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Chloroquine Induced Stevens Johnson Syndrome: A Case Report

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Abstract: The appraised incidence of the Stevens-Johnson syndrome ranges between 1.2 and 6 per million populations per year but the mortality rate is 15%. A 14 year old boy from rural area of Kadapa was admitted in the general medicine department with complaints of skin lesions all over the body with involvement of oral lesions since 10 days. He had a history of fever (high grade and not associated with chills) for the past 10 days and was administered inj. Lariago (Chloroquine-64.5 mg/ml) followed by oral chloroquine (Tablets Lariago, Chloroquine phosphate 250 mg, 2 tables stat, 1 tablet after 6 h, 1 O.D. for 1 day) for empirical treatment of malaria by a local physician. After 24 hours, he developed red patches over the abdomen and extremities associated with burning sensation and itching, which was progressed to all over the body. This adverse reaction is dose-related and can be labeled as Type A class of adverse effect. It can be considered as definite, Probable / conditional adverse drug reaction as per causality assessment of suspected adverse drug reactions. Thus, the hint of this written report is to create awareness about the rare but potentially fatal drug reaction like Stevens-Johnson syndrome with chloroquine which is ordinarily used for endemic malaria in India.
Keywords: Adverse drug reaction, Chloroquine, Malaria, Stevens Johnson syndrome

INTRODUCTION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are occasional but severe cutaneous drug reactions jeopardizing patient's life. Incidence of SJS and TEN is 2.6-7 persons per million populations per year in United States [1]. It is 1.1 and 0.93 per million per year for SJS and TEN correspondingly in Germany [2]. Drugs are most normally concerned for causing 77-95% of cases [3, 4]. SJS/TEN have been observed with more than 100 drugs. SJS and TEN comprise<10% and >30% of the body surface area respectively. The third circumstance named as SJS-TEN overlay falls in-between SJS and TEN [5]. Patient may primarily present with SJS, which later progresses into TEN or SJS-TEN overlap. Diagnosis mostly relies on clinical signs and histopathology of skin lesions [6, 7]. The particular mechanism of SJS/TEN still remains largely unknown. Immunological mechanisms, reactive drug metabolites or interactions between these two are recommended. Several studies and case reports on SJS/TEN have been done in India as well as abroad since the description of SJS case by Stevens and Johnson in 1922.

Chloroquine is a 7-chloro, 4-aminoquinoline anti-malarial and a very persuasive blood schizonticidal drug. It is very effective against the erythrocytic forms of all four plasmodial species. It is a weak base and it buffers intracellular pH, thereby inhibiting cellular invasion by parasitic organisms. It also inhibits haem polymerase; the enzyme that polymerizes haem to haemozoin [8]. Intracellular accumulation of haem is toxic to the parasite. Chloroquine is completely absorbed orally, extensively distributed and has a large volume of distribution. It is usually given orally and can also be given by I.M., S.C., or as slow I.V. infusion. It has a half-life of ~ 50 h. It is the mainstay for the treatment of malaria and chemoprophylaxis of malaria.

Adverse reactions commonly associated with chloroquine include severe gastritis, difficulty in accommodation, blurring of vision, corneal opacity, toxic psychosis, photosensitive dermatoses and even retinal damage on prolonged use [9]. However, the Stevens-Johnson syndrome and toxic epidermal necrolysis with chloroquine have been rarely noted [10]. Here we report a case of SJS which was induced by chloroquine phosphate (rarely implicated in the causation of SJS).

CASE REPORT

A 14 year old boy from rural area of Kadapa was admitted in the general medicine department of the Rajiv Gandhi Institute of medical sciences, Kadapa (India) with chief complaints of skin lesions all over the body with involvement of oral lesions since 10 days. He had known history of epilepsy since 18 months and on sodium valproate for last one year and on phenytoin for

two months. He had a history of fever (high grade and not associated with chills) for the last 10 days prior taking any medication. Medication sstarted were inj. Chloroquine (64.5 mg/ml) followed by oral chloroquine (Tablets Lariago, Chloroquine phosphate 500 mg, 2 tables stat, 1 tablet after 6 h, 1 O.D. for 1day) for empirical treatment of malaria by a local physician, antihistamine (levocetrizine), anti-cough and cold preparation, and inj. Paracetamol (Fevastin). After 24 hours, he developed red patches over the abdomen and extremities associated with burning sensation and itching, which was progressed to all over the body (Fig. 1, 2).

