



A CASE REPORT: CARBAMAZEPINE INDUCED STEVEN JOHNSON'S SYNDROME

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Article Received on 05/09/2015

Article Revised on 26/10/2015

Article Accepted on 15/11/2015

ABSTRACT

Adverse drug reactions (ADRs) are one of the leading causes of death among hospitalized patients and occur in 0.3 to 7 per cent of all hospital admissions. These may vary from mild rashes to severe reactions such as Stevens-Johnson syndrome (SJS). Antiepileptic drugs-induced SJS is a life-threatening severe cutaneous adverse reaction. We report here a case of carbamazepine induced SJS in a 18 year old male patient presenting in emergency ward of our college. The patient responded to the treatment and was prescribed Inj. Pheniramine Maleate and inj. Prednisolone 10 mg and remained symptom free since then.

KEYWORDS: Carbamazepine, Drug induced Stevens - Johnson syndrome, Anti- Epileptics, Drug Reaction.

INTRODUCTION

The World Health Organisation defines Adverse Drug Reactions (ADR) or adverse reaction "as a response to a drug, which is noxious and unintended, which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of a disease or for the modification of physiological functions." World statistics show that 5 - 10% of the hospital admissions are attributed to adverse drug reactions, and 0.3% of adverse reactions are fatal in nature.^[1]

Cutaneous drug reactions are the most common type of adverse drug reactions. These are due to drugs applied locally or taken systemically and often manifested as rashes. Often associated with a history of exposure to new drugs, such as sulfonamides, penicillin, seizure medications (eg, phenytoin, carbamazepine), quinolones, cephalosporins, allopurinol, corticosteroids, or NSAIDs.^{[2][4]}

Carbamazepine is a tricyclic compound effective in treatment of bipolar depression. It was initially marketed for the treatment of trigeminal neuralgia but has proved useful for epilepsy as well. Carbamazepine shows activity against maximal electroshock seizures.

Carbamazepine inhibits high-frequency repetitive firing in neurons in culture. It also acts presynaptically to decrease synaptic transmission.^[3]

Steven Johnson syndrome is a more severe form of erythema multiforme in which mucous membranes of the mouth, eyes and occasionally genitals may also be involved.

During ADR monitoring we reported a typical case of Steven Johnson syndrome following the subsequent administration of carbamazepine.

CASE REPORT

An 18year old male of weight 50 kgs, was admitted to the emergency department of Era's lucknow medical college and hospital on the 8th of august 2015 with chief complaints of high grade fever, headache and rashes over the trunk, upper and lower limb followed by difficulty in swallowing since past 6 days.

The patient was apparently asymptomatic 1 month back when he was diagnosed with mania and was prescribed oral carbamazepine 200mg twice a day.

After 21 days of oral administration of the drug he developed hyperpyrexia and rashes which were vague in presentation and distribution.

From the 24th day, he started developing rashes which appeared as red, raised lesions beginning from trunk and progressing towards neck and then involving both arms and flexor surface of forearms over a period of 3-4 days with progressing intensity and severity along with

genital, ocular, oral ulcerations and red eye, finally presented to the emergency of our institute in the above mentioned condition. The ulcers involved the eyelids also.

On physical examination, the patient was well oriented with time, place and person and had lesions as described earlier. Intraoral examination revealed ulcerations on the entire lips, mucosa, tongue and palate. The ulcerations were tender.

Ophthalmic examination showed conjunctivitis and sub conjunctival hemorrhages. On general examination, BP was 110/80 mm of Hg, Pulse- 94 beats/min, temperature 101degrees F, Respiratory rate- 16/min, chest auscultation and abdominal palpation did not reveal any significant finding. The following investigations were done Hb 12.2 gm/dl, TLC 4500/mm³, ESR 46 mm/1st hour, X-ray chest-normal, slide from skin scraping negative for gram negative organisms, bleeding time, clotting time and platelet count were normal.

