



Acetaminophen induced Stevens Johnson syndrome - Toxic Epidermal Necrolysis Overlap Syndrome: A rare Adverse Reaction

Saiprasad Onkareshwar Kavthekar¹, Amith K¹, Anil Bapurao Kurane¹, Yoganand J. Phulari²

¹Department of Paediatrics, D.Y. Patil Medical College, D. Y. Patil Education Society (Deemed to be University), Kolhapur- 416003, Maharashtra, India.

²Department of Dermatology, D.Y. Patil Medical College, D. Y. Patil Education Society (Deemed to be University), Kolhapur- 416003, Maharashtra, India.

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Abstract

Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are hyper sensitive life - threatening rare dermatological reactions. In SJS - TEN overlap syndrome, the extent and severity of epidermal detachment is 10- 30%. Drugs like sulfonamides, nonsteroidal anti- inflammatory agents, antibiotics and anticonvulsants are the commonest precipitants. Here, we present a rare case of SJS - TEN overlap syndrome in a previously normal 11 years old girl after acetaminophen intake for fever. This case report is intended to make paediatricians aware that the adverse reaction like SJS - TEN overlap syndrome can develop with a drug like acetaminophen which is supposed to be the safest antipyretic in paediatrics.

Introduction

Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are hypersensitive life threatening rare dermatological conditions caused by either viral infections, malignancies or adverse drug reactions.¹ The difference between the SJS and TEN is the extent and severity of epidermal detachment; it is less than 10% in SJS, more than 30% in TEN and 10 - 30% in SJS - TEN overlap syndrome.² In SJS, mucocutaneous nonpruritic lesions appear in clusters while TEN is characterized by multiple large blisters that subsequently coalesce with extensive sloughing of skin and mucous membranes.³ The incidence of SJS has been estimated to be around one to six per million persons per year with a mortality rate of one to five percent which rises up to 30% in TEN.⁴ Drugs particularly sulfonamides, nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics and anticonvulsants are the commonest precipitants of SJS and TEN.⁵ Amongst NSAIDs, acetaminophen is the commonest used drug to control fever and considered as one of the safest drugs in children. Here, we report a rare case of SJS - TEN overlap syndrome in a previously normal healthy girl after intake of acetaminophen.

Case report

A 11 year old healthy girl was hospitalized for generalized nonpruritic skin rash since last two days. She also had cold and fever two days back and was prescribed tablet acetaminophen 500 mg as an antipyretic by a family physician. She consumed half tablet of acetaminophen twice daily 12 hours apart (Total one tablet/500 mg). Her fever subsided but next day she developed swelling around lips and eyes, for which she

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*Corresponding Author

Amith K
Junior Resident,
Department of Paediatrics,
D.Y. Patil Medical College,
D. Y. Patil Education Society
(Deemed to be University),
Kolhapur - 416003, Maharashtra, India.
Email:amithk313@gmail.com

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was treated with tablet cetirizine 10 mg. Subsequently, swelling around lips and eyelids increased along with oral ulcerations and skin rash all over body (Figure 1). According to parents the rashes developed as red macular lesions on face and neck and later extended symmetrically involving firstly her upper limbs, trunk, and lastly legs. On general examination she had toxic look but hemodynamically stable. Erythematous maculopapular lesions were present covering around 25-30% body surface area. As the rash progressed it started coalescing to form plaques on lips, eyes, neck, upper limbs, trunk and genital region. There were few blisters on back and trunk, with positive Nikolsky's sign and no skin tenderness (Figure 2). Rest of the systemic examination was normal. On the basis of typical history of drug ingestion and occurrence and progression of typical rash along with its extent and severity, she was confirmed clinically a case of SJS-TEN overlap syndrome.

Her investigations revealed haemoglobin - 12.6g/ dl, total leukocyte count – 7700/mm³ with neutrophils 74%, lymphocytes 25%, eosinophils of 1% and platelets- 2,05,000/mm³ with raised C reactive protein(10mg/dl). Her liver and renal function test and serum electrolytes were normal. Urine and blood cultures were sterile. Mycoplasma pneumonia serology was also sent and which turned out to be negative. Her chest X-ray was also normal. Histologic analysis of skin showed full thickness epidermal necrosis.

