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Case Report

Triple Threat: A Case Report of Phenytoin, Lamotrigine and Oxcarbazepine Induced Toxic Epidermal Necrolysis

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ABSTRACT

Rationale: Toxic Epidermal Necrolysis (TEN) is a potentially life-threatening dermatologic disorder that can be triggered by medications, infections, vaccines, or idiopathic causes. According to reports from the EuroSCAR study, certain drugs such as Lamotrigine, Carbamazepine, Phenytoin, Nevirapine, Sulfonamides, and Allopurinol pose a high risk of causing TEN. **Patient Concerns:** A 55-year-old male presented with a maculopapular rash all over his body persisting from last six days. After a thorough review of the patient's medical and medication history, it was a suspected reaction induced by Lamotrigine, Oxcarbazepine, and Phenytoin, which were prescribed to manage his seizure episodes. **Diagnosis:** The patient was diagnosed with Toxic Epidermal Necrolysis triggered by Lamotrigine, Oxcarbazepine, and Phenytoin. **Intervention:** Treatment included discontinuation of all offending drugs and administration of various medications, including Inj. Dexamethasone, Inj. Taxim 1 g, T. Cetirizine 10 mg, T. BC/Ca/Vit C/Cap A&D, Fubiset cream for erosions, Dologel oral paste, Candid mouth paint, Kenocort oral paste for oral erosions, saline soaking for haemorrhagic crusting over lips, Povidone iodine mouth gargling, kenocort paste for scrotal erosion, Emollient, Inj. H. Actrapid, and T. Amlodipine. **Outcomes:** The patient responded well to treatment, with resolution of the rashes after five days of treatment. He was discharged from the hospital with instructions to continue T. Prednisone 5 mg OD, T. Cetrizine 10 mg OD, Dologel oral paste, Kenocort oral paste, and Candid mouth paint. **Conclusion:** This case highlights the critical importance of vigilant medication management and early intervention in suspected drug-induced cutaneous adverse reactions. **Lesson:** Patients using suspected drugs should be monitored closely. If they encounter any suspected adverse reactions, these drugs should be dechallenged immediately for better outcomes. This situation emphasizes the importance of proactive education for both patients and healthcare providers regarding potential adverse drug reactions, especially in high-risk populations, to prevent similar incidents from occurring in the future.

Key words: Toxic Epidermal Necrolysis, Anti convulsants, Adverse drug reaction, Maculopapular rash, Case report.

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INTRODUCTION

Toxic Epidermal Necrolysis (TEN) is a severe condition characterized by extensive shedding of skin and mucous membranes, posing a risk of sepsis and death. As described by Alan Lyell in 1956, it resembles a scalding skin eruption. While most cases result from immune reactions to specific drugs, other factors like infections, tumors, and vaccinations are also linked. Steven-Johnson Syndrome (SJS) shares a similar disease process but differs in the degree of skin detachment: TEN affects over 30% of body surface area, while SJS affects less than 10%.[1] Global data suggests an estimated incidence of 1.2-6 cases per million patient-years for SJS and 0.4-1.2 cases per million patient-years for TEN.[2]

Here's a report of a patient diagnosed with hemorrhagic stroke (CVA), where the treatment approach is tailored to the specific cause and severity of the bleeding. Generally, medications such as anti-convulsants, anti-hypertensives, and osmotic diuretics are utilized.[3] However, anti-convulsants like phenytoin and newer drugs like lamotrigine can have severe side effects, ranging from minor gastrointestinal issues to life-threatening conditions like SJS and TEN. Reports indicate that approximately 10% of patients treated with lamotrigine and phenytoin experience drug eruptions.[4]

