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Case Report

Phenytoin induced Stevens Johnson syndrome: a case report

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ABSTRACT

Stevens-Johnson syndrome (SJS) is a rare consequence of hypersensitivity reaction precipitated by certain drugs and viral infections. It is an idiosyncratic drug reaction usually associated with drugs like anti-epileptics, non-steroidal anti-inflammatory compounds and antibiotics. The overall incidence of this entity is very low and is life-threatening if undiagnosed and untreated. The syndrome is characterized by purpuric macules and bullous eruptions involving the mucous membrane which may be followed by systemic manifestations. The mechanism of SJS due to drugs is not fully defined. Delayed Hypersensitivity reaction mediated by T lymphocytes in response to a drug is thought to be responsible. Here authors present a case of SJS induced by phenytoin in an adult male. The case warrants the need of adopting a meticulous approach while prescribing phenytoin. The case is being reported to accentuate the importance of adverse drug reactions and to emphasize the importance of reporting such reactions ensuring efficient pharmacovigilance.

Keywords: Adverse drug reactions, Phenytoin, Pharmacovigilance, SJS

INTRODUCTION

Antiepileptic drugs are associated with severe skin reactions such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).[1] Phenytoin is one of the most commonly prescribed antiepileptic. And is known to cause a plethora of adverse drug reaction.[2]

Stevens Johnson syndrome(SJS) and toxic epidermal necrolysis (TEN) are rare and severe manifestations of idiosyncratic reaction to certain drugs. The may also be caused by infections like herpes but are more commonly associated with drugs. SJS and TEN are two entities of the same condition differing only in the percentage of body surface area involved. Usually <10% body surface area (BSA) involvement is seen in SJS, 10-30% BSA in SJS-TEN overlap and >30% BSA detachment is seen in TEN.

Among the drugs - antiepileptic's, antibiotics like sulfonamides and isoniazid and NSAIDS are the common culprits.[3] The full blown form of the syndrome is preceded by a prodromal phase of flu like symptoms which evolve over 1-3 weeks to cutaneous manifestations in the form of macular eruptions over the trunk, face and upper limb.[4] Involvement of mucous membrane is seen in 90% of cases. Diagnosis is made on clinical suspicion and confirmed by biopsy.

Prognosis depends upon the age of patient, presence of comorbidities and area of detachment.[4] Septicaemia is the most common complication of SJS and the major contributor towards mortality.[5] Here we report a case of SJS in an 18-year male after he was put on prophylactic dose of phenytoin.

CASE REPORT

History

An 18-year-old male patient presented with history of epilepsy and was prescribed tablet phenytoin100 mg orally twice daily. After consumption of the medication for twenty days, patient developed non pruritic rashes all over the body and fever, for which he consulted at K.R. hospital. Later the patient developed oral ulcers and lip ulcers associated with fever. These lesions first appeared on abdomen and then spread to limbs and face and then gradually progressed to involve the oral mucosa, eyes and genitals. He is a known case of polio and has post polio deformity involving the right wrist and leg.

General examination

The general condition of the patient was good, patient was conscious, oriented, with all his vital signs in normal range. Patient had increased salivation, redness of eyes, photophobia, difficulty in opening eyes, inability to eat and difficulty in talking. There was discharge of pus from oral cavity. There was deformity of the right wrist and leg due to polio.

Systemic examination

No other significant abnormalities were detected.

Local examination

Erythematous plaques with central dusky hue were present over chest, bilateral forearms. Multiple papulo-vesicular lesions were present over bilateral forearms, arms and legs. Hyperpigmented macules were present over bilateral thighs and legs. Erosions and haemorrhagic crusting were present over lower and upper lip. Whitish plaques were present on tongue and buccal mucosa. There was purulent discharge from erosion in the mouth and ear. Erosions were present over bilateral upper eyelids. Erosions were also present over glans penis.

Investigations

All the routine investigations were performed. HCT-30.7%, MCV-71.6%, MCH-23.5%, MCHC-32.9%, with normal RBC count and haemoglobin levels. All other investigations were normal.

Management

- The anti-epileptic Phenytoin was withdrawn immediately.
- Patient was treated with I.V methylprednisolone and fresh frozen plasma transfusion.
- Skin erosions, painful oral ulcers and ophthalmic lesions were treated symptomatically.
- Supportive measures included I.V fluids and correction of electrolyte imbalance.

