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Case Report

Stevens-Johnson Syndrome/ Toxic Epidermal Necrolysis Overlap Induced by Concurrent Phenytoin and Quetiapine Administration: A Case Report

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Abstract

Steven Johnson syndrome (SJS) is a rare mucocutaneous drug reaction characterized by epidermal necrosis and detachment. Although both phenytoin and quetiapine have been individually associated with SJS, their concurrent administration is uncommon.

A 61 years old female who developed painful erythematous patches followed by blistering and mucosal erosion markedly seen on the back, face, proximal limbs and trunk after a single dose of taking both the drugs together for the first time. The clinical features and extent were consistent with SJS/TEN overlap. The Severity of Illness Score for Toxic Epidermal Necrolysis (SCORTEN) was calculated of 4, indicating a high risk of mortality. Both the drugs were immediately discontinued and systemic steroids along with supportive treatment showed marked improvement in the patient.

This case highlights the potential for severe adverse effects due to co-administration of medicines. Early recognition and prompt withdrawal of the causative agents are key to preventing the side effects and enhancing the outcomes in drug induced SJS.

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Introduction

Steven Johnson syndrome (SJS) is a severe, immune mediated skin disease characterized by wide spread skin detachment and mucosal damage. SJS involved less than 10% of the body surface area (BSA), whereas Toxic epidermal necrolysis (TEN) involves more than 30%.[1] Between 10-30% lies SJS/TEN overlap. Both conditions are associated with high morbidity and mortality. Medications such as antibiotics, anticonvulsants and antipsychotics are the major triggers in over 75% of the cases.[2] Early detection and removal of the offending drug are critical steps to prevent complications such as sepsis and end organ damage.

Phenytoin, an aromatic anticonvulsant, is a well-established cause of SJS/TEN, particularly in individuals with HLA-B*15:02 allele.[3] Quetiapine, an atypical antipsychotic is more commonly associated with drug reaction with eosinophilia and systemic symptoms (DRESS) than with epidermal necrolysis.[4] Concurrent use of both drugs have really been seen to cause severe cutaneous adverse reactions. The pathogenesis involves cytotoxic T cell activation leading to keratinocyte apoptosis and extensive epidermal loss.

This case describes a patient who developed SJS/TEN overlap following initiation of both drugs together, highlighting the importance of taking caution when prescribing multiple drugs together and the crucial role of early detection.

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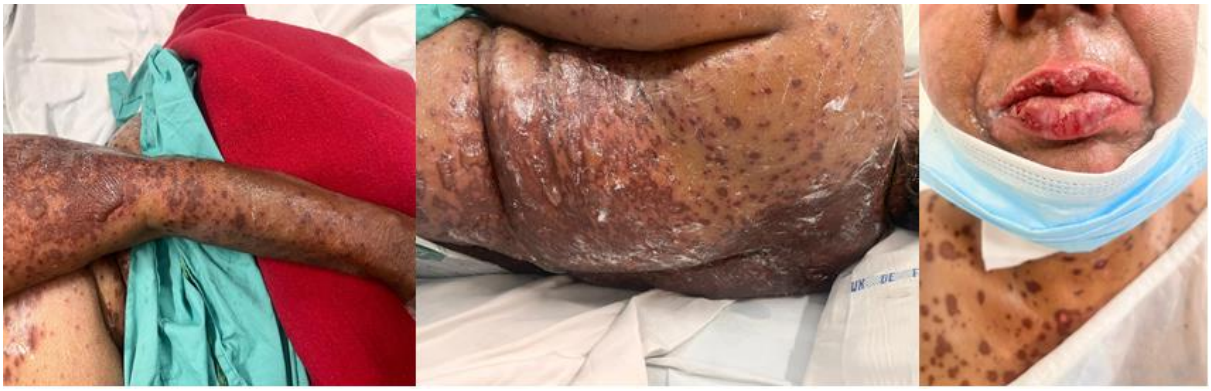

Figure 1 Erythematous maculopapular lesions of different diameters demonstrated on patient's body.

Case Report

A 61 years old woman known case of bipolar disorder presented to dermatology outpatient department with the following complaints from four days:

1. Flaccid, fluid filled blisters on the trunk, abdomen, back, arms and legs- 1 day.
2. Mucosal erosions involving the lip and genitalia- 1 day.
3. Fever- 4 days.

The patient was fine until four days prior to presentation when she developed intermittent low grade fever with rigors and chills without any associated gastrointestinal or respiratory symptoms She noted a pruritic, erythematous papular rash on her back which slowly progressed to flaccid blisters spreading to her entire body which later ruptured leaving behind areas of desquamation and hemorrhagic crusting. This was followed by mucosal involvement including erosions of lips and labia minora leading to painful mastication and dysuria. The patient stated that she took tablet Phenytoin and tablet Quetiapine together for the first time four days back after a doctors prescription change as she was taking phenytoin since 2 years and also took quetiapine for a short interval 2 years back. There was no prior history of any dermatological condition, drug reaction or known allergy **(Figure 1)**.

