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A Case Report on Stevens-Johnson Syndrome Induced by Phenytoin

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Authors' contributions

This work was carried out in collaboration among all authors. Author SB designed the study, was chiefly involved in management of this patient and wrote the first draft of the manuscript. Author SS also contributed in drafting of this manuscript and management of the patient. Author JL managed literature searches and author AG read, edited and approved the final manuscript.

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Case Report

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ABSTRACT

Drugs are known to cause various adverse drug reactions ranging from a skin rash to severe skin reactions like Stevens-Johnson syndrome (SJS). Stevens-Johnson syndrome is a life threatening immune complex mediated hypersensitivity mucocutaneous reaction mainly affecting skin and the mucous membrane, presenting as severe mucosal erosions with widespread erythematous, cutaneous macules or atypical targets. Various drugs are known to cause skin reactions which include antiepileptics, analgesics, antibiotics, and proton-pump inhibitors. Carbamazepine and Phenytoin are among the leading antiepileptic drugs causing drug induced Stevens-Johnson syndrome (SJS). Here we report a case of SJS induced by phenytoin. A 17-year-old male reported with extensive ulceration of the oral cavity and haemorrhagic crustations on the lower lip which occurred 2 days after the intake of phenytoin. He was treated with corticosteroids and oral topical anaesthetics. We all must be careful while prescribing drugs and be aware of the adverse effects of the drugs especially the life threatening one.

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1. INTRODUCTION

One of the major causes of morbidity and mortality are the Adverse Drug Reactions (ADRs) which accounts for 6% of the total hospital admission of the patients with 0.3 to 7 percent of deaths [1,2]. SJS is life threatening ADRs and one of the leading causes of mortality. Stevens Johnson syndrome (SJS) was termed by Steven and Johnson in 1922 and described as “A new eruptive fever with stomatitis and ophthalmia” [3]. SJS is a severe mucocutaneous hypersensitive reaction with an incidence rate of 0.05 to 2 persons per million populations per year [2,4,5]. Various drugs have been identified as causative agent for SJS like antimicrobials (sulfonamides, penicillins and cephalosporins), NSAIDs and anti-epileptics (Carbamazepine and phenytoin) [1,6]. SJS may present with skin and mucous membrane lesions characterized by blisters and erosions. Although, adverse reactions are rare, but still, they are major threat to the patient’s welfare and increases burden on economy and healthcare system which results into the withdrawal of drugs from market and death of the patient. Recently, a significant association of PHT induced SJS/TEN with HLA-B*1502 allele had been observed in Asian populations [1,7,8]. We report here a case of Stevens-Johnson syndrome due to phenytoin.

2. CASE REPORT

A 17-year-old male reported to the Oral Medicine and Radiology department with a complaint of painful ulceration of oral cavity and lip from last 1 week, leading to difficulty in opening mouth and eating food. History of present illness revealed that there was burning sensation followed by ulcers in oral cavity and lips (Fig. 1). The past medical history revealed that the patient met an accident and had leg fracture 10 days back. The patient was prescribed tablet phenytoin 300 mg for 7 days by a local medical practitioner. Within 2 days the patient had burning sensation followed by painful ulceration in the oral cavity and lips. There was no history of skin, eye or genital involvement.

Intra-oral examination revealed diffuse irregular shaped erosions covered with pseudomembrane present on both right and left buccal mucosa, labial mucosa and floor of the mouth. Haemorrhagic crustations were present on the upper and lower lip. On palpation lesion was non scrapable and tender with a rough texture. Haemorrhagic crusts had profuse bleeding on cleaning.

Laboratory investigations revealed leucocytosis with 14050 per mm^3, differential neutrophil count 48.9%, lymphocytes 38.2%, monocyte 6.2%, eosinophil 6.5%, basophil 0.2% and raised C-reactive protein (CRP-17 mg/L). Hemodynamically patient was stable. Based on clinical examination, medical history, and physical examination our diagnosis was SJS.

The patient was treated with systemic steroids; tablet prednisolone 30 mg once daily for 7 days. Further reduced to 20 mg once daily for next 7 days. Gradually, 10 mg and 5 mg for consecutive 7 days were administered. Benzydyamine hydrochloride 0.15% oral rinse for oral ulcers. Topical application of Clotrimazole cream 1% and Kenacort (triamcinolone) 0.1% ointment, 3 times daily for lips and mucosal lesions was advocated. The patient was reviewed after a week. Lesions had healed significantly in the oral cavity. Recall after 2 weeks revealed almost resolved lesions on all the surfaces and completely recovered approximately in 30 days (Figs. 2 and 3).