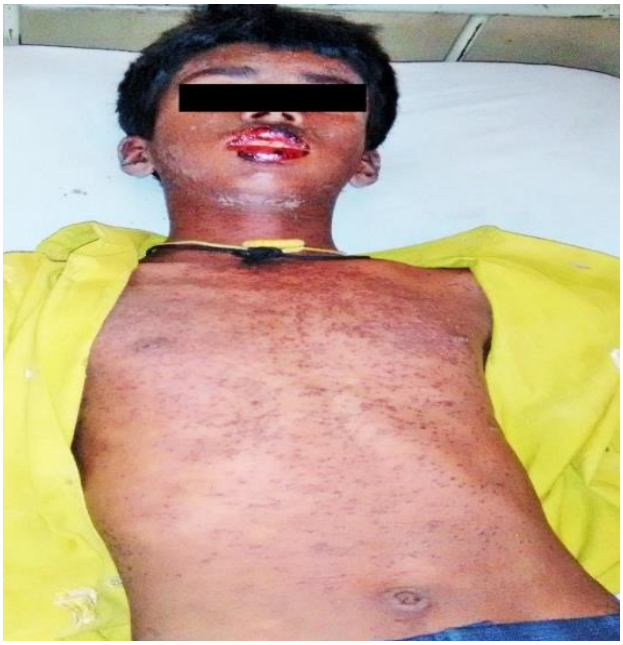

Figure 1: Oral erosions and haemorrhagic lesions.

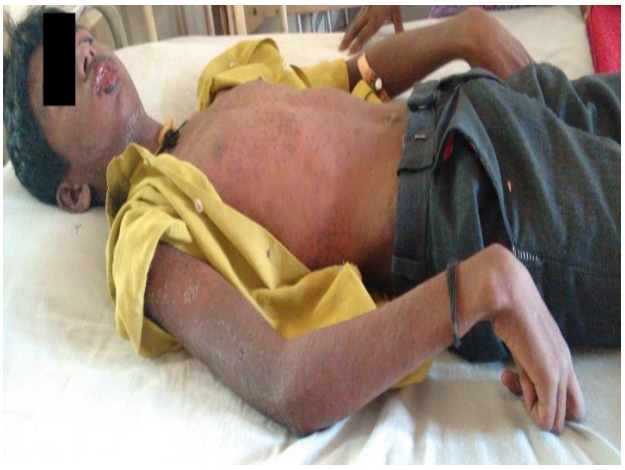

Figure 2: Targetoid lesions over trunk and limbs.

DISCUSSION

According to WHO, adverse drug reaction is defined as "any response to drug which is noxious or unintended and occurs at a dose normally used in man for prophylaxis, diagnosis or treatment of diseases or for modification of physiological function".[6]

Among the reported adverse drug reactions cutaneous drug reactions are the most common. SJS though rare, is considered as a severe form of erythema multiform spectrum.[7] Clinically, SJS and TEN are characterized by polymorphic lesions like erythematous macules, papules, plaques, vesicles and bullae with predilection for the distal extremities and are Nikolsky's sign positive. "Target" lesion with bull's eye appearance is characteristic of SJS and TEN. Oral, genital, and conjunctival mucosa is often involved in the form of erosion or ulceration.[8]

A study conducted by CY Yang et al, on Severe cutaneous adverse reactions to antiepileptic drugs in Asians showed that among antiepileptic's, Carbamazepine (CBZ) and phenytoin (PHT) were the most common causative AEDs for SJS/TEN. Phenytoin-related severe cutaneous adverse reactions frequently impair the internal organs, leading to the highest mortality among the different antiepileptic drug-related cutaneous reactions.[9] According to the EuroSCAR study, use of certain medications are associated with high risks of SJS or TEN. Prescribing any of them requires thorough evaluation of expected benefits and monitoring of early signs and symptoms for such adverse reactions. These drugs, namely, are - Nevirapine, Lamotrigine, Carbamazepine, Phenytoin, Phenobarbital, Cotrimoxazole and other anti-infective sulfonamides, Sulfasalazine, Allopurinol, Oxicam-NSAIDs.[10]

Currently, no treatment modality has been established as a standard for these patients. Due to rarity of these disorders, there are no randomized controlled trials of pharmacological agents in the treatment of TEN. However, there are case reports of successful treatment with I.V immunoglobulins, systemic corticosteroids, plasmapheresis, cyclosporine, cyclophosphamide, anti-tumour Necrosis Factor-α (TNF-α) and haemodialysis but with limited data to be recommended as first line treatment.[11]

CONCLUSION

Adverse drug reaction especially cutaneous drug reactions which are easier identified should always be monitored for. SJS although a rarer form of these cutaneous drug reactions should always be suspected in patients on drugs with predilection to cause these reactions. Antiepileptic's like phenytoin, carbamazepine, lamotrigine and other drugs like antibiotics and NSAID's are other causative drugs and patients taking them should be counselled and monitored. There is no specific treatment for SJS and so early diagnosis and management are of great importance. Reporting these adverse drug reactions is necessary and only efficient pharmacovigilance can pave the way for a better health care.

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