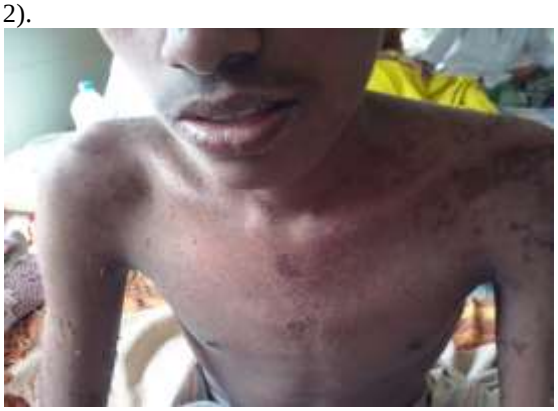

Fig. 1: Patches Over the Trunk and Shoulders

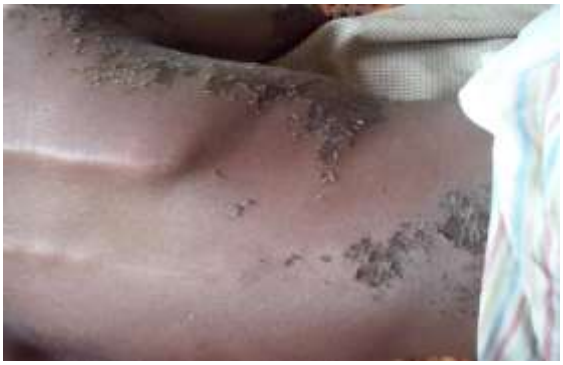

Fig. 2: red patches over the abdomen back of the trunk

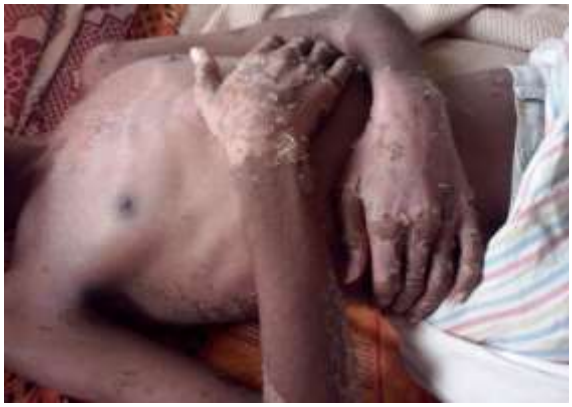

Fig. 3: The red patches over the extremities

He was conscious and coherent, his heart rate was 74/min and blood pressure was 100/60 mm Hg. Cutaneous examination showed involvement of about 80 % total body surface area, with generalized erythematous rash associated with scaling more over anterior aspect of neck. There were ulcerations on oral mucosa and unable to open the mouth completely. Investigations revealed the following: Widal test-negative, Hb- 11 gm%, WBC- 6900 cells/cu.mm, N-70%, L-26%, E-4%, ESR-25 mm/hr., RBS- 112 mg/dl, blood urea-14 mg/dl and serum creatinine-0.7 mg/dl. He was administered corticosteroid (betamethasone), antiallergic (pheneramine maleate), antibiotic (amoxicillin+clavulanic acid), antihistamine (cetirizine), anti-ulcerative (pantoprazole), chlorpheneramine maleate and multivitamin preparations. Betamethasone ointment (0.1%) and liquid paraffin for topical application. Parenteral therapy was gradually stopped. The patient showed steady improvement with the therapy given, and was discharged after 10 days.

DISCUSSION

Thus the above defined Stevens-Johnson syndrome has a sequential relationship to chloroquine administration. However, re challenge is not justified due to ethical constrains. This adverse reaction is dose-related and can be labeled as Type A class of adverse effect. It can be considered as definite, Probable / conditional adverse drug reaction as per causality assessment of suspected adverse drug reactions [11]. The appraised incidence of the Stevens-Johnson syndrome ranges between 1.2 and 6 per million population per year but the mortality rate is 15% [12]. There are limited reports of chloroquine-induced Stevens- Johnson syndrome but it is often ignored in its adverse effect profile [13, 14]. Abarna Devi Sanmarkan *et al*. [15] reported that maximum number of SJS cases was in the age group of 11–20 years, males preponderated the SJS group and 87% of SJS had oral mucosal involvement. Drug as an etiology was recognized in almost all the studies and the main group of drugs causing SJS was antimicrobials. South Indian studies had conveyed higher percentage of cases with fluoroquinolones. As described by Sanmarkan *et al*., [15] skin lesions led mucosal lesions in 50% of patients. No detailed explanation of corticosteroid use was found in the studies. Corticosteroids are considered debatable in the management of SJS/TEN despite their use for more than 30 years. No randomized controlled trials are available to inaugurate their efficacy [16]. It is difficult to analyze the effect of steroids from this study due to limited description of their use.

CONCLUSION

Thus the hint of this written report is to create awareness about the rare but potentially fatal drug reaction like Stevens-Johnson syndrome with

chloroquine which is ordinarily used for endemic malaria in India.

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