IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
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Human Journals
Case Report
December 2023 Vol.:29, Issue:1

Carbamazepine Induced Steven Johnson Syndrome - Toxic Epidermal Necrolysis - A Case Report

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Submitted: 25 November 2023
Accepted: 30 November 2023
Published: 30 December 2023

HUMAN JOURNALS
ijppr.humanjournals.com

Keywords: Steven Johnson Syndrome, Toxic epidermal necrolysis, Carbamazepine, papules, Bullae, SCORE-TEN assessment

ABSTRACT

Stevens-Johnson syndrome (SJS) is a rare, lethal serious disorder of the skin and mucous membranes of the eyes, mouth, and genitals. It's usually a reaction to medication that starts with flu-like symptoms, followed by a painful rash that spreads and blisters. Then the top layer of affected skin dies and starts to detach. Stevens-Johnson syndrome is a medical emergency that usually requires hospitalization. SJS is usually associated with some types of anticonvulsants, including carbamazepine, lamotarigine, phenobarbital, phenytoin and valproic acid, NSAIDS (ibuprofen), antibiotics (sulphonamides, penicillins). A 60 year old female was admitted to the Dermatology department with chief complaints of rashes all over the body and oral ulcers since 2 days. The patient suffered from fever and body pain along with vomits since 3 days. The patient was apparently asymptomatic 3 days back, when she developed the above symptoms for which she consulted a regional hospital where she was prescribed tab. tegritol 200 mg od. Patient had been taking Tab. Tegritol (carbamazepine) 200 mg OD, since a month and 3 days before she developed oral ulcers which were insidious in onset and gradually progressed leading to redness in the eyes along with pus discharge and later progressing over the trunk and extremities. She had a history of itching prior the onset of lesions. No history of diarrhea, photosensitivity, any irritant topical applications, insect bite, or aggravating factors. The patient was assessed with the SCORETEN SCALE and 4 parameters were present with a predicted mortality rate 62.2%.

INTRODUCTION:

Stevens-Johnson syndrome (SJS) is an erratic, lethal serious disorder of the skin and mucous membranes of eyes, mouth, genitals. (1-3). It's generally a reaction to medication that starts with flu-like symptoms, tailed by a painful rash that spreads and blisters. Then the top layer of affected skin dies and starts to detach. Stevens-Johnson syndrome is a medical emergency that usually necessitates hospitalization (4-5). SJS is usually associated with some types of anticonvulsants, including carbamazepine, lamotrigine, phenobarbital, phenytoin and valproic acid, NSAIDs (ibuprofen), antibiotics (sulphonamides, penicillin) (5-6). Treatment emphasizes on eliminating the cause, caring for wounds, controlling pain and diminishing complications as skin regrows. It can take weeks to months to recover. A further severe form of the condition is called toxic epidermal necrolysis (TEN). They are only differentiated on the body surface area by epidermal detachment. SJS and TEN differ as, Epidermal detachment of $< 10\%$, 10–30% and $> 30\%$ are designated as SJS, SJS/TEN and TEN, respectively. The mortality rate ranges from 1 to 5% for SJS, and 25 to 35% for TEN (6-7).

CASE REPORT:

A 60 year old female was admitted to the Dermatology department with chief complaints of rashes all over the body and oral ulcers since 2 days. The patient suffered from fever and body pain along with vomits for 3 days. The patient was asymptomatic 3 days back, when she developed the above symptoms for which she consulted a regional hospital where she was prescribed Tab. Neuroprime plus OD, Tab. Vomikind MD4 OD, Tab. Propranolol 10 mg OD, Tab. Rabelace DSR OD, Tab. Pandoc OD, Tab. Glyciphage SR 500 mg OD, Tab. Telmisartan AM OD, Tab. Tegretol 200 mg OD.

The patient had been taking Tab. Tegretol (carbamazepine) 200 mg OD, since a month and 3 days before she developed oral ulcers which were insidious in onset and gradually progressed leading to redness in the eyes along with pus discharge and later progressing over the trunk and extremities. She had a history of itching prior the onset of lesions. No history of diarrhea, photosensitivity, any irritant topical applications, insect bite, aggravating factors.

