WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 8, Issue 12, 1167-1172. Case Study ISSN 2277– 7105

PARACETAMOL INDUCED TOXIC EPIDERMAL NECROLYSIS: A CASE REPORT

Dr. R. Ganesan[1]*, Dr. S. Muthu Subramaniam[2], Jasno Saji John[3] and Sruthimol V.[4]

[1]Department of General Medicine, Vijaya Group of Hospitals, Vadapalani, Chennai.

[2]Consultant Dermatologist, Vijaya Group of Hospitals, Vadapalani, Chennai.

[3,4]Pharm-D Interns, K.K. College of Pharmacy, Gerugambakkam, Chennai

Article Received on
05 Sept. 2019,
Revised on 26 Sept. 2019,
Accepted on 16 Oct. 2019
DOI: 10.20959/wjpr201912-16092

***Corresponding Author**
Dr. R. Ganesan
Department of General Medicine, Vijaya Group of Hospitals, Vadapalani, Chennai.

ABSTRACT

Background: Toxic epidermal Necrolysis (TEN) is an adverse reaction that can be induced by various drugs; the associated mortality rate is 20–25%. Paracetamol is widely used as an over-the-counter analgesic and antipyretic drug. It's a remarkably safe drug devoid of serious side effects in therapeutic doses; Paracetamol is very rarely implicated to be a culprit of TEN. **Case Prsentation**: We report a case of 29 years old male presented with complaints of bilateral lower limb swelling and itching with blisters and scaling of skin all over the body after taking Paracetamol. Skin biopsy was consistent with toxic epidermal necrolysis. The patient was initiated with Cyclosporin and supportive treatment was given, to which he responded very well. **Conclusion:** clinicians must be more cautious while prescribing and should monitor patients for severe drug reactions, including TEN. Patients should also be educated regarding the adverse effects of NSAIDs.

KEYWORDS: Toxic epidermal necrolysis, Paracetamol, Adverse reaction.

INTRODUCTION

Cutaneous adverse drug reactions (ADR) range from trivial manifestations, such as morbilliform eruptions, to severe life-threatening reactions, including Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).[1,2] Toxic epidermal necrolysis (TEN) is a serious, life-threatening, cutaneous adverse drug reaction with a high mortality rate (20–25%).[3-5] The disorder is characterized by a rapidly developing blistering exanthema of purpuric macules and targetoid lesions accompanied by mucosal involvement and variable

skin detachment. TEN is defined as skin detachment exceeding 30%.[6] Strong associations have been reported between TEN and a number of drugs, including anticonvulsants, allopurinol, anti-infective sulfonamides and nevirapine.[4]

CASE REPORT

A 29 year old male with no comorbidities, presented with complaints of bilateral lower limb swelling and itching with blisters and scaling of skin all over the body after taking Paracetamol.

History of present illness: The patient had taken Paracetamol (3tablets/day for 3 days) for his back pain. After a week, he developed Left foot swelling and itching; hyper pigmented skin. On the next day, few bullae on left foot/leg were seen. Initially he was treated abroad with antibiotics, antihistamines and painkillers (Paracetamol) and new lesions developed on thighs that evening. The following day, he came back to India and was diagnosed as leg cellulitis and was treated with antibiotic, anti-inflammatory agent, antihistamine, painkiller (Paracetamol–2tablets/day for 6 days) and new lesions on trunk was seen with widespread blistering.

On examination, patient was conscious, oriented, afebrile, bilateral pedal edema. There were lichenoid appearing skin and peeling in the trunk. In thighs and leg, there were atypical targetoid lesion present, tense bullae, erythematous skin with peeling, nikolsky's sign positive, oral cavity – single vesicle palate, congestion of conjunctiva present.

Routine blood and urine investigations were normal. Skin biopsy was consistent with toxic epidermal necrolysis.

He was treated symptomatically and supportive treatment was given to which he responded very well and was discharged on medical advice.

