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Case Study

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CARBAMAZEPINE INDUCED STEVENS-JOHNSON SYNDROME-TOXIC EPIDERMAL NECROLYSIS OVERLAP SYNDROME

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ABSTRACT

Stevens Johnson syndrome/Toxic epidermal necrolysis-overlap syndrome refers to cases in which 10% to 30% of the body surface area is detached. A persistent fever and flu-like symptoms may occur prior to the appearance of erythematous macules (red spots) covering a large area of the body, as well as painful blistering of the skin and mucous membranes. Frequently, the eyes are involved. Carbamazepine is one of the most common culprit among the drugs which causes Stevens Johnson syndrome/Toxic epidermal necrolysis. The aim of reporting the case report is to create awareness among patients and healthcare professionals so that they will be more vigilant towards the unwanted drug effects. This is a case of drug induced Stevens Johnson syndrome/Toxic epidermal necrolysis overlap syndrome in a patient who was prescribed with carbamazepine for the treatment of neuropathic pain, reported at the hospital with severe mucocutaneous lesions. This case necessitates the importance of awareness among patient and healthcare professionals regarding the untoward effects of drugs and timely detection as well as management of the condition.

KEY-WORDS: Steven-Johnson syndrome/Toxic epidermal necrolysis, carbamazepine, adverse drug reaction,

INTRODUCTION

Stevens- Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are extreme adverse reactions characterized by mucosal and cutaneous disorders and it is characterized by fever and systemic complications.[1] SJS is rare, often a life threatening clinical condition due to an immune complex mediated reaction that involve the skin and the mucous membrane and manifested as severe cutaneous adverse reactions (SCAR).[2] It was first identified and reported by A.M. Stevens and F.C. Johnson in 1922 and thereby named as SJS.[3] Incidence of this condition is reported in 1–6 cases per million population every year throughout the world.[4] Lyell coined the term toxic epidermal necrolysis in 1956 to identify patients who have experienced significant epidermal loss due to necrosis, resulting in a blistered skin surface. SJS can result in serious epidermal necrolysis in extreme cases.[1] Anticonvulsants, Antibiotics (particularly sulphonamides), Allopurinol, and nonsteroidal Anti-inflammatory drugs are all common SJS precipitants. Drugs are accountable for 75% of cases in adults. Antibiotics and anticonvulsants pose the highest risk among drugs.[2,3] One of the major causal medications for SJS and TEN is carbamazepine (CBZ), a first line anti-epileptic medication (AED).[1] In addition to that, bacterial and viral infections are reported rarely as the causative agents of SJS/TEN. Besides, genetic factors also play a major role, people of Chinese and south east Asian origin with HLA B*1502 were found to develop this disorder and it occurs slightly more in women than in men.[5]

Patients can present with Stevens-Johnson syndrome symptoms that progress to toxic epidermal necrolysis in a matter of days. Fever and influenza-like symptoms that are not caused by an infectious disease often appear one to three days before the mucocutaneous lesions of these two conditions. Initially, these eruptions are symmetrically distributed on the face and upper trunk.[1]

These are the regions that are normally the most severely impacted. The rash spreads quickly, reaching its peak in four days or less in some cases. In most cases, the first skin lesions are poorly formed macules with darker purpuric centres that coalesce. Cases with a small area of epidermal detachment, less than 10% are referred to as SJS, while those with a large area of detachment, more than 30% are referred to as TEN. When 10-30% of the

epidermis is detached, the two syndromes are known to overlap.[1]

Dysphagia due to the lesions on the periorbital area and dysuria due to the same in genitourinary tract are the common difficulties experienced by the patients. Conjunctivitis is also a commonly seen symptom.[5]

CASE HISTORY

A 67-year-old woman presented with generalized dermatitis was admitted in the hospital due to erythematous eruptions and difficulty in swallowing. She had a history of severe neck pain and Carbamazepine, Amitriptyline, and a combination of paracetamol and aceclofenac was prescribed from another hospital. On the third day after initiating the above medications, patient developed a mild fever and generalized weakness. Following days, the severity increased to sore throat, oral ulcers and dysphagia and blisters on the trunk and limbs. On the ninth day of continuing to take the above medications, erythematous maculopapular rashes were formed on the body and the patient visited the emergency department of our hospital. Physical examination during admission, revealed generalized dermatitis with blisters, large erosions of the palms and soles, painful crusted erosions on lips and the patient was diagnosed with SJS/TEN overlap syndrome possibly due to carbamazepine. Her medical history also revealed the presence of diabetes mellitus and she was on glimepiride and metformin. Upon admission, carbamazepine was withdrawn and the patient was administered with IV antibiotics, corticosteroids, proton pump inhibitors, antihistamines and other supportive measures. After three weeks of treatment, the skin lesions had disappeared, and the patient was discharged in good clinical condition.