The patient had no family history of SJS.

Personal History: known case of DM and HTN and was on medications Tab. Glyciphage SR 500mg BD and Tab. Telmisartan AM OD respectively. Not a known case of bronchial

asthma, TB. No addictions. There was no documentation of any drug allergies. She had a normal appetite. The bowel and bladder were irregular for 10 days.

General examination: Patient was C/C/C, well-built and nourished. No PICKLE.

Cutaneous examination: Multiple erythematous papules coalescing to form erosions predominantly seen over the anterior and posterior trunk. Multiple flaccid bullae are seen on the posterior trunk.

Oral cavity: Multiple oral erosions were seen on the hard palate and B/L buccal mucosa and lips.

Nasal cavity: Not involved.

Eyes: B/L conjunctivitis seen with pus discharge

Genitals: Multiple erythematous papules coalescing to form erosions seen in the inguinal region.

Scalp: Not involved

The reports showed elevated ESR 80mm 1st hour and 110mm 2nd hour (reference range: <20mm), and also elevated C- reactive protein 12 mg/lt (reference range: 6mg/lt).

Diagnosis: Based on the clinical findings, past medical history and physical examination our diagnosis was Carbamazepine induced Stevens-Johnson Syndrome. Oteven Johnson Syndrome- Toxic Epidermal Necrolysis.

The reports showed elevated ESR of 80mm 1st hour and 110mm 2nd hour (reference range: <20mm), and also elevated C- reactive protein 12 mg/lt (reference range: 6mg/lt).

The patient was prescribed:

Drug	Dose	ROA	Frequency	Day 1	Day 2	Day 3	Day 4	Day 5
IVF NS	75 ml/hr	IV		+	+	+	+	-
Inj. Pan	40 mg	IV	OD	+	+	+	+	+
Inj. Avil	2cc/5ml	IV	SOS	+	+	+	+	+
Glymed lotion	Required quantity	Cutaneous	BD	+	-	-	-	-
Fucid C cream	Required quantity	Cutaneous	BD	+	+	+	+	+
Listerine mouthwash	1 cap	Oral wash	TID	+	+	+	+	+
Tab. Psorid	50 mg	PO	BD	-	+	+	+	-
KMnO4 Compressions			TID	-	+	+	+	+
Hexigel oral gel			BD After food	-	+	+	+	+
Mucopain gel			TID 5 minutes before food	-	+	+	+	+
Inj. Linezolid	600 mg	IV	BD	-	+	-	+	+
Inj. Meropenem	1 gm	IV	TID	-	-	+	+	+
Inj. Heparin	2500	IV	TID	-	-	+	+	+
Tab. Lanol ER		PO	TID	-	-	+	+	+
Tab. Forcan	150 mg	PO	BD	-	-	-	+	+
Candid mouth paint			BD	-	-	-	-	+
Cap. Psorid	100mg	PO	BD	-	-	-	-	+
Inj. Lantus	10 units	SC	BD	-	-	+	-	+
Inj. Dalacin	600 mg	IV	TID	-	-	-	-	+

The patient's attendees were counselled and a high-risk consent was made to sign by them. On the next day, on observation, the epidermal detachment had increased than before.

Score TEN assessments showed:

1) Age > 40 years +
2) Epidermal detachment > 10% BSA +
3) Serum Urea > 10mmol/L +
4) Serum glucose > 14mmol/L +

4 parameters present with a predicted mortality rate 62.2%

The next day, the patient complained that itching was increased and blood glucose levels were 315 mg/dl for which Inj. HAI was advised according to GRBS. On examination multiple bullae of variable sizes were seen over posterior trunk. Multiple erythematous to violaceous papules and erosions seen all over the body. Acral cyanosis seen over distal extremities. B/L eye congestion + with pus discharge. Vitals were stable.

