A Case Report on Steven Johnson Syndrome

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Abstract

Steven-Johnson syndrome is a type IV hypersensitivity reaction which causes toxic epidermal necrolysis throughout the human body**,** it typically involves burning rash that develop into papules and into ecthyma, lesions can be found in both limbs and in face which is bullous in nature. intake of certain types of drugs which includes anti-biotics, epilepsy medicines and Nsaids are the class of drug which trigger SJS/TEN. It has high morbidity and mortality rate than compared to any other dermatological conditions and it is a rare condition. **case presentation:** we report an eventful case of a 16-year-old girl who developed SJS induced by drug Carbamazepine. The patient was prescribed with Tab. Carbamazepine for the treatment of depression and low mood later the following week upon the intake of medication patient started to develop high-grade fever along with severe rash and lesion has been found all over the body. Skin-punch biopsy studies revealed patient had SJS and symptomatic treatment has been started for the patient. **Clinical discussion:** carbamazepine and other ant-psychotic drugs are well known to trigger SJS/TEN. Carbamazepine plasma concentration values differ from person to person and have a latency duration up to 15 days which could trigger SJS. A special approach should be made for the management of drug-induced SJS and early finding of the disease symptoms are the key for the management of the symptoms. **Conclusion:** Fever and other FLU like symptoms should be noted has they are signs of SJS after the intake of carbamazepine. Treatment should be approached by prompt treatment. Proper counselling to patient should prevent the further development of this condition and approach of carbamazepine in the treatment of depression should be revised.

Key words: Steven Johnson syndrome, toxic epidermal necrolysis, Carbamazepine, Bipolar disorder, human leukocyte antigen (HLA).

Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are twoexamples of very uncommon but potentially fatal adverse skin responses. Certain drugs are often the cause of both of these conditions. Antiepileptic medicines (also known as AEDs), nonsteroidal anti-inflammatory drugs (often known as NSAIDs), and some antibiotics are examples of medications that have been shown to cause these kinds of responsesClick or tap here to enter text..Both in the United States and elsewhere in the globe, carbamazepine (also known as CBZ) is one of the more established antiepileptic medicines (AEDs). It is one of the most widely utilised antiepileptic drugs (AEDs) since both neurologists and non-neurologists are extremely familiar with its range of efficacy as well as its positive and negative aspects[(4)].Carbamazepine, lamotrigine, and phenobarbital are examples of psychotropic drugs that have a high potential for epidermal necrolysis[(5)].The exact mechanism by which these illnesses develop has not been determined as of yet. It is thought that dysregulation of the immunologic response is one of the most significant causes of the condition. It is now believed that the primary mechanism is the apoptosis of keratinocytes, which results in the cells dying[(6)]. Detachment of the epidermis that is less than ten percent, between ten and thirty percent, or more than thirty percent is referred to as SJS, SJS/TEN, or TEN,

respectively.SJS has a death rate ranging from 1 to 5%, whereas TEN has a mortality rate between 25 and 35%[7].Fever, sore throat, and exhaustion are the classic early symptoms of SJS, which are often misunderstood and hence treated with antibiotics. Fever, sore throat, cough, and burning eyes for 1–4 days are common symptoms of SJS, SJS/TEN, and TEN[8].Mucous membrane lesions and ulcers form, most often in the mouth and lips but sometimes in the vaginal and anal areas.Those located in the mouth are notoriously uncomfortable and might hinder a person's ability to take in liquids. One of the most prevalent triggers of adverse drug reactions in patients is the medication carbamazepine, which is used for a variety of medical conditions including epilepsy, bipolar disorder, trigeminal neuralgia, and chronic pain.[9]The reported frequency of a significant hypersensitivity response to carbamazepine is between one in one thousand and one in one ten thousand new exposures to the medicine.[10]

Case report

Patient was admitted to SRM hospital on October 18, 2022 at 9 in the morning with a complaint of fluid-filled lesions, purpuric rashes, blisters, vesicles, and ulcers all over the body, including the conjunctiva, oral mucosa, and genitalia, for four days. Patient was also experiencing pain. Patient had a high-grade viral fever 5 days prior to the beginning of rashes, for which she sought treatment at a private hospital in the form of acyclovir. The patient does not have any follow-up cases of seizures disorder, epilepsy, trigeminal neuralgia, or acute manic and mixed episodes associated with bipolar illness.

Patient had history of depression and low mood because of Higher studies and exams for which patient sought help in the hospital and got prescribed Tab. Carbamazepine to treat the condition. On the same following week patient developed skin rashes all over the body and had high grade fever for which patient got Tab. Acyclovir has treatment. Patient stopped Tab. Carbamazepine after intake for 4 days later which she developed Steven-Johnson syndrome.

Physical findings on admission

Patient was febrile (101.9°F), no pallor/icterus/cyanosis/clubbing/pedal edema/generalised lymphadenopathy.