DISCUSSION

Toxic epidermal necrolysis (TEN) is a rare, acute, and life threatening mucocutaneous disease that is usually drug related.[7]

TEN results from extensive keratinocyte cell death, which leads to separation of large areas of the skin at the dermo-epidermal junction. In TEN, keratinocyte death occurs due to

apoptosis. Tumor necrosis factor alpha, interleukin-6, and Fas ligand are the important mediators of keratinocyte death (apoptosis) in TEN.[8]

A multivariate analysis showed a weak association with acetaminophen.[4] The US Food and Drug Administration reported that acetaminophen is associated with a risk of serious skin reactions, including TEN, also stated that SJS/TEN can occur with first time use of acetaminophen or at any time while it is being taken.[9]

Duration between the drug intake and first onset of symptom in SJS/TEN ranges from 5 to 31 days.[10] In our case, it took 7 days for the first symptom to develop.

Paracetamol is among the most extensively used analgesic and anti‑pyretic because of easy availability and cost-effectiveness. Despite being considered relatively safe, adverse reactions including cutaneous hypersensitivity reactions have been reported.[11] Identification of NSAIDS as a causative agent is difficult because of their widespread OTC use and as co-prescription.[12]

Khawaja et al,[13] reported a case of Acetaminophen induced SJS and TEN with widespread macula-papular rash, stinging in the eyes, oral mucosal ulcerations, and high-grade fever. Similar features were seen in this case, but there was the absence of high-grade fever and oral mucosal ulcerations.

The first step in the management was an immediate withdrawal of the offending agent followed by supportive care. Garcia Doval *et al.*, report that earlier the drug is withdrawn, better the prognosis while exposure to drugs with longer half-lives increases the risk of death. Supportive care must include the management of fluid and electrolyte requirements.[14]

In this case, the patient was treated successfully with Cyclosporin 300 mg/day for 7 days, 50% liquid paraffin + 50% soft paraffin applied all over the area affected, potassium permanganate solution for bathing, Clindamycin for antibacterial prophylaxis and for congestion of conjunctiva Ciprofloxacin eye drops and propylene glycol was given.
Several studies have confirmed the benefit of cyclosporine in TEN.[15]

Cyclosporine is an immunosuppressant commonly used in preventing organ rejection after organ transplantation. In dermatology practice, it is commonly used in the treatment of skin disorders such as psoriasis and atopic dermatitis. Cyclosporine acts by calcineurin inhibition.

By calcineurin inhibition, cyclosporine decreases the production of various inflammatory cytokines. It also has anti-apoptotic action.[15,16] In the treatment of TEN, it is not clear whether cyclosporine acts through its immunosuppressive effects or anti-apoptotic effects. Most of the reports with successful treatment of TEN with cyclosporine have not reported any mortality, indicating its effectiveness and safety in the treatment of SJS/TEN. By shortening the recovery time, cyclosporine also reduces the cost of the treatment.[17]

In a study conducted by Saoji et al,[17] only cyclosporine was used without steroids indicating that only cyclosporine as monotherapy is effective in TEN which is similar to our case.

H. Watanabe et al,[18] reported a case of TEN due to Acetaminophen showed almost 100 % skin detachment, which correlates with our case.

CONCLUSION

This case report reports the fact that severe hypersensitivity reactions can occur with Paracetamol, which can be possibly dangerous and life‑threatening. Therefore, clinicians must be more cautious while prescribing and should monitor patients for severe drug reactions, including TEN. Patients should also be educated regarding the adverse effects of NSAIDs.

ACKNOWLEDGEMENT

We would like to thank Dr. Saarumathe Chandrabose for her valuable support and helping hands throughout this study.