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CASE REPORT

A 55-year-old male patient presented at Government General Hospital, Kadapa, complaining of high-grade fever, loose stools, loss of appetite for a week, and a maculopapular rash appearing over the chest, abdomen, and later spreading to all limbs over the past six days. Additionally, he reported dysphagia for five days due to multiple erosions and hemorrhagic ulcers on the lips, tongue, bilateral buccal mucosa, and hard palate. The patient has a medical history of hypertension, diabetes, and a hemorrhagic stroke diagnosed a month ago. He is currently on medications including T. phenytoin 100 mg OD, T. olmesartanmedoxomil and chlorthalidone 30/12.5 mg OD, T. citicoline and piracetam 500/800 mg OD, T. Benfonerve forte OD, T. atorvastatin 40 mg OD, T. lamotrigine 100 mg OD, T. clinidipine 5 mg OD, T. oxcarbazepine 100 mg TID, Cap V-M Goal (vitamin supplement) OD. On examination, the patient appeared drowsy but conscious, obeying commands, and exhibiting pallor. Cutaneous examination revealed diffuse erythematous to purpuric macular lesions with some coalescing patches on the trunk, along with skin tenderness on bilateral upper and lower limbs, genitals, palms, and soles and a positive pseudo-Nikolsky sign. Erosions, with the largest measuring 3x2 cm and the smallest 1x1 cm, were noted on the back. Oral examination revealed a white plaque on the hard palate, suggesting oral candidiasis. Mucopurulent discharge was observed on ocular examination, and ill-defined erosions were present on the scrotum. Diffuse purpura was noted on bilateral palms and soles, while the scalp, hair, and nails appeared normal.

The physicians in the male medicine ward referred the patient to a dermatologist on day 2 for their opinion on diagnosis and further treatment, resulting in the diagnosis of toxic epidermal necrolysis induced by phenytoin, lamotrigine, and oxcarbazepine. Treatment involved discontinuation of all offending drugs and administration of various medications, including Inj. Dexamethasone, Inj. cefotaxime 1 g, T. Cetirizine 10 mg, T. BC/Ca/Vit C/Cap A&D, Fubiset cream [Fusidic acid and betamethasone valerate]for erosions, Dologel [Choline salicylate, Benzalkonium chloride & Lignocaine HCL liquid gel], Candid [Clotrimazole in glycerine, Propylene glycol] mouth paint, Triamcinolone oral mucosal paste for oral erosions, saline soaking for hemorrhagic crusting over lips, Povidone iodine mouth gargling, Triamcinolone paste for scrotal erosion, Emollient, Inj. H. Actrapid, and T. Amlodipine. The patient responded well to the treatment, with decreased erythema in the scrotal area, skin degeneration noted on the nape of the neck and back, and resolution of rash on bilateral upper and lower limbs observed by day 5. The patient recovered from this serious suspected reaction after rigorous treatment for 12 days, as shown in Figure 2. He was discharged from the hospital with the advice to continue T. Prednisone 5 mg OD, T. Cetrizine 10 mg OD, Dologel oral paste, Triamcinolone oral paste, Candid [Clotrimazole in glycerine, Propylene glycol], mouth paint.

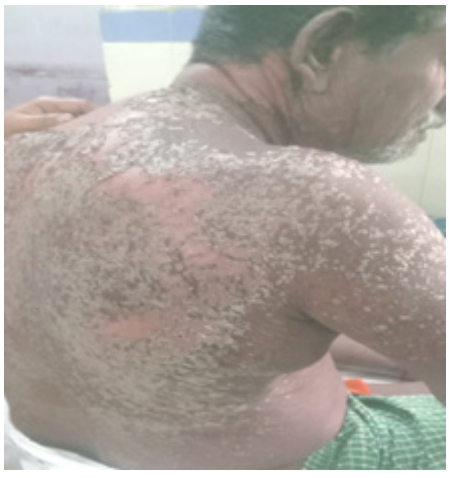

Figure 1: Before management.

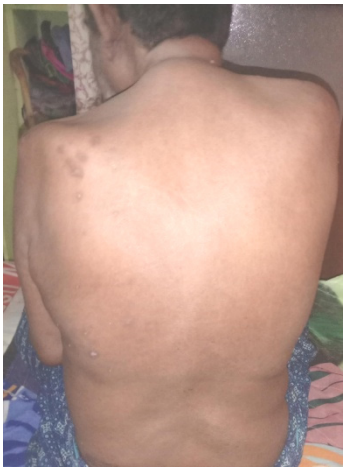

Figure 2: After management.