The patient was immediately admitted with diagnosis of drug induced Steven Johnson's Syndrome and Tab. Carbamazepine was immediately stopped. Patient was started with Intravenous fluids (1.5 liters/day) to replace the lost fluids, Intravenous Cefotaxime (1 gram every 12 hourly) for infection prophylaxis, Inj. Pheniramine Maleate 25 mg and inj. Prednisolone 10 mg qid.

Oral ulcer was managed with the candid mouth paint. Ofloxacin eye drops 0.3% was advised for eye lesion and Lotion Calamine was applied gently over the skin following strict aseptic measures. Causality assessment using Naranjo's algorithm categorized the adverse drug reaction as probable (score=5) and by WHO scale was also classified to be probable.

Patient started showing improvement after 2 days of treatment, had normal body temperature with BP-130/80 mm of Hg, Pulse 80 beats/minute, Respiration at 16/minute, urinary output of 1.5-1.8 liters/day and with an overall improved general condition.

We reported the ADR in vigiflow for further assessment by National Coordinating Centre (NCC). Systemic steroid, Inj. Prednisolone 10 mg qid for 7 days, which was gradually tapered to 10 mg tid for 7 days, 10 mg bid for 5 days, then Tab Prednisolone 10 mg once daily for 5 days respectively. Inj. Cefotaxime was also stopped after 7 days. Patient recovered completely after 22 days.

DISCUSSION

Stevens-Johnson syndrome is an immune-complex-mediated hypersensitivity reaction that typically involves the skin and the mucous membranes.^{[5][6]}

It is a rare mucocutaneous blistering disorder of considerable severity. Reactions produced by systemic

administration of drugs are usually sudden in onset, generalised and bilaterally symmetrical.^[7]

Its more severe form is called toxic epidermal necrolysis (TEN). SJS has a polyetiologic pattern, drugs being the most common cause, for eg. Anticonvulsants, sulphonamides, aminopenicillins, NSAIDs, allopurinol, etc.^[8]

Other risk factors for SJS include: HIV, viral infections, genetic factors, vaccination, graft versus host disease, malignancy, and idiopathic. Patients are at a greater risk of this type of drug reaction during the first 4 weeks of therapy, particularly between 1 and 3 weeks.

The exact pathophysiology of the interactions between drugs, their metabolites, viruses, cytokines, lymphocytes, genetic predisposition, pharmacogenomics, and keratinocyte apoptosis has not been fully explained. It is characterised by the detachment of epidermis from the papillary dermis at the epidermal-dermal junction, manifesting as a papulomacular rash and bullae as a result of keratinocyte apoptosis. Keratinocyte apoptosis mediated by cytotoxic T-lymphocytes (CD8) in SJS and TEN is modulated by plasma TNF-alpha and interferon-gamma, which are increased in patients with SJS and TEN. The main pathway is thought to be granulysin-mediated, but the issue remains controversial and the potential involvement of one or a number of pathways has not been resolved. There may be multiple pathways which play an important role depending on the genetic disposition of the patient and/or the type of drug precipitating the immunological response.^[8]



Carbamazepine is a dibenzazepine derivative with antiepileptic and psychotropic properties. Carbamazepine is also used in the treatment of trigeminal neuralgia and has been tried with variable success in glossopharyngeal neuralgia and other severe pain syndromes associated with neurological disorders and also in the management of bipolar disorder unresponsive to lithium.^[9]

Systemic corticosteroids were applied (prednisone given orally) after clinical and histological diagnosis were confirmed in this case.^[10] It has been reported that higher daily doses of some drugs are associated with an increased risk of SJS compared to lower doses, as is the case for allopurinol. However there is as yet no evidence about the relationship between carbamazepine dosage and SJS.

CONCLUSION

This was a case of Carbamazepine induced Steven Johnson's syndrome. It is important to note that carbamazepine re-administration should be avoided in patients with a previous history of SJS or adverse skin reaction to carbamazepine by obtaining an accurate medical history.

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