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Toxic Epidermal Necrolysis by Lamotrigine - A Case Report of Fatality

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ABSTRACT

Toxic epidermal necrolysis (TEN) is an immune mediated fatal adverse muco-cutaneous drug reaction characterized by extensive exfoliation of the epidermis and mucous membrane. It may result in sepsis and death. In most cases, TEN is caused by certain drugs & vaccines. TEN involves more than 30% of body surface area. Steven Johnson Syndrome also shows the same disease process and same spectrum of drug-induced epidermolysis.

A 37-year-old patient who was on Lamotrigine, Escitalopram & Clonazepam for multiple somatoform disorder developed generalized vesicular rash with fever after 2 weeks of initiation of lamotrigine. The patient was admitted to the hospital and Lamotrigine was taken off. Patient was given conservative management. Adverse drug reaction was reported to Adverse drug reaction monitoring centre (AMC) and severity was assessed by WHO-UMC Scale. Patient died after 5 days of admission. Score of Toxic epidermal necrolysis (SCORTEN Scale) is used to assess severity of the illness and to predict mortality rate. Early Diagnosis, withdrawal of offending agent, timely proper supportive management can help in lowering the mortality.

Keywords: Toxic epidermal necrolysis, Lamotrigine, Adverse drug reaction, Multiple somatoform disorder, Steven Johnson Syndrome, Score of Toxic epidermal necrolysis

INTRODUCTION

Toxic epidermal necrolysis (TEN) is a potential life threatening acute muco-cutaneous syndrome characterized by extensive exfoliation of the epidermis and mucus membrane, which may result in sepsis and death. In most cases, TEN occurs as a consequence of immune reaction to certain drugs & vaccines. [1] TEN involves more than 30% of body surface area and is characterized by extensive full thickness epidermal necrosis with epidermal detachment. There is dermal or epidermal inflammation along with mononuclear cells seen in skin biopsy. [2]

CASE PRESENTATION

A 37-year-old female patient was on Lamotrigine, Escitalopram & Clonazepam for multiple somatoform disorder. After 2

weeks, the patient developed generalized papulovesicular rash with fever which was diagnosed as Varicella infection & Acyclovir was added to the patient. After 4 days, the papulovesicular rash transformed into bullous eruption and denuded skin around the face and on the trunk appeared. Lamotrigine was stopped immediately after admission to the hospital, but generalized mucosal erosion and hemorrhagic crust on the lips and mucosal surface developed. Nikolsky sign was positive in this patient. Drug drug interaction checked but nothing significant interaction outcome was revealed. Patient was admitted in HDU and conservative management started. Adverse drug reaction was reported to Adverse drug reaction monitoring centre (AMC). Causality assessment was done by WHO-UMC Scale and it was found to be possible. Patient died after 5 days of admission.

Picture showing a case of Toxic Epidermal Necrosis by Lamotrigine

PATHOPHYSIOLOGY

TEN presents as acute eruption characterised by epidermal loss and multi-site mucositis with systemic symptoms. Increased incidence is found in women (sex ratio is 2:1).

Primarily, TEN is a drug induced phenomenon, characterised by diffuse epithelial keratinocyte necrosis. It is mainly initiated by Drug induced cytotoxic T lymphocyte, MHC Class I restricted drugs which leads to clonal expansion of CD8 + Cytotoxic T cell, that infiltrate the skin and induce keratinocyte apoptosis. Other factors like TNFα, IFNγ and Inducible nitric oxide synthase(iNOS) are also linked to this process. [3]

DIFFERENTIAL DIAGNOSIS

Staphylococcal scalded skin syndrome
Pemphigus vulgaris
Bullous pemphigoid
Erythema multiforme major
Acute generalized exanthemas pustulosis
Generalized bullous fixed drug eruption
Paraneoplastic pemphigus
Linear IGA bullous dermatosis [4]

LIST OF DRUGS ASSOCIATED WITH TOXIC EPIDERMAL NECROLYSIS

Antibiotics: Sulfonamides, Chloramphenicol, Penicillin Quinolone
Anti-Epileptic: Barbiturate, Carbamazepine, Phenytoin, Lamotrigine

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): Oxybutazone, Piroxicam
Anti-Viral Drugs: Oseltamivir, Abacavir [5]

DISCUSSION

Most cases of TEN are mainly drug induced. It occurs within 1-3 weeks of initiation of treatment. It starts with flu like syndrome and then cutaneous eruption starts (ill-defined dusky erythematous macular rash and bullae then it forms sheet like blisters). The rash usually starts in face, pre-sternal area and then all over body. Steven Johnson Syndrome also shows the same disease process and same spectrum of drug-induced epidermolysis. Staphylococcal Scalded Skin Syndrome have also similar presentation but there is no involvement of mucosa. TEN involves more than 30% of total body surface area, while SJS affects less than 10%. Mucosal affection (erythema and erosion) occurs in 90% cases of TEN, Oropharynx, eye and genitalia are also affected. Respiratory involvement may lead to serious effects. The release of massive number of cytokines, lead to metabolic acidosis, sepsis and multi organ dysfunction. In routine blood investigation, anaemia and lymphopenia are most common. Neutropenia is an unfavourable prognostic factor for TEN. Score of Toxic epidermal necrolysis (SCORTEN Scale) is used to assess severity of the illness and to predict mortality rate. [2]

CONCLUSION

TEN is recognized as severe form of SJS. In acute phase it is accompanied by variety of systemic complications & may proceed to multi organ failure. So early diagnosis and stoppage of offending drugs causing TEN/SJS, can be determined from pharmacovigilance data.

Declaration by Authors

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