Oral Cavity: Multiple oral erosions seen over the hard palate, tongue and B/L buccal mucosa with mild slough and decreased opening of oral cavity.

Ophthalmologist review: On Examination

Feature	Right eye	Left eye
VA	CF	CF
EOM	Full and free	Full and free
Lids	Edematous, meta hyperplastic eyelashes +	Edematous, meta hyperplastic eyelashes +
Conjunctiva	Congestion ++ Purulent discharge +	Congestion ++ Purulent discharge +
Cornea	Clear	Clear
Pupils	NSRL	NSRL
Iris	Normal	Normal
Lens	Cataract +	Cataract +

Advice: Pull the lower eyelids 10-15 times a day to prevent symblepharon formation and clean the discharge using NS/ Distilled water TID. Review after 5 days.

Medications:

1) FML-T QID for 1 week
2) Optidew eye drops every hour
3) Lacrigel eye ointment BD

Dietician's review:

A strict diabetic soft diet was recommended and was advised to have small and fragmented meals at regular intervals. Ensure DM care powder 3 scoops in 100 ml water was advised.

The following day, the patient complained about an increase in lesions, peeling of skin and generalized body pain. The vitals were stable. On examination, multiple papules with erosions were seen predominantly on the trunk, upper extremities and face. Multiple bullae of variable size seen over trunk and posterior back.

Psychiatric review:

On examination, the patient had no seizures, mood was low. The patient had passive death wish and crying spells for 4 days. The patient did not show signs of feeling anxious, fearful or constant worrying thoughts. Patient suffered from one episode of panic attack on the last day. The symptoms were suggestive of psychosis. The psychiatrist did not recommend any psychotropic medications but advised relaxation techniques.

Examination on the next day showed that the patient was conscious and coherent. The erosions were healing, pus appeared in a few intertriginous areas and the peeling had slowed down.

Pulmonologist's review:

On observation, the patient has SOB, cough and fever. The following medications were prescribed nasal spray avamys 2/2., Tab. Montek- FK at night.

ENT review:

On observation, the patient has a cold, blocked nose and pain. There was presence of dried crusts in the nose. The doctor prescribed Nasoclear nasal drops 2 drops TID, Tab. Felver plus BD.

On the fourth day from admission, the patient died, due to the uncontrolled spread of blisters, and increased skin detachment. The SCORETEN assessment had prior shown to have 62.2% mortality rate.

DISCUSSION:

Stevens-Johnson syndrome and Toxic epidermal necrolysis (TEN) is a rare, life-threatening drug induced skin disease with a mortality rate of about 30%. The clinical hallmark of TEN is a marked skin detachment instigated by widespread keratinocyte cell death accompanied with mucosal involvement. The meticulous pathogenic mechanism of TEN is still uncertain. Recent advances in this field have directed to the identification of several factors like the HLA-B*1502, that might contribute to the induction of excessive apoptosis of keratinocytes

(3,7-8). HLA-B*1502 screening is highly recommended in patients requiring carbamazepine therapy (9,10). In this case, we present a case of Prescription error and ADR which was not properly identified. The treatment involved immediate DE challenging of the drug. In this case report, of Carbamazepine induced SJS-TEN. Once the patient complains about side effects from carbamazepine, they should be assessed with standard scales like Naranjo causality assessment. Our patient was assessed using the SCORETEN scale which showed 4 points which meant the patient had 63.3% mortality rate, therefore the Carbamazepine-induced SJS-TEN was a severe ADR.

CONCLUSION:

The patients should be properly monitored while taking medications like anticonvulsants, antibiotics, NSAID's. If any side effects are observed, immediate withdrawal should be made and the drug in future. Early detection and proper management can improve the conditions. The prescribers and Clinical Pharmacists should be careful while prescribing such drugs. The clinical pharmacists should provide proper counselling to the patients and explain about the medications, disease, and the drug-related side effects and they must be educated about reporting any adverse reaction immediately and not ignore them. If any ADR is reported, the patients must be given appropriate instructions to avoid those medications in the future.

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