3. DISCUSSION

Stevens-Johnson syndrome is a rare, severe, mucocutaneous immune complex mediated hypersensitivity reaction described by Hebra in 1866 and Albert Mason Stevens and Frank Chambliss Johnson in 1992 [4]. SJS characterized by rapidly enlarging and spreading blisters and target-like lesions involving skin and mucosal, with a mortality rate up to 40% [1]. The diagnostic criteria of SJS/TEN are based on the history given by the patient and clinical morphology. Hypersensitive mucocutaneous reaction is defined as SJS when skin detachment is of less than 10% of body surface area, an overlap of SJS/TEN when skin detachment is of 10- 30% and TEN when detachment of greater than 30% [1]. Earlier, SJS was considered as EM major, but now it is considered as distinct entity due to its severity, presence of constitutional signs, atypical target lesions, involvement of more than one mucosal site, and residual sequelae [3]. In the oral cavity, SJS causes widespread ulcerative lesions. Prodromal symptoms in SJS initiate within 1–3 weeks of starting a new drug, and lasts for 1–2 weeks, presenting with flu-like symptoms, sore throat,

headache, fever, arthralgias, myalgias and rashes along with dry eyes, urethritis and vulval ulcers in few cases [7]. Our patient reported burning pain in prodromal phase, followed by mouth ulcers but the eye and genital ulcerations were absent. SJS have been proposed to have many risk factors including drugs, viral infections, malignant disorders, and graft rejection. Drugs are the most common cause of SJS including NSAIDs, antipsychotics, antibiotics, and antiepileptics [4]. Phenytoin and Carbamazepine have been reported to be the most leading cause of SJS[1]. In our case patient had hypersensitivity reaction to the phenytoin. In literature, there has been reported wide range of incidences of SJS with phenytoin (13.37% and 3.33%) [1,9]. Clinically, SJS present as widespread erythematous macules forming flat atypical target lesions followed by the full thickness epithelial necrosis [3]. Our case showed widespread ulceration of oral cavity, crusting of lips which bleeds on touch. Diagnosis of SJS is based on patient history of infection or intake of specific drug, clinical presentation such as erythematous macules, blisters, haemorrhagic erosions and crustations along with histological analysis of skin biopsy showing typical full thickness epidermal necrolysis due to extensive keratinocyte apoptosis [1]. Management constitutes the stoppage of the offending drug immediately followed by supportive care. Supportive care must include the management of fluid and electrolyte requirements [10]. Necrotic skin should not be debrided in infective stage. Antibiotics are indicated in case of the infection. Use of corticosteroid, initiated during initial stage and tapered off gradually shows tremendous improvement in SJS mucocutaneous lesions [3,11,12]. In our case, topical analgesic and antifungal were given along with corticosteroids. We prescribed tablet prednisolone 30 mg once daily for 7 days. Further tapered to 20 mg for next 7 days. Gradually, 10 mg and 5 mg for consecutive 7 days. His condition improved gradually with no sequelae during 20- 25 days of follow-up.

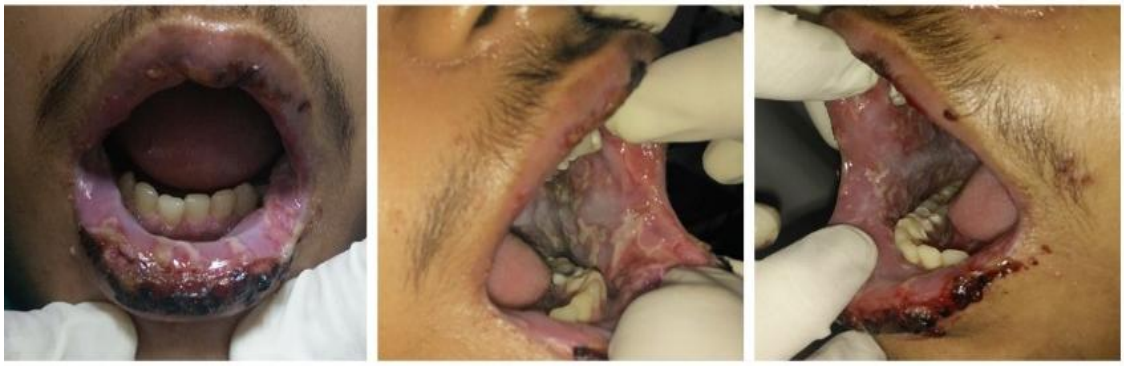

Fig. 1. Initial presentation showing encrusted lesion on lips and intra-oral erosions with covered pseudomembrane