Systemic examination

CVS- S1S2 + RS-NVBS

CNS-NON-FOCAL NEUROLOGICAL DEFICIT PA- SOFT, NON-TENDER

Laboratory investigation;

Haematology	**Values**
Haemoglobin (Hb)	12.2 g/dl
WBC	15,500 cells/cu.mm
Platelet	2,00,000
S. Na+	131 mmol/L
S. Cl-	105 mmol/L

1)

Differential leukocyte count (DLC) showed eosinophilia with N52.4/L41.7/M4.8/E0.8/B0.3

2)

Liver function test	**Values**
Bilirubin total	0.28 mg/dl
Direct bilirubin	0.10 mg/dl
Alkaline phosphate	139 mg/dl
Total protein	6.3 g/dl
Albumin	3.7 g/dl

3)

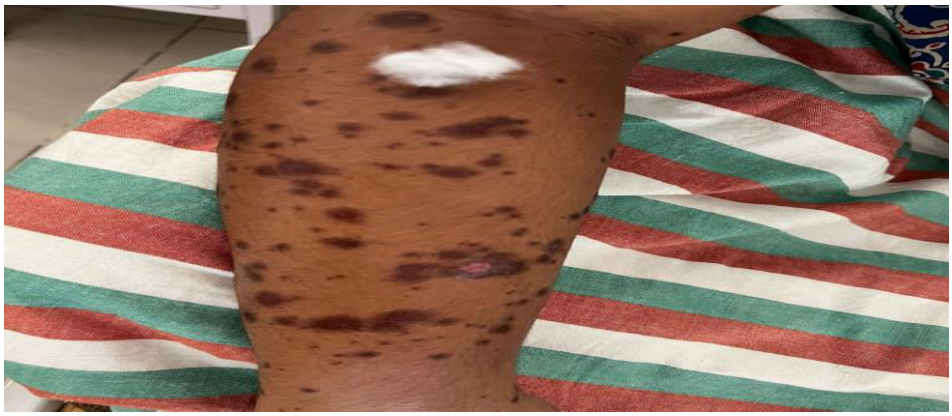
Lipid profile test	Values
Cholesterol	139 mg/dl
LDL	105 mg/dl
VLDL	20 mg/dl
HDL	73 mg/dl
TGL	102 mg/dl

4)

Renal function test	Value
UREA	12 mg/dl
BUN	06 mg/dl
CREATININE	0.4 mg/dl
URIC ACID	2.2 mg/dl

Dermatological examination

Multiple well defined Violaceous to hyper pigmented plaques with presence of ecthyma along with mild crusting has been noted on face, chest, back, abdomen, upper and lower limbs. Multiple vesicles few embedded over the plaque has been found over the face, trunk, limbs. Crusted plaques with honey colored have been observed over nose. Whitish plaques have been observed in the oral cavity seen in tongue, buccal mucosa, and lips. pus discharge from lips has been observed and patient have complaints of opening mouth. Erythematous plaques and vesicles have been observed in palms, soles, and scalp. **Fig:1-2**



Fig(1):Carbamazepine induced hyper pigmented plaques present in fore arm of the 16yr old girl.

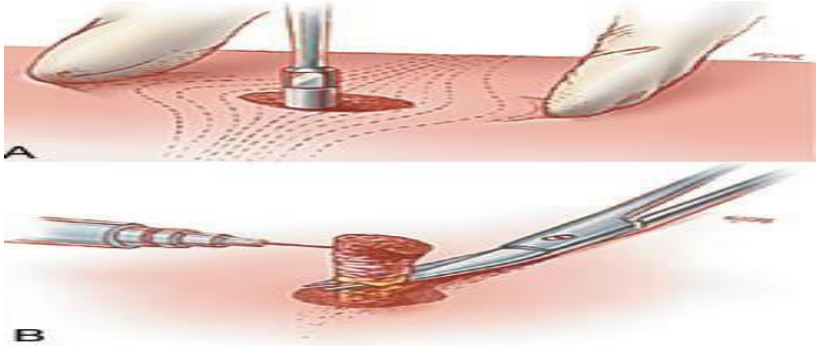


Fig (2): punch biopsy procedure

Treatment given

The diagnosis of SJS has been done by 4mm punch biopsy studies where samples are collected from the right fore arm. The biopsy report confirmed SJS and patient given intravenous fluid of dextrose and sodium chloride, injection dexamethasone 4 mg has been administered intramuscularly has STAT for the first week, INJ. pantoprazole 40 mg intravenous before meals once a day, TAB. Azithromycin 500 mg od and supplements have been administered. Later, patient shifted from INJ. dexamethasone to TAB. Prednisolone 20 mg which was later tapered on and stopped. Patient showed symptomatically better hence been discharged on advice after 9 days.