DISCUSSION

Stroke is a common cause of epilepsy, especially among older adults. More than half of all seizures in elderly people are related to stroke. The likelihood of having seizures after a stroke can vary. For ischemic strokes (caused by blocked blood flow), seizures occur in around 4-10% of cases. For hemorrhagic strokes (caused by bleeding in the brain), seizures occur in about 4-27% of cases. These seizures can be categorized as acute symptomatic seizures, occurring within a week of stroke onset, or unprovoked seizures, which manifest more than a week after stroke. About half of seizures in patients with Intracerebral Hemorrhage (ICH) occur at the onset of bleeding. Administering anticonvulsants, particularly in cases of ICH, has shown promise in reducing early seizures and improving neurological outcomes.[5] According to American Heart Association guidelines, prophylactic anticonvulsant therapy, typically with phenytoin, is recommended for one month following spontaneous intracerebral hemorrhage, after which therapy should be discontinued unless seizures occur.[6] However, these drugs can lead to severe and life-threatening adverse reactions like Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). TEN is characterized by widespread keratinocyte necrosis triggered by certain medications or their

metabolites, resulting in epidermal detachment and blistering, as seen in Figure 1. According to Mehtha M *et al.*, mucocutaneous reactions typically manifest 8-16 days after starting anticonvulsant therapy, in our patient, a reaction was observed 12 days into treatment.[7] The case showed a probable causal relationship when assessed using the WHO-UMC causality assessment scale, requiring aggressive management.

CONCLUSION

It's essential to educate patients taking medications such as phenytoin, lamotrigine, oxcarbazepine, and others in this class about their potential severe adverse reactions, like TEN, which can be life-threatening. Patients need to understand both the health benefits and risks associated with these medications. They should also be informed about the importance of dechallenging if they experience a serious adverse reaction and the necessity of seeking immediate medical attention for further care and management. Providing drug alert cards to these patients can assist in managing other potential medical conditions and help reduce the risks associated with drug reactions.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

TEN: Toxic epidermal necrolysis; **WHOUMC:** World Health Organisation- Uppsala Monitoring Centre; **SJS:** Steven-Johnson Syndrome; **CVA:** Cerebro vascular accident; **ICH:** Intracerebral hemorrhage; **OD:** Once daily; **TID:** Thrice daily.

PATIENT CONSENT

The patient referenced in this case report has provided consent for publication, acknowledging the reports nature and understanding that their identity will be kept confidential. The patient is satisfied with the medication they received.

SUMMARY

Toxic Epidermal Necrolysis (TEN) is a severe, life-threatening condition affecting the skin and mucous membranes, often triggered by drug reactions. It involves extensive skin detachment, covering over 30% of the body surface area, distinguishing it from Stevens-Johnson Syndrome (SJS), which affects less than 10%. Anti-convulsants such as phenytoin and lamotrigine are common causes, with approximately 10% of patients experiencing severe side effects.

A 55-year-old male with a history of hypertension, diabetes, and a recent hemorrhagic stroke presented with high-grade fever, loose stools, appetite loss, and a spreading maculopapular rash. He also reported dysphagia due to oral erosions. His medications included phenytoin, lamotrigine, and oxcarbazepine. Examination revealed erythematous to purpuric lesions, skin tenderness, a positive pseudo-Nikolsky sign, and mucosal erosions. TEN was diagnosed, likely induced by phenytoin, lamotrigine, and oxcarbazepine. Treatment included discontinuation of these drugs and administration of dexamethasone, cefotaxime, cetirizine, vitamins, and topical treatments. Significant improvement was noted within five days, with full recovery after 12 days. Upon discharge, the patient was prescribed prednisone, cetirizine, and topical treatments, showing marked recovery from the drug-induced TEN.

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