REFERENCES

1. Letko, E., D. N. Papaliodis, G. N. Papaliodis, Y. J. Daoud, A.R. Ahmed, and C. S. Foster. Stevens-Johnson syndrome and toxic epidermal necrolysis: a review of the literature. *Ann. Allergy Asthma Immunol*, 2005; 94: 419-436.
2. Pereira, F. A., A. V. Mudgil, and D. M. Rosmarin. Toxic epidermal necrolysis. *J. Am. Acad. Dermatol*, 2007; 56: 181-200.
3. Roujeau JC, Kelly JP, Naldi L et al. Medication use and the risk of Stevens-Johnson syndrome or toxic epidermal necrolysis. *N Engl J Med.*, 1995; 333: 1600–1607.
4. Mockenhaupt M, Viboud C, Dunant A et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: assessment of medication risks with emphasis on recently marketed drugs. The EuroSCARstudy. *J Invest Dermatol*, 2008; 128: 35–44.

5. Lee HY, Chung WH. Toxic epidermal necrolysis: the year in review. *Curr Opin Allergy Clin Immunol*, 2013; 13: 330–336.
6. Bastuji-Garin S, Rzany B, Stern RS, Shear NH, Naldi L, Roujeau JC. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. *Arch Dermatol*, 1993; 129: 92–96.
7. French LE, Prins C: Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. In: Bolognia JL, Jorrizo JL, Schaffer JV editors. Dermatology 3rd edition. New York: Elsevier, 2013; 319–33.
8. French LE, Prins C. Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. In: Bolognis JL, Jorizzo JL, Rapini RP, editors. Dermatology. 2nd ed. Noida: Elsevier, 2008; 287-99.
9. FDA Drug Safty Communication. FDA warns of rare but serious skin reactions with the pain reliever/fever reducer acetaminophen, 2013; 8-1. http://www.fda.gov/Drugs/DrugSafety/ucm363041.htm
10. Sanmarkan AD, Sori T, Thappa DM, Jaisankar TJ. Retrospective Analysis of Stevens-Johnson syndrome and Toxic Epidermal Necrolysis over a Period of 10 Years. *Indian J Dermatol*, 201; 56(1): 25-9.
11. Kvedariene V, Bencherioua AM, Messaad D, Godard P, Bousquet J, Demoly P. The accuracy of the diagnosis of suspected Paracetamol (acetaminophen) hypersensitivity: results of a single-blinded trial. *Clin Exp Allergy*, 2002; 32: 1366-9.
12. Svensson CK, Cowen EW, Gaspari AA. Cutaneous drug reactions. *Pharmacol Rev.*, 2001; 53: 357-79.
13. Khawaja A, Shahab A, Hussain SA. Acetaminophen induced Steven Johnson syndrome-toxic epidermal necrolysis overlap. *J Pak Med Assoc*, 2012; 62: 524–7.
14. Garcia-Doval I, LeCleach L, Bocquet H, Otero XL, Roujeau JC. Toxic epidermal necrolysis and Stevens-Johnson syndrome: Does early withdrawal of causative drugs decrease the risk of death? *Arch Dermatol*, 2000; 136: 323–7.
15. Rai R, Srinivas CR. Suprapharmacologic doses of intravenous dexamethasone followed by cyclosporine in the treatment of toxic epidermal necrolysis. *Indian J Dermatol Venereol Leprol*, 2008; 74: 263-5.
16. Bilimoria FE, Shah BJ. Drug reactions. In: Valia RG, Valia AR, editors. IADVL Textbook of Dermatology. 3rd ed. Mumbai: Bhalani, 2008; 1633-64.
17. Vikrant Saoji, Shilpa Hazare, Sanjiv Choudhary. Cyclosporine in toxic epidermal necrolysis. *Indian J Drugs Dermatol*, 2016; 2(1): 24-27.

18. Watanabe H, Kamiyama T, Sasaki S, Kobayashi K, Fukuda K, et al. Toxic epidermal necrolysis caused by acetaminophen featuring almost 100% skin detachment: Acetaminophen is associated with a risk of severe cutaneous adverse reactions. *J Dermatol.*, 2016; 43(3): 321-4.