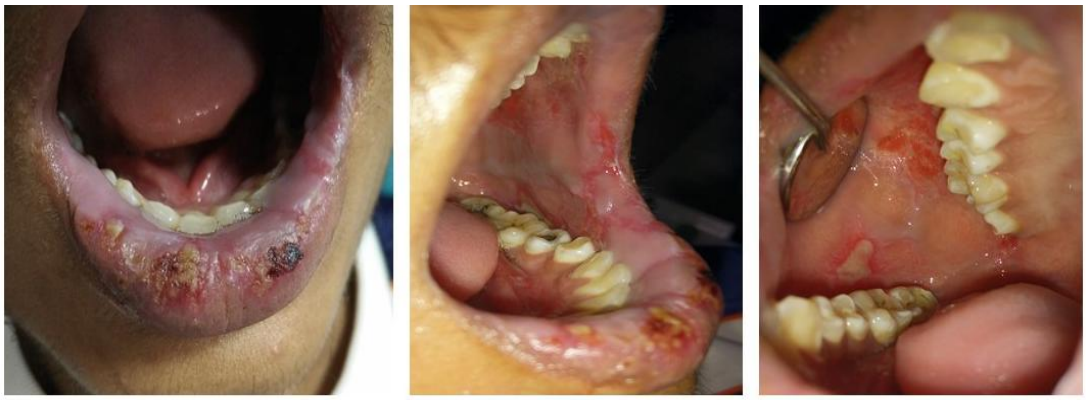

Fig. 2. Healing of crustations of the lips and erosions of the buccal mucosa

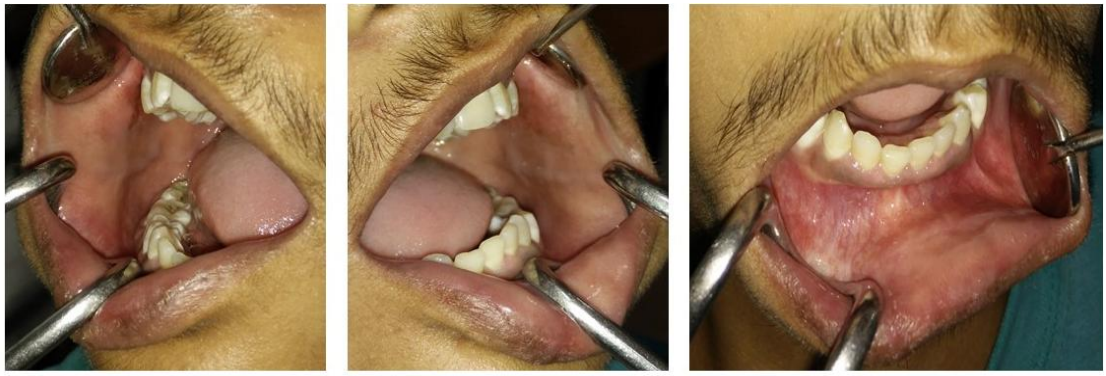

Fig. 3. Healed lesions of the lips and buccal mucosa

Hence, concluded that before prescribing phenytoin or any drug patient allergic to, a detailed history of past drug allergy, family history of drug allergy should be thoroughly investigated. Immediate withdrawal of the offending drug and supportive care is the mainstay of treatment in SJS.

4. CONCLUSION

Patients started with any common drug regimen may a potential risk of developing SJS. This case report reports the fact that life threatening hypersensitivity reactions can occur with very commonly used drugs like phenytoin. Increased clinical alertness is required to identify hypersensitivity reactions like rash, vesiculobullous lesions, and clinical symptoms such as fever, nausea, and abdominal pain and to make early diagnosis to reduce changes of the secondary infection and subsequent complications. The offending drug should be discontinued and supportive care given as a part of the therapeutic approach. Corticosteroids are a choice of therapy for SJS in most of the cases. Therefore, clinicians must be more careful while prescribing commonly and widely used drugs.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the adv ancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

Patient was informed and consent was taken.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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