We immediately stopped the offending drug i.e. acetaminophen and she was managed with intravenous 0.9% DNS, injection ampicillin (100 mg/ kg/ day six hourly) and injection cloxacillin (50 mg/ kg/ day eight hourly) for 10 days, along with injection dexamethasone (0.3 mg/ kg/ day 12 hourly) for five days and tapered over next five days. Topical steroid (Fluticasone propionate) and tobramycin eye drops for skin and eye lesions were used respectively along with triamcinolone acetonide mouth gel for oral lesions. She was put on high protein diet and treated under strict aseptic precautions.

First two days, the patient remained toxic but hemodynamically stable. New lesions like bullae around chest, flexor aspect of arm and legs started with increasing diameter. Later due to coalescing of bullae, desquamation and crusting occurred. She showed regression of skin rashes after eight days along with resolution of eye, mouth and genital lesions and discharged after 10 days of treatment (Figure 3). On follow up after one week, she had total disappearance of skin rashes, eye, mouth and genital lesions with few hypopigmented skin rash sequel.

Discussion

SJS was first described in 1922 as an acute mucocutaneous syndrome in two young boys with prolonged course and potentially lethal outcome.⁶ In 1956, Alan Lyell described four patients with an eruption resembling scalding of the skin which is called TEN.² SJS and TEN are considered to be two ends of spectrum of severe epidermolytic adverse cutaneous drug reactions differing only by

their extent of skin detachment.⁷ The pathogenesis of SJS and TEN is not fully understood but is believed to be immune mediated, as re-challenging in an individual with the same drug can result in rapid recurrences of SJS and TEN.⁸ CD8+T cells as well as the cytolytic molecules FasL and granulysin are key players in the pathogenesis by triggering keratinocyte apoptosis.⁷

In our patient, there was typical history of only ingestion of acetaminophen and no other drug along with typical pattern of rash and histology picture, she was confirmed with SJS-TEN overlap syndrome as the severity and extent of skin lesions was higher than that found in SJS alone but lesser than TEN. There were very few differential diagnoses like DRESS (Drug reaction with eosinophilia and systemic symptoms) syndrome, erythema multiforme etc which were ruled out. We did not perform re-challenge test with acetaminophen administration to authenticate the diagnosis of SJS / TEN overlap syndrome as we felt it was not justifiable and ethical. Patient was managed with antibiotics, corticosteroid and supportive local skin, eye and mouth care successfully without any complications. Similar to our case report, Biswal et al also reported acetaminophen induced SJS-TEN overlap syndrome in 11 year old girl.⁹

Figures

Figure 1. Bilateral eyelid and lip oedema with early bullous lesions on admission



Figure 2. Extensive maculopapular lesions with few ruptured bullous lesions on abdomen and chest.



Figure 3. Post treatment healing of lesions on face, trunk and limbs with crusting on lips.



7. Harr T, French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome: A review. *Orphanet J Rare Dis.* 2010;5(1):1-1. DOI:10.1186/1750-1172-5-39
8. Halevi A, Ben-Amitai D, Garty BZ. Toxic epidermal necrolysis associated with acetaminophen ingestion. *Ann Pharmacother.* 2000;34(1):32-4. DOI:10.1345/aph.19064
9. Biswal S, Sahoo SS. Paracetamol induces Stevens-Johnson syndrome-toxic epidermal necrolysis overlap syndrome. *Int J Dermatol.* 2014;53(8):1042-4. DOI:10.1111/ijd.12355

Conclusions

The paediatrician should be aware and alert as severe life-threatening hypersensitivity skin reactions like SJS-TEN can happen with a simple drug like acetaminophen which is supposed to be the safest drug in children.

References

1. Chan HL, Stern RS, Arndt KA. The incidence of erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. *Arch Dermatol.* 1990;126(1):43-7. DOI:10.1001/archderm.1990.01670250049006
2. Lyell A. Toxic epidermal necrolysis: an eruption resembling scalding of the skin. *Br J Dermatol.* 1956;68(10):355-61. DOI:10.1111/j.1365-2133.1956.tb12762.x
3. 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(1):92-6. DOI:10.1001/archderm.1993.01680220104023
4. French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome: Our current understanding. *Allergol Int.* 2006;55:9-16. DOI:10.2332/allergolint.55.9
5. Joyce JE. Stevens-Johnson Syndrome. In Kliegman RM, eds. *Nelson Textbook of Pediatrics.* 21st edition. 2020;2(673.2):3482-83
6. Stevens AM, Johnson FC. A new eruptive fever associated with stomatitis and ophthalmia: report of two cases in children. *Am J Dis Child.* 1922;24:526-33. DOI:10.1001/archpedi.1922.04120120077005