN, Gupta PP. Toxic epidermal necrolysis (Lyell's syndrome) due to streptomycin. *Indian J Chest Dis Allied Sci* 1980; **22**: 73-76.
6. Udawat H, Khandelwal V, D'Souza P, Goyal RK. Toxic epidermal necro-lysis secondary to carbamazepine in a patient with human immunodeficiency virus infection. *J Assoc Physicians India* 2001; **49**: 918-19.
7. Arora S, Venibabu H. Cotrimoxazole induced toxic epidermal necrolysis in a case of human immunodeficiency virus infection. *Indian J Chest Dis Allied Sci* 1998; **40**: 125-29.
8. Gordin FM, Simon GL, Wofsy CB, Mills J. Adverse reactions to trimethoprim-sulphamethoxazole in patients with AIDS. *Ann Intern Med* 1984; **100**: 495-99.
9. Bowen DL, Lane HC, Fauci AS. Immunopathogenesis of the acquired immunodeficiency syndrome. *Ann Intern Med* 1985; **103**: 704-09.