Owing to a lack of resources in this case's rural environment, a skin biopsy and histopathology of the affected area were not performed.Based on the clinical presentation, the patient was diagnosed as having carbamazepine-induced SJS/TEN overlap syndrome that covered the majority of the body surface area. The SCORE of Toxic Epidermal Necrosis (SCORTEN) criteria were used to determine prognosis, and a score of 2 was assigned. About 28.5% of the total body surface area is affected by detached/detachable skin lesions. The Naranjo causality assessment algorithm rated the reaction as "probable," awarding it a score of 5 and it was also rated as “probable” by the World Health Organization–Uppsala Monitoring Centre (WHO–UMC) causality assessment scale.

DISCUSSION

Carbamazepine is used for trigeminal neuralgia and also has anti-epileptic and psychotropic properties. Stevens-Johnson syndrome/Toxic epidermal necrolysis is one of the serious adverse effects of carbamazepine. Carbamazepine do not always cause such reactions; however, it is vital to monitor the patient When the drug is administered.[6]

The various factors responsible for the development of SJS/TEN include drugs, viral infections (herpes simplex virus), genetic factors, neoplasia (carcinomas and lymphomas) etc. However, the most common cause is the use of medications and carbamazepine has a strong association with its incidence.[6]

Devi et al reported in their study that anticonvulsants mainly carbamazepine (more than 80%) was the major cause of SJS especially in the first eight weeks of treatment.[6] Another study reported its incidence with analgesics.[7] These studies suggested that the increased number of prescriptions of carbamazepine and analgesics could be the main reason for the increased frequency of SJS due to these drugs.[6,7] Initially the patient experiences fever, myalgia, and general weakness for 1 to 3 days followed by the development of cutaneous lesions which are equally scattered on the upper part of the body especially on face and trunk. These poorly defined macules with darker purpuric centers coalesce and within 3-4 days the rash extends to other areas also. The management of SJS/TEN includes early detection of the adverse reaction and withdrawal of the offending drug; otherwise it may lead to serious deterioration of the patient condition.[8]

In this case also carbamazepine was withdrawn and the patient was supported with IV antibiotics, corticosteroids, antihistamines etc. After 3 weeks of hospital admission the skin lesions were subsided and the patient got discharged.

CONCLUSION

Finally, we'd like to point out that patients who start on any high-risk drug regimen run the risk of developing SJS/TEN overlap syndrome. Patients should be given medications with adequate prescription counselling informing them about possible side effects so that if they experience any unexpected side effects, they can seek medical help right away.As a result, the severity of adverse reaction may be mitigated. The presence of drug allergy should be appropriately investigated. In the event that a patient is discovered to be allergic to a specific drug class, it is possible to consider pharmacogenetic testing.

The initial presenting symptom is normally oral erythema and ulcerations, which the patient may dismiss. There have been several reported cases in the literature where the appearance of oral lesions led to an early diagnosis of SJS.

In order for the patient to have oral feeds and maintain nutritional balance, symptomatic treatment of the oral lesions is required. Hypersensitivity reactions like rash, vesiculobullous lesions, and/or other clinical symptoms like fever, nausea, and abdominal pain necessitate

increased clinical vigilance Early detection allows the clinician to avoid secondary infection and its associated complications. The offending medication should be stopped and never used again.

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REFERENCES

1. Roujeau J, Stern R. Severe Adverse Cutaneous Reactions to Drugs. *New England Journal of Medicine*, 1994; 331(19): 1272-1285.
2. Ruminski MA, Wisneski SS, Dugan AE. Stevens-Johnson Syndrome: What a Pharmacist should know. *US Pharm*, 2013; 38(7): 69-79.
3. Stevens AM, Johnson F. A new eruptive fever associated with stomatitis and ophthalmia: report of two cases in children. *Am J Dis Child*, 1922; 24: 526.
4. Chan HL, Stern RS, Arndt KA, et al. The incidence of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis: a population based study with particular reference to reactions caused by drugs among outpatients. *Arch Dermatol*, 1990; 126(1): 43–47.
5. Wang XQ, Lang SY, Shi XB, Tian HJ, Wang RF, Yang F. Cross-reactivity of skin rashes with current anti-epileptic drugs in Chinese population. *Seizure*, 2010; 19(9): 562–566
6. Devi K, George S, Criton S, Suja V, Sridevi PK. Carbamazepine – The commonest cause of toxic epidermal necrolysis and Stevens-Johnson syndrome: A study of 7 years. *Indian J Dermatol Venereol Leprol*, 2005; 71(5): 325-8.
7. Pinninti R, Jami S, Ameen K. Aceclofenac induced Stevens-Johnson/toxic epidermal necrolysis overlap syndrome. *J Pharmacol Pharmacother*, 2013; 4(1): 69-71.
8. Bae HM, Park YJ, Kim YH, Moon DE. Stevens-johnson syndrome induced by carbamazepine treatment in a patient who previously had carbamazepine induced pruritus - a case report -. The Korean Journal of Pain, 2013 Jan; 26(1): 80-83.