Upon examination, her pulse was 110/min, Temp 101 F, BP 100/70 mmHg. She was not in an obvious respiratory distress. There was a widespread erythematous polymorphic papules and flaccid blisters on the trunk, back, arms, and legs involving almost 25% of the patient's body with areas of hyperpigmentation. A few of the blisters were ruptured, revealing underlying denuded dermis. Nikolsky's sign was negative where as Asboe Hansen sign was positive. Perineum showed erythema, swelling, and erosions involving the vulva, labia with a yellow coat. There were ill-defined erosions on the buccal mucosa. The tongue was covered with a thick, white-to-yellow coat. Lips were swollen and erythematous with a whitish coat that bled on touch. Her SCORTEN at time of admission was 4-5 due to which the patient was managed in the ICU. Histpathological confirmation was not performed due to patient's critical condition and high SCORTEN and priority was given to her urgent management. All suspect medications were discontinued. Systemic therapy included intravenous methylprednisolone (1 mg/kg/day) and antihistamines (Pheniramine Maleate 22.75mg 8-hourly). Supportive care involved fluid resuscitation. Topical management comprised moderate potency steroids mixed with white soft paraffin. Ophthalmologic review led to a prescription for artificial tears for mild uveitis. Psychiatric consultation recommended switching to Tab. Risperidone (1mg daily).

Significant clinical improvement was observed over two weeks. Blisters dried with evident reepithelialization. Healing of oral and genital mucosa permitted resumption of oral intake. Ocular symptoms resolved. The patient was discharged in

Figure 2 Erythematous maculopapular lesions at different stages of healing.

stable condition on risperidone, with scheduled follow-up appointments. She received counselling regarding strict avoidance of the offending drugs **(Figure 2)**.

Discussion

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are severe, life-threatening mucocutaneous reactions most commonly triggered by medications.[1,2] This case describes SJS/TEN in a patient following initiation of quetiapine and phenytoin, both of which are associated with severe cutaneous adverse reactions. Clinical features included widespread blistering, oral and genital mucosal involvement, and a positive Asboe-Hansen sign, allowing diagnosis without the need for biopsy. Histopathological confirmation was not pursued due to patient's critical condition and high SCORTEN score.

SJS/TEN results from immune-mediated keratinocyte apoptosis, typically involving drug-specific T-cell activation. Phenytoin is a well-established and common trigger, specifically in individuals with the HLA-B*15:02 allele, a strong genetic predictor for its development in Asian populations.[3,6] Recent studies in other populations, such as in Iran, have further confirmed this association.[7] Quetiapine, an atypical antipsychotic, is less commonly implicated than phenytoin and is more frequently associated with other hypersensitivity reactions like DRESS.[4] However, emerging case reports, including a very recent one by Su& Kao, have documented SJS/TEN overlap syndrome induced by quetiapine, solidifying its potential as a rare culprit.[8] Causality assessment was further evaluated using the ALDEN(Algorithm of Drug Causality for Epidermal Necrolysis) score, a validated and widely used tool for identifying the most probably culprit drug in SJS/TEN cases.[9] However, interpretation was partially limited due to concurrent exposure to two potential culprit drugs and history of prior uneventful exposure to both agents. Although ALDEN supported a higher likelihood for phenytoin compared to quetiapine, this finding is in keeping with established epidemiological and pharmacogenetics evidence. The combination of these two high-risk medications, as seen in our patient, may have contributed to increased immunological susceptibility; however, a true synergistic effect remains speculative and is not well established in current literature.[8]

Management consisted of immediate discontinuation of the offending drugs, which is the first step of treatment.[2] Therapeutic measures included intravenous corticosteroids, antihistamines, and meticulous topical care to promote skin healing. Ophthalmology addressed mild uveitis and ocular dryness, while psychiatry transitioned the patient to an alternative antipsychotic, risperidone.

The patient showed significant improvement over two weeks, with resolution of mucositis and blistering, stressing the importance of prompt diagnosis and intervention. This case shows the importance for caution when prescribing high-risk medications, particularly in combination, and also the significance of patient education regarding drug reactions.

Conclusion

This case shows the potential for Quetiapine and Phenytoin to induce SJS/Ten overlap, which is a life threatening condition requiring prompt recognition and multidisciplinary management for better prognosis, reducing morbidity and mortality. This

report emphasize the importance of the clinicians awareness of drug induced SJS/TEN particularly when prescribing high risk medications and highlights the need for patient education to prevent further episode.

Declaration of patient consent Authors certify that they had obtained all appropriate patient's consent.

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Author's contribution

SK: Identification and management of the case and manuscript writing.

AUB: Diagnosis, management of the case and critical review of the manuscript.

All authors have given final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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