Discussion

One of the most well-known psychotropic drugs that may cause SJS is carbamazepine.Carbamazepine plasma concentrations are not linearly proportional to dosage. However, there is a lot of fluctuation in the claimed therapeutic dosage range of 6-12 g/ml.Carbamazepine-induced SJS had a median latency duration (interquartile range) of 15 days (12-20).Using the Algorithm of Drug causality for Epidermal Necrolysis (ALDEN) scoring system for SJS/ TEN, carbamazepine scored +6.There is substantial evidence linking carbamazepine to SJS.There are several potential causes of SJS, but the most prevalent are viral infections (the herpes simplex virus being the most common infectious agent) and neoplasia (carcinomas and lymphomas). However, medicine usage is by far the most prevalent culprit. Antibiotics, anticonvulsants, and non-steroidal anti-inflammatory medicines like allopurinol also seem to be at fault.It has been widely believed that carbamazepine-induced SJS is an isolated, dose-independent, and unexpected adverse event that occurs only in rare cases[11]Devi et al. performed a 7-year research and discovered that anticonvulsants were the most common cause of SJS, particularly in the first 8 weeks of therapy, and the major medication responsible (more than 80%) was carbamazepine[12].The existing evidence suggests that the occurrence of SJS/TEN due to carbamazepine is a delayed hypersensitivity immune response that is predictable and specific. This reaction involves certain human leukocyte antigen (HLA) alleles that are specific to carbamazepine and other drugs in particular populations[13]The precise mechanism underlying hypersensitivity reactions remains unclear.Exposure to carbamazepine leads to proliferation of lymphocyte and T-cell clones.Late ocular complications are reported in 50% of patients, with dry eyes, trichiasis, symblepharon, distichiasis, visual loss, entropion, ankyloblepharon, lagophthalmos, and corneal ulceration being the most commonly occurring complications in descending order of frequency.The majority of diagnoses are made clinically; however, skin biopsies are useful for confirmation[14]. Recognising the rash early and discontinuing the medicine immediately are the cornerstones of therapy, coupled with symptomatic relief.

Conclusion

It's important to pay attention to any signs of fever after taking carbamazepine, since these might be precursors of SJS/TEN. Secondary infections and problems may be avoided by an interdisciplinary approach and prompt treatment. Careful titration of the medicine and early diagnosis of adverse effects can aid in preventing life-threatening disorders like SJS and other side effects associated with carbamazepine, which is increasingly utilised for numerous reasons.Therefore, it is necessary to provide medications with consciousness while also being aware of the conditions of the patients, whether the patient is a Geriatric or paediatric population.

References

1. Roujeau, JC., Kelly, JP., Naldi, L., Rzany, B., Stern, RS., Anderson, T., (1995). Medication Use and the Risk of Stevens–Johnson Syndrome or Toxic Epidermal Necrolysis. New England Journal of Medicine.14(24):1600–8.
2. Levi, N., Bastuji-Garin, S., Mockenhaupt, M., Roujeau, JC., Flahault, A., Kelly, JP., (2009). Medications as Risk Factors of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Children: A Pooled Analysis. Paediatrics. 11(2) :297–304.
3. Raucci, U., Rossi, R., Da Cas, R., Rafaniello, C., Mores, N., Bersani,G., (2013).Stevens-Johnson Syndrome Associated with Drugs and Vaccines in Children: A Case-Control Study. PLoS One. 8(7):682-685.
4. Gierbolini, J., Giarratano, M., Benbadis, SR.,(2016). Carbamazepine-related antiepileptic drugs for the treatment of epilepsy - a comparative review. Expert Opin Pharmacother. 2(7):885–888.
5. Mitkov, M V., Trowbridge, RM., Lockshin, BN., Caplan, JP., (2014). Dermatologic Side Effects of Psychotropic Medications. Psychosomatics.55(1):1–20.
6. Darlenski, R., Kazandjieva., J, Tsankov, N.,(2015). Systemic drug reactions with skin involvement: Stevens-Johnson syndrome, toxic epidermal necrolysis, and DRESS. Clin Dermatol. 33(5):538–541.
8. Maverakis, E., Wang, EA., Shinkai, K., Mahasirimongkol, S., Margolis, DJ., Avigan, M., (2017). Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis Standard Reporting and Evaluation Guidelines. JAMA Dermatol.153(6):587-591.
9. Leeder, JS.,(1998) Mechanisms of Idiosyncratic Hypersensitivity Reactions to Antiepileptic Drugs. Epilepsia.39(7):8–16.
10. Tennis, P., Stern, RS.,(1997). Risk of serious cutaneous disorders after initiation of use of phenytoin, carbamazepine, or sodium valproate: A record linkage study. Neurology.1(2):542–546.
11. Johnston, A., Uetrecht, J., (2015). Current understanding of the mechanisms of idiosyncratic drug-induced agranulocytosis. Expert Opin Drug Metab Toxicol. 11(2):243–257.
12. Devi, K., George, S., Criton, S., Suja, V., Sridevi, P., (2005). Carbamazepine - The commonest cause of toxic epidermal necrolysis and Stevens-Johnson syndrome: A study of 7 years. Indian J Dermatol Venereol Leprol.71(5):325-331.
13. Dodiuk-Gad RP, Chung WH, Valeyrie-Allanore L, Shear NH. (2015). Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis: An Update. Am J Clin Dermatol.; 19;16(6):475–93.
14. Yip, LW., Thong, BY., Lim, J., Tan, AW., Wong, HB., Handa, S., (2007). Ocular manifestations and complications of Stevens Johnson syndrome and toxic epidermal necrolysis: an Asian series. Allergy